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IJMS INTERNATIONAL JOURNAL of MEDICAL STUDENTS

Original Article

The Weight of Schoolbags and Musculoskeletal Pain in Children of Selected Schools in Thimphu, Bhutan: A Cross-sectional Study.

Thinley Dorji,[1,2] Saran Tenzin Tamang,[3] Sonam Yoezer,[3] Kuenzang Wangdi.[4]

Abstract

Background: The carriage of loads on the back in children, >10% of one's body weight (BW), induces postural change and morbidity related to spinal pain. We studied the weight of schoolbags and the prevalence of musculoskeletal pain related to carrying schoolbags among children in Thimphu, Bhutan. **Methods:** This was a cross-sectional study, with a multistage cluster sampling, conducted amongst grade 8 and 10 students. Data were collected using a standardized self-administered questionnaire and weights of students and schoolbags were measured. Descriptive statistics were used to present the findings. Means were compared using t-test and risk factors were identified using logistic regression. **Results:** There were 131 students whose schoolbags weighed >10% body weight (BW). The mean weight of schoolbags was 4.6 ±1.5 kg for grade 8 students and 4.0 ±1.5 kg for grade 10 students. Musculoskeletal pain in at least one body region was reported by 411 students. Schoolbags weighing >10% BW and carrying the bags over only one shoulder were significant risk factors for reporting musculoskeletal pain. There were 197 students whose schoolbags did not have any safety feature; students did not use them consistently even if they were present. **Conclusions:** The weight of school bags that were more than the recommended ,10% BW was a strong factor in reporting musculoskeletal pain. Parents and students may be educated on the use of schoolbags with safety features. Measures such as providing storage facilities in schools may reduce the weight of bags.

Keywords: Ergonomics; Musculoskeletal Pain; Teens; Weight-Bearing; Adolescents (Source: MeSH-NLM).

Introduction

The carriage of loads on the back on a daily basis puts considerable strain on the bodies of children causing spinal pain in the cervical, thoracic and lumbar regions.[1] Backpacks cause changes in the spinal posture in children with reported reduction of the lumbar lordosis, especially if the weight carried exceeds 10% of one's body weight.[2–5] There is a dose-response relationship between the spinal postural changes and weight of posterior loads in school children[2,6] and negative impact on the forward lean, pain and skin pressure on children's bodies.[7] Estimates of the global point prevalence of spinal pain in 12-18 year old school students varies between 15-70%[1,8] In Bhutan, 14.3% of the population in the age group 15-49 years old presented to hospitals with "musculoskeletal disorders" in 2017, but the exact burden of spinal pain is unknown.[9]

While there is an upward trend of the prevalence of low back pain among the paediatric population, concerns have been raised about the diverse effect of musculoskeletal pain in children and their compounded effects in adulthood.[8,10] The prevalence of musculoskeletal pain is reported higher in those who carry heavy schoolbags.[8,11–14] Carriage of schoolbags with safety features are an important area of intervention.[15] However in Bhutan, there are no standard schoolbags for students. The distances travelled by students carrying schoolbags can vary from few minutes to up to two hours, often requiring walking up mountains or slopes.[16] Students carry many items other than just books and lunch boxes that add to the weight of the schoolbag.[7]

In recent times the weight of school bags has become a topic of concern for educators and parents in Bhutan.[17] This study was conducted to determine the average weight of schoolbags in proportion to children's body weights, and the prevalence of musculoskeletal pain among schoolchildren in Thimphu, Bhutan.

Methods

Design and setting

This cross-sectional study was conducted among students studying in grades 8 and 10 under Thimphu, the capital city and the largest district by population in Bhutan. Bhutan is a small Himalayan kingdom in Southeast Asia with a population of 0.7 million. In 2017, there were 5,074 students in grades 8 and 10 in Thimphu.[16] The sample size was calculated for proportions. The expected prevalence of musculoskeletal pain, given a lack of baseline data, was set at 0.5, the margin of error 0.05, a confidence level 95%, and a design effect of 1 to give a final sample size of 441 with a 15% drop out rate.

Study sample

Multistage sampling technique was used. Six schools (three with grade 8 and three with grade 10) were randomly selected using lottery method from the list of schools in Thimphu district.[16] From each selected school, sections were randomly selected using a lottery method to recruit a cluster of approximately 70 ±5 students. Subjects who were diagnosed by a medical doctor as having spinal and musculoskeletal problems and those with physical handicaps were excluded.

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Study questionnaire

Data were collected using a study questionnaire that was developed for this study. The study tool partly consisted of a self-administered questionnaire in English that was pre-tested in a set of twenty students in grade 8 and twenty in grade 10 at a school. Following this, the language was simplified in several questions and two diagrams were introduced to indicate the body parts to report pain and the type of schoolbag used (backpack or satchel). The questionnaire in English was adequate and did not require translation to Dzongkha, the national language. Part A of the tool collected basic information such as age and level of physical activity. Part B collected information on musculoskeletal pain with questions derived from the Standardized Nordic Body Map Questionnaire, a validated tool used to study self-declared musculoskeletal symptoms.[18] Part C collected information on the type of school bag and their safety features. In Part D, the investigators measured the height and weight of students, the weight of school bag using standard techniques and tools calibrated by the Bhutan Standards Bureau and assessed the schoolbags for the four safety features (padded shoulder strap, chest strap, hip strap and compartments).

Data analysis

The data were cleaned, entered and analysed in IBM SPSS 23.0 (trial version). The weight of schoolbag relative to student's body weight were classified into those with ≤10% BW and >10% BW. Data were analysed using descriptive statistics to determine the presence/absence of musculoskeletal pain. The difference in the mean weight of school bags among students in the two grades was assessed using t-test. Adjusted analysis was performed using logistic regression to identify the risk factors for pain in the 9 body regions (neck, upper back, low back, shoulders, elbows, hands/wrists, hips/thighs, knees and ankles) in the 12-month period prior to data collection. The following factors were included in blocks to calculate adjusted odds ratio: age, sex, time spent on activities after school (screen time, playing sports), usage of safety features (padded shoulder strap, chest strap, compartments), mode of carrying (over one shoulder or both shoulders) and bag weight relative to student's body weight (≤10% BW and >10% BW).

Ethics clearance

Ethics clearance was obtained from the Research Ethics Board of Health, Ministry of Health, Bhutan (REBH/PO/2017/043 dated 26 April, 2017). Administrative approval was obtained from the Ministry of Education, Bhutan and respective school principals to conduct the study. Informed assent was taken from each student and consent was taken from their parent/guardian.

Results

Characteristics of participants

A total of 441 students studying in grades 8 (n = 190) and 10 (n = 251) participated in the study. There were 232 females (***Table 1***). The mean age of students studying in grade 8 was 13.6 (±1.3) years and those in grade 10 was 15.8 (±1.1) years. Half of the participants (216, 49.0%) walked to school while the rest used public (146, 33.1%) and private transport (79, 17.9%).

Table 1. The proportion of the weight of schoolbag relative to body weight among students of Thimphu, Bhutan in 2017.

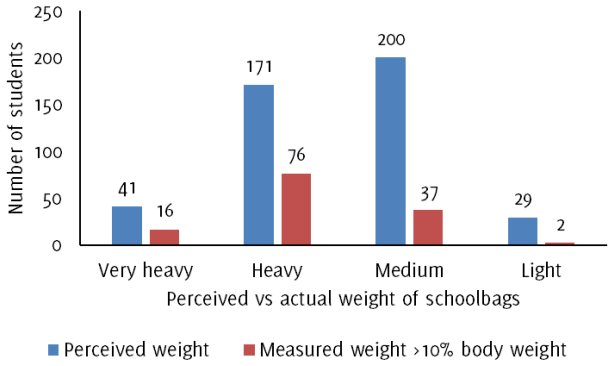
Grade and gender		Bag Weight to BW (%)						Total
		10%		>10 to <15%		15%		
		n	(%)	n	(%)	n	(%)	
Grade 8	Male	57	(61.3)	26	(28.0)	10	(10.7)	93
	Female	52	(53.6)	33	(34.0)	12	(12.4)	97
Grade 10	Male	95	(81.9)	20	(17.4)	1	(0.9)	116
	Female	106	(78.5)	25	(18.5)	4	(3.0)	135

BW = body weight

Schoolbag weight and safety features

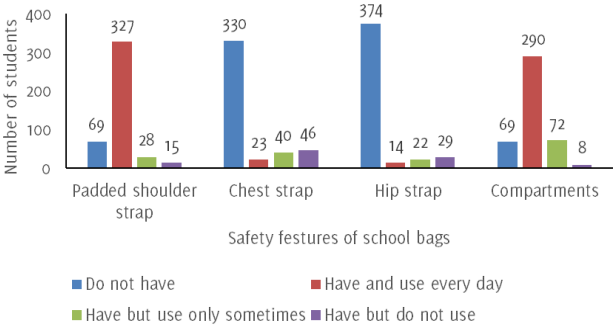
The mean weight of schoolbags was 4.6 ±1.5 kg (range: 0.9-8.1 kg) among grade 8 and 4.0 ±1.5 kg (range: 0.6-8.2 kg) among grade 10 students. This difference in means of schoolbag weights between the two grades was 0.7 kg, $p < 0.001$. The mean weight of textbooks carried to school on the day of the survey was 1.9 (±0.7) kg among grade 8 and 1.6 (±0.5) kg among grade 10 students. Textbooks constituted nearly half of the total weight of the bag (40.4% for grade 8 and 40.1% for grade 10). The percentage of students that carried bags heavier than 10% BW is shown in ***Table 1***. A negative Pearson's correlation $r = -0.237$, $p < 0.001$ was noted between perception on the schoolbag weight and actual weight of the schoolbag relative to BW (***Figure 1***).

Figure 1. The comparison between the perceived bodyweight and actual heavy schoolbag measured as >10% body weight among students of Thimphu, Bhutan in 2017.



The majority of the students (439, 99.6%) carried backpacks while two carried satchels. The backpacks were assessed for the presence of four safety features. The frequency of use of these safety features are shown in ***Figure 2***.

Figure 2. The frequency of use of backpack safety features by students of Thimphu, Bhutan in 2017.



Musculoskeletal pain

The majority of the participants (411, 93.2%) reported having musculoskeletal pain in at least one of nine regions of the body during the preceding 12 months. Self-reported pain in different regions across both grades and sex are detailed in ***Table 2***.

Among those who complained of musculoskeletal pain, over a quarter of them (114, 27.8%) had missed school due to the pain in the preceding 12 months. The majority of them attributed it to pain in one region (79, 69.3%). The three most commonly reported areas were: lower back (37, 32.5%), shoulders (30, 26.3%) and upper back (28, 24.6%). Of those who reported having missed school, half (59, 51.8%) had sought medical help (visited a doctor, *drungtsho* (traditional physician), or traditional/local healer).

After adjusting for age, sex, time spent on activities after school, and usage of safety features, children who carried schoolbags weighing >10% of body weight (adjusted OR = 2.75; 95%CI 1.27, 5.60; $p < 0.001$) and those carrying heavy bags over just one shoulder (adjusted OR = 5.72, 95%CI = 1.07, 30.41; $p = 0.041$) were more likely to report musculoskeletal pain.

Table 2. Self-reported pain in different body regions as mapped in the Standardized Nordic Body Map Questionnaire among students of Thimphu, Bhutan in 2017.

		Grade 8				Grade 10				Overall	
		Male		Female		Male		Female			
		n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Body Region											
Neck		34	(36.6)	46	(47.4)	54	(46.6)	51	(37.8)	185	(42.0)
Upper back		37	(39.8)	40	(41.2)	46	(39.7)	60	(44.4)	183	(41.5)
Lower back		33	(35.5)	43	(44.3)	55	(47.4)	69	(51.1)	200	(45.4)
Hips/Thighs		28	(30.1)	20	(20.6)	30	(25.9)	52	(38.5)	130	(29.5)
Knees		31	(33.3)	34	(35.1)	39	(33.6)	50	(37.0)	154	(34.9)
Ankles		33	(35.5)	17	(17.5)	30	(25.9)	39	(28.9)	119	(27.0)
Shoulder	**Right**	11	(11.8)	12	(12.4)	18	(15.5)	10	(7.4)		
	Left	3	(3.2)	4	(4.1)	9	(7.8)	14	(10.4)	269	(61.0)
	Both	43	(46.2)	46	(47.4)	38	(32.8)	60	(44.4)		
Elbow	**Right**	5	(5.4)	5	(5.2)	5	(4.3)	7	(5.2)		
	Left	4	(4.3)	2	(2.1)	1	(0.9)	3	(2.2)	57	(12.9)
	Both	2	(2.2)	8	(8.2)	6	(5.2)	9	(6.7)		
Wrists/ Hands	**Right**	13	(14.0)	11	(11.3)	14	(12.0)	15	(11.1)		
	Left	6	(6.5)	1	(1.0)	-	-	8	(5.9)	107	(24.3)
	Both	6	(6.5)	14	(14.4)	6	(5.2)	13	(9.6)		

Discussion

Nearly half of the students in grade 8 and less than a quarter of students in grade 10 carried school bags heavier than recommended. These proportions are lower than that reported for students in Ireland and Kuwait (70% each), but similar to that reported for Uganda (31%).[6,8,12] The mean weight of schoolbags was heavier among grade 8 students than grade 10 students despite the fact that older students were prescribed more textbooks (20 textbooks for 9 academic subjects in grade 10 compared with 15 textbooks for 6 subjects in grade 8). Older students might be carrying only the notebooks that are required for the day or borrow textbooks from other students.

The prevalence of musculoskeletal pain in our sample was considerably higher (93.2%) than those reported: 88.2% in Uganda, 69.3% Spain; 60% in India.[12,14,15,19–21] All these studies document self-reported pain but only few have quantified the severity of the pain reported using tools such as visual analogue scale.[8,22] Comparison between these studies must be interpreted with the scope of definitions used for each study. We used the Standardized Nordic body map for anatomical localization of musculoskeletal pain.[13,18,20] Though its body map picture is useful especially when administered among children, its use in our setting has not been validated and could have led to over-reporting of musculoskeletal pain.

There was a significant difference between how heavy students perceived their bags to be and the actual weight of the bags. In addition to the factors that determine the perception of load heaviness,[23] socio-cultural context plays an important role in our setting. Many of the parents of the current school children grew up in an era where there were no roads and report of having carried loads that were heavier than the current schoolbags and in traditional ways without safety measures of contemporary comparisons. Load perception may also be linked to recognition and reporting of musculoskeletal pain.

The negative impact of physiological and anatomical changes in the thoraco-lumbar spine resulting from chronic load bearing may be reduced by using bags with safety features. Most of the school bags that we studied did not have safety features; even if these features were present, many students did not use them. This calls for interventions to encourage students to adopt healthy backpack habits. Vidal et al reported an intervention programme of a combination of theory and practical feedback sessions that may be easily adopted in the classrooms in our setting.[19]

In our sample, carrying school bags weighing >10% bodyweight and carrying the bag over one shoulder compared to carrying it strapped over two shoulders were significant risk factors in reporting musculoskeletal pain. Reports of such pain at such an early age are of concern given that Bhutan has over 214,000 students in total, which makes up 30% of the country's population.[16,24] Adolescents who report musculoskeletal pain are at an increased risk of mental disorders especially anxiety and mood disorders, subsequent increased mental healthcare use and an increased odds of being absent from work in the long term.[25,26] In the short term, students have stayed absent from school due to musculoskeletal pain. The proportion of students who missed school due to musculoskeletal pain are higher than that reported in other studies.[12] In our study, age and sex were not risk factors for musculoskeletal pain.[11,22,27]

Recommendations

Heavy schoolbags can be addressed by making sure that parents and their children are aware of the risks, encouraging use of methods to reduce risk (use of safety features, carrying the bag over both shoulders) and effective ergonomic education.[20] Providing secure storage facilities[19] in schools is a viable option for Bhutan where education is provided free of cost. Awareness needs to be created among parents and teachers on the selection and use of schoolbags that have safety features.

Limitations

In our study, the weight of schoolbags was measured only on the day of data collection. The cumulative effect of heavy schoolbags over the academic year and pain prevalence in the short- and long term were not assessed.[8] Musculoskeletal pain was self-reported and we had not collected clinical details about the pain. Therefore, we were unable to test for other effects that could have influenced the reporting of pain and also the goodness-of-fit of the logistic regression model. The study was conducted in one large urban and suburban area, Thimphu. The distance from school, type of school bags and mode of transport are different in rural areas and therefore a similar study is recommended. For the multistage clustered sampling technique used in this study, we were unable to perform weighted analysis due to lack of adequate factors collected during the study.

Conclusions

The prevalence of musculoskeletal pain was high. Nearly a third of the students carried schoolbags that were heavier than that recommended. The weight of a schoolbag relative to the body weight was a significant risk factor for experiencing musculoskeletal pain.

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Author Contributions

Conceptualization: T.D., S. T. T., S. Y., and K. W. Methodology: T.D., S. T. T., S. Y., and K. W. Validation: T.D., S. T. T., S. Y., and K. W. Formal Analysis: T.D., S. T. T., S. Y., and K. W. Data Curation: T.D., S. T. T., S. Y., and K. W. Resources: T.D., S. T. T., S. Y., and K. W. Writing – Original Draft: T.D., S. T. T., S. Y., and K. W. Writing – Review & Editing: T.D., S. T. T., S. Y., and K. W. Supervision: T.D., and K. W. Project Administration: T.D., S. T. T., S. Y., and K. W.

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Case Report

Spine ABC, A Multidimensional Case Report from A to Z: Aneurysmal Bone Cyst of the Spine.

In memory of Dimitrios Konstantinou

Eliza (Eleni-Zacharoula) Georgiou,[1] Savvina Prapiadou,[1] Helen P. Kourea.[2]

Abstract

Background: Aneurysmal bone cysts (ABC) are uncommon entities which cause expansile and destructive bone lesions and are characterized by reactive proliferation of connective tissue. They usually grow rapidly with hypervascularity. ABC's incidence on the spine is 1.5 in 10 million. Most cases present with pain of unexplained origin. **The Case:** Presented in this paper is an ABC case in the spinous process of the L2 vertebra of a 20-year-old Greek female patient. The main symptom was persistent back pain, without neurological symptoms, of four years' duration. Treatment consisted of surgical curettage of the lesion. In this case report, we tried to describe not only the pathology of this disease but also the subsequent psychosocial symptoms that accompany it. We managed to accomplish that by exploiting the knowledge of an experienced pathologist, the help of the physicians responsible for this case, the interest of some sensitized medical students, and of course, the experience of the patient herself since the patient is also the lead author. **Conclusion:** The focal point of this article is that even though ABCs might lead to excruciating pain, this pain can be alleviated with the proper treatment, especially if the communication between physician and patient is optimal.

Key Words: Aneurysmal Bone Cyst, Spine, Pain, Neoplasms (Source: MeSH-NLM).

Introduction

The aneurysmal bone cyst (ABC) is a benign tumor-like lesion that is described as "an expanding osteolytic lesion consisting of blood-filled spaces of variable size separated by connective tissue septae containing trabeculae or osteoid tissue and osteoclast-type giant cells.[1] ABC's general incidence is 1.4 in a million, the median age is 13 years.[2] Although benign, ABC can be locally aggressive. Its expansile nature can cause pain, swelling, deformity, disruption of growth plates or joint surfaces, neurological symptoms (depending on the location), and pathologic fracture.[3]

In this case report, the patient's identity is intentionally disclosed to the reader. As the patient, one of my main goals for writing this case report was to describe the evolution of my experience. More specifically, I wanted to highlight how this rare lesion shifted my perspective on chronic pain.

As medical students, we study extensively the pathology, anatomy and pathophysiology of every disease. However, we usually lack the ability to communicate with our patients and completely understand how they feel, mainly due to gaps in our educational system. This incident helped me see my future as a medical doctor from a different point of view. Having this rare lesion on my body, I realized just how devastating chronic pain can be. I understood that our role and responsibility as doctors is to not only to offer the appropriate disease related-treatment to our patients but also to truly listen to them , to show compassion and empathy, and to aid and guide them in the alleviation of the psychosocial symptoms they might be experiencing . In short, I recognized the importance of advocating for their well-being in whatever way we can and includes (and possibly begins with) rendering the correct diagnosis and using any and every resource available to us.

Key Points:

- The true etiology and pathophysiology of ABCs is unknown.
- Patients with an aneurysmal bone cyst (ABC) usually present with pain, swelling, a mass at times rapidly enlarging, or pathologic fracture in the affected area, or even a combination of the above. The symptoms are usually present for several weeks to months before the diagnosis is rendered.
- There are plenty of case studies for ABCs but none of them focuses on the fact that this pain is capable of confining you in bed. Additionally, they don't place enough emphasis on the fact that the pain can be alleviated with the proper treatment. ABCs might not be severe or risky but it's terrifying to imagine living your life in constant pain.

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The Case

History and Physical Examination

The patient (16y, female, Greek) initially presented both on the orthopedic and athletic clinic with chronic back pain, intense spinal muscular spasms bilaterally and a clinical picture of slight left-curved scoliosis. Due to the patient's involvement in professional basketball, *no further examination or imaging was considered necessary* since the symptoms were directly attributed to intensive sport-related stress to the body. Non-steroidal Anti-Inflammatory drugs (NSAIDs)

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and muscle relaxants were prescribed. Physiotherapy sessions were also performed without causing any pain alleviation. One year after the onset of the pain, the patient was discouraged from continuing professional basketball and subsequently resigned. The pain and the symptoms persisted for 4 years.

Differential Diagnosis

Differential diagnosis at the time consisted of muscle strains, intervertebral disc herniation, trauma in the area and psychogenic pain.

After 4 years from the initial onset of pain (age of patient 20y), the patient relapsed and became bedridden. A Magnetic Resonance Image (MRI) scan with contrast was performed. **(*Figure 1*)**. MRI showed supernatants of the spinous process of the L2 vertebral body, an imprint located between the spinous processes of L1- L2 vertebrae. The lesion was clearly circumscribed and was not surrounded by swelling. It was measured with maximum dimensions of 1.2x1.6x0.6 cm. This alteration produced signal intensity similar to the cerebrospinal fluid (CSF) in T2 weighted sequences and signal intensity close to the bone marrow in T1 weighted sequences. It was considered necessary for the lesion to be further investigated by *Computerized Tomography (CT)* scanning focusing at L2 to document the relation of this lesion to the spinous process. **(*Figure 2*)**.

The altered lesion was elucidated in this test as it was located in the spinous process of L2. The upper part of the lesion showed a labyrinthine edge and had broken mildly the bone. It had maximum dimensions in the sagittal level of 1,6 x 1,4 cm. The lesion had clear and smooth confines, and mildly extended to the bone without breaking the cortex. No other visible bone alteration was apparent from the study of the bone section shown. Based on the above imaging findings, the lesion had mainly benign characteristics. The protagonist of differential diagnosis was an *aneurysmal bone cyst*. The chance of giant cell tumor was considered low.

Management and Outcome

The opinions regarding treatment were discordant. Paracetamol and muscle relaxants (3 pills of 1000mg paracetamol & orphenadrine per day) were prescribed for 6 months without pain remission. The patient was *bedridden* for that time interval and consequently *she could not accomplish her daily obligations*. She was not able to attend the lectures and workshops of her medical school which caused her academic performance to decline. At the same time, she was isolated in her home because she could not cope with the physical requirements of social events.

After that period of time, surgical removal of the L2 spinous process and cyst wall was performed through a 4cm incision. The resected material consisted of multiple tissue fragments measuring 4x3.5x0.7cm, including pieces of bone, striated muscle and fibrofatty tissue. NSAIDs were given for 2 weeks after surgery. The patient avoided the sitting position, torsional movements and lifting weights for 2 months.

Biopsy

The biopsy material included mainly cancellous bone containing hematopoietic bone marrow, skeletal muscle and fibrofatty tissue fragments. Focally, among the bone spicules and marrow elements there were small fragments of a cystic lesion, lined by flattened endothelium, containing few red blood cells. These findings were consistent with ABC.

Recovery

The recovery included the empowerment of the muscles that support the spine. NSAIDs were given for 2 weeks after the surgery and an orthopedic band was used to support spinal muscles. One year after the surgery, there are episodes of bilateral numbness in the legs and back pain in the area of the posterior iliac process usually lasting a week. These symptoms may be attributed to the operation-related development of connective tissue that presses the spinal cord.

Figure 1. MRI scan. The MRI showed supernatants of the spinous process of the L2 vertebral body, an imprint located between the spinous processes of L1- L2 vertebrae.

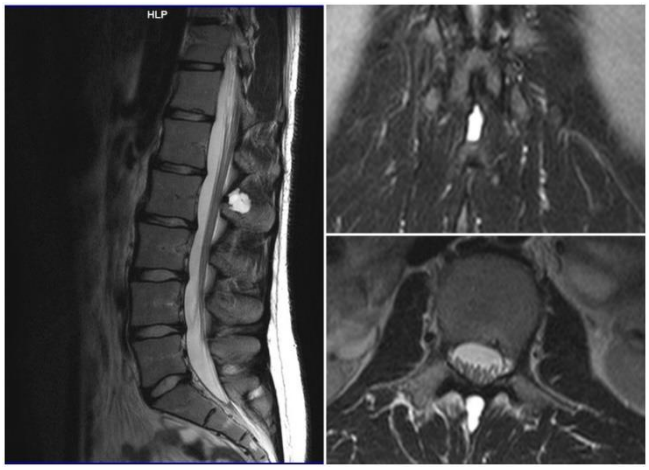
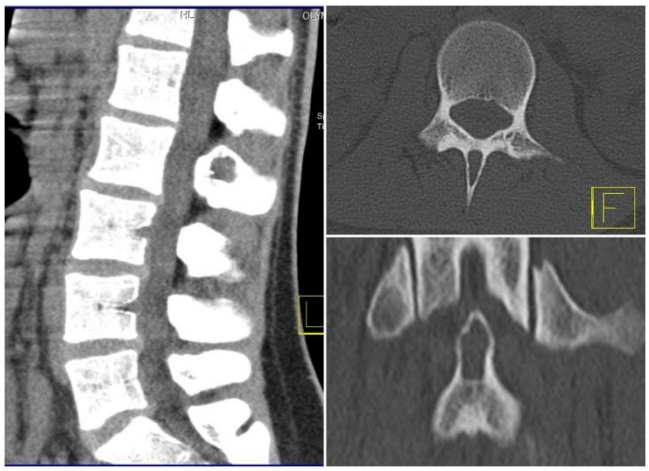


Figure 2. CT scan. The altered lesion was elucidated in this test as it is located in the spinous process of L2.



However, the patient is capable of lifting weights, of engaging in sports and of living without the constant need for NSAIDs. The remission of the pain makes her capable of not only improve her physical health, but also her psychosocial life because she can make long term plans without the fear of a relapse and the excruciating pain it is accompanied by.

Discussion

Epidemiology

The annual incidence of primary aneurysmal bone cyst was 0.14 per 100.000 individuals; however, the true incidence is difficult to calculate because of the existence of spontaneous regression and clinically silent cases. In a published review of 897 cases of ABC, the following rates of occurrence were reported **(Table 1)** and as we stated on the abstract, the occurrence of spine ABCs is 1.5 in 10 million [3].

Table 1. Rates of occurrence.

Sites of involvement	Frequency
Tibia	17.5%
Femur	15.9%
Vertebra	11.2%
Pelvis	11.6%
Humerus	9.1%
Fibula	7.3%
Foot	6.3%
Hand	4.7%
Ulna	3.8%
Radius	3.1%
Other	9.2%

Etiology & Pathophysiology

In this case, due to limited resources, we were unable to investigate the etiology and pathophysiology of ABC. However, through a literature review we found that true etiology of ABCs is as of yet unknown. Most investigators believe that ABCs are the result of a vascular malformation within the bone; however, the ultimate cause of the malformation is a topic of controversy. There are three commonly proposed theories **(Table 2).**[4]

The true pathophysiology of ABCs is also unknown.[5] Different theories about several *vascular malformations* exist; these include arteriovenous fistulas and venous blockage. The vascular lesions then cause increased pressure, expansion, erosion, and reabsorption of the surrounding bone. The malformation is also believed to cause local hemorrhage that initiates the formation of reactive osteolytic tissue. Findings from a study in which manometric pressures within the ABCs were measured support the theory of altered hemodynamics. Most primary ABCs demonstrate a *t(16;17)(q22;p13) fusion of the TRE17/CDH11-USP6 oncogene.* This fusion leads to increased cellular cadherin-11 activity that seems to arrest osteoblastic maturation in a more primitive state. This process may be the neoplastic driving force behind primary ABCs as opposed to secondary ABCs, which seem to as a reaction to underlying disease process.[6,7]

Table 2. Etiology theories of ABCs.

Etiology theories of ABCs		
ABCs may be caused by a reaction ***secondary to another bone lesion*** (ABCs in the presence of another lesion are called secondary ABCs, and treatment of these ABCs is based on what is appropriate for the underlying tumor).	ABCs may arise ***de novo***; those that arise without evidence of another lesion are classified as primary ABCs.	ABCs may arise in an area of previous ***trauma.***

Clinical Presentation

Patients with an aneurysmal bone cyst (ABC) usually present with pain, swelling, a mass at times rapidly enlarging, or pathologic fracture in the affected area, or even a combination of the above. The symptoms are usually present for several weeks to months before the diagnosis is rendered. Neurologic symptoms associated with ABCs in the spine may develop secondary to pressure or tension of nerves over the lesion. Pathologic fracture occurs in about 8% of ABCs, but the incidence may be as high as 21% in ABCs that have spinal involvement.

Treatment

Aneurysmal bone cysts (ABCs) are generally treated *surgically*[8] which was the approach that was followed by our patient. Rarely, asymptomatic ABCs may be seen in which there is clinically insignificant destruction of bone. In such cases, close monitoring alone of the lesion may be indicated because of the evidence that some ABCs spontaneously resolve. When a patient is monitored in this manner, the diagnosis must be certain, and the lesion should not be increasing in size.

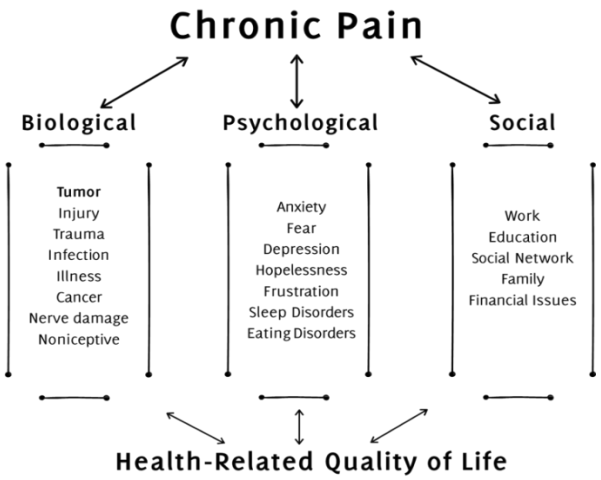
Some anatomic locations may be difficult to access surgically. If this situation is encountered, other methods of treatment, such as intralesional injection and selective arterial embolization, may be successful. In the future, advances in *osteoinductive materials* (eg, genetically engineered bone morphogenic protein) may offer a less invasive treatment of ABC.[8,9]

Psychosocial Aspect

Throughout this case report we described several of the psychosocial symptoms of the patient which were a direct result of the chronic pain caused by the ABC. Additionally, we thoroughly explained the biometric aspects of ABC. The emphasis that was placed on both aspects of the patient's condition is meant to highlight the importance of a biopsychological approach of every patient.

The biopsychosocial approach was developed by Drs. George Engel and John Romano in 1977. While traditional biomedical models of clinical medicine focus on pathophysiology and other biological approaches to diseases, the biopsychosocial approach emphasizes the importance of understanding human health and illness in their fullest contexts. The biopsychosocial approach systematically considers biological, psychological, and social factors and their complex interactions in understanding health, illness, and healthcare delivery.[11]

Figure 3. Biopsychosocial model of chronic pain and consequences on the quality of life [12]



Chronic pain affects a large proportion of the population, imposing significant individual distress and a considerable burden on society, yet treatment is not always instituted and/or adequate. Comprehensive multidisciplinary management based on the biopsychosocial model of pain has been shown to be clinically effective and cost-efficient, but is not widely available (***Figure 3***).

Many of the issues relating to physicians could be addressed by improving medical training, both at undergraduate and postgraduate levels – for example, by making pain medicine a compulsory core subject of the undergraduate medical curriculum. This would improve physician/patient communication, increase the use of standardized pain assessment tools, and allow more patients to participate in treatment decisions. Patient care would also benefit from improved training for other multidisciplinary team members; for example, nurses could provide counseling and follow-up support, psychologists offer coping skills training, and physiotherapists could have a greater role in rehabilitation. Equally important measures include the widespread adoption of a patient-centered approach, chronic pain being recognized as a disease in its own right, and the development of universal guidelines for managing chronic, non-cancerous pain.[13]

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This case report is written in memory of Dimitrios Konstantinou.

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Author Contributions

Conceptualization: E.Z.G. Writing – Original Draft: E.Z.G. Writing – Review & Editing: S.P., and H.P.K. Visualization: E.Z.G. Supervision: H.P.K. Project Administration: E.Z.G.

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Case Report

Recurrent Subacute Subdural Hematoma in a 67-Year-Old Female with Late Alzheimer's Disease: A Case Report.

Paul Marcel Morgan.[1,2]

Abstract

Background: Chronic Subdural Hematoma (CSDH) is becoming an urgent public health issue due to an increase of incidence in aging populations like Taiwan. Though trauma still stands as the primary mechanism of CSDH, it is often overlooked in the elderly, especially those with mid-to-late stage Alzheimer's Disease (AD). Coincidentally, the clinical presentation of mid-to-late stage AD shares significant overlap with CSDH. AD creates an immense challenge for physicians and family members to identify early signs of CSDH. **The Case:** We report a peculiar case of a 67-year-old female with a history of AD who presents to the Emergency room in Belmopan City, Belize, with recurrent CSDH. On admission her consciousness was disturbed and late stage dementia presented an enormous challenge for logical and meaningful history taking. Axial non-contrast computed tomography showed a crescent-shaped isodense subdural hematoma in the left hemisphere of the parietal lobe. She was stabilized and treated conservatively with corticosteroids, beta blockers, angiotensin-converting enzyme (ACE) inhibitors and diuretics. **Conclusion:** It is important for physicians to recognize and develop protocols to identify early signs of CSDH in patients with late stage AD. Early management is a key factor in minimizing more serious complications like recurrence, seizures, and tension pneumocephalus.

Key Words: Chronic Subdural Hematoma, Alzheimer Disease, Trephining (Source: MeSH-NLM).

Introduction

Chronic subdural hematoma (CSDH) is one of the most common neurosurgical conditions in which blood accumulates between the arachnoid mater and the dura mater.[3-7] The world wide annual incidence of CSDH is estimated at 8.2 per 100 000 per year in people above the age of 65.[1, 8] CSDH is becoming a more urgent public health issue due to an increase in incidence in aging populations such as in Taiwan.[1]

CSDH is a slow accrual of encapsulated fluid containing blood and degradation products that sit between the dura mater and the arachnoid mater.[3, 7] CSDH is predominant among the elderly and a long standing theory suggests that head trauma is the primary risk factor - accounting for over 70% of cases.[1, 7, 8] Vascular malformations, brain tumors, alcoholism and seizures are also significant predisposing factors that should also be taken into consideration.[7] Recently though, the trauma theory has been subjected to intense scrutiny as it takes roughly 4 to 7 weeks following a head injury for a CSDH to become symptomatic.[7] However, this time frame has some inconsistencies as even a slow venous hemorrhage would accumulate quickly enough to become symptomatic within just a few days.[7, 9]

The presentation of CSDH varies significantly from no symptoms to headache, seizures, decreased memory, and confusion.[1, 3, 5, 7-9] Coincidentally, the presentation of mid-to-late stage AD shares significant overlap with those of CSDH.[2] This situation creates an immense challenge for physicians to identify early signs of CSDH and its re-occurrence in patients with concurrent AD. However, it must be considered that the majority of CSDHs are largely attributed to trauma, intracranial hypotension and defective coagulations.[2, 12]

Inflammation, is known to play a crucial role in the development of CSDH.[7] Despite its role in tissue repair, prolonged inflammatory responses directly contributes to fluid accumulation and angiogenesis leading to new membrane growth through CSDH.[7] IL-6 and IL-8 have also been elucidated as important inflammatory cytokines implicated in fibrinolysis. IL-6 and IL-8 are produced by a host of cell types including monocytes, fibroblasts, and endothelial cells.[7]

The pathology of the enlargement of the CSDH is very complex but this condition is treated most effectively through surgery.[7] Middle Meningeal Artery (MMA) embolization and burr hole evacuation are relatively simple procedures, recurrences remain one of the major bottlenecks in treatment.[6, 7, 9]

Case Report

On January 29th, 2019 a 67-year-old female patient with a history of stage III hypertension, subdural hematoma, and late state dementia presented to the Department of Accident and Emergency at Western Regional Hospital in Belmopan City, Belize, due to consciousness disturbance, syncope, and left-sided hemiparesis. The symptoms were most pronounced on the day leading up to admission. On admission her consciousness was disturbed and late stage dementia presented an enormous challenge for logical and meaningful history taking. The patient's family denied the use of antiplatelet and anticoagulants. Her Glasgow Coma Scale was E4V2M5 (11). Vital signs in the ER revealed a temperature of 36.1°C, pulse rate of 61, respiratory rate of 14, oxygen saturation of 90%, and a blood pressure of 120/70. Fluid resuscitation was initiated and blood samples were taken. Prior to this second round of admission, she was admitted on January 1st 2019 for a burr hole craniotomy (trephination) to irrigate and drain a subdural hematoma in the left hemisphere of the parietal lobe.

ER workup revealed microcytic anemia with hemoglobin 10.8 g/dl (norm 13-18 g/dl), hemotocrit 32.1% (norm 40-54%) and MCV 78 fl (norm 80-94 fl) without increased WBC (white *blood cells).* Glucose level were normal (106 mg/dl) and urine analysis was unremarkable.

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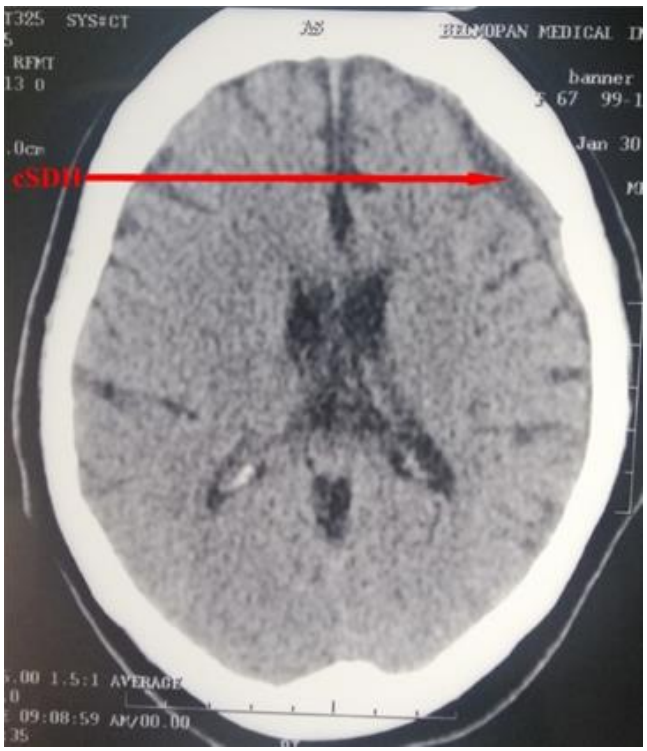
The CT was performed using a multidetector scanner Brivo CT325. Continuous helical slices of 5 mm thick sections across the entire neurocranium were performed. Reconstruction at 3 mm slices and 1.5 mm intervals were also obtained. The osseous tissues and pneumotized cavities were studied using bone window which revealed a recent left parietal burr hole.

The CT imaging revealed an extra axial crescent shape isodense collection affecting the left parietal region associated with effacement of the cerebral sulci in the left parietal lobe due to edema. The cerebellar hemispheres, vermis, brainstem and cerebellar-pontine angles appeared normal in density and contour. The ventricular system also appeared normal in size and position relative to the midline. Infratentorial and supratentorial cisternae and the external subarachnoid were also unremarkable.

Figure 1. Axial non-contrast CT image showing a crescent shaped isodense subdural hematoma in the left hemisphere of the parietal lobe. The right hemisphere, ventricular system, and deep structures of the brain appear normal with no midline shift.



Although there are various effective modalities of treatment for CSDH, using burr-hole evacuation or Middle Meningeal Artery (MMA) embolization, there were no neurosurgery facilities or trained neurosurgeons to perform any invasive interventions.

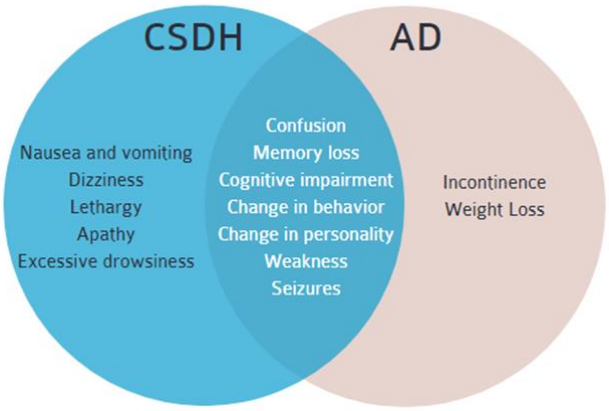
Our patient's fluids were maintained with 500cc of Ringer's lactate solution and treatment was conservative with 200 mg/kg qd IV infused mannitol and 12 mg of IV infused dexamethasone over of 30 to 60 minutes to reduce intracranial pressure associated with brain edema. 50 mg qd captopril and 25 mg BID of atenolol were prescribed for control of hypertension. The patient was then transferred to the largest referral trauma center in Belize City, Belize, Karl Heusner Memorial Hospital (KHMH) for further expert intervention.

Discussion

Though trauma still stands as the primary mechanism of CSDH it is often overlooked in the elderly population and consequently creates a degree of retrospective haze around its true time and place.[7] The most frequently presented symptoms in CSDH have been intellectual deterioration and change in personality which eerily mirror the presenting symptoms of mid-to-late stage AD[10] Late-onset AD is most commonly diagnosed in patients after the age of 60 with a global prevalence of 6%.[1, 8]

Symptoms of mid-to-late stage AD include confusion, cognitive impairment, change in behavior and personality, memory loss, weakness, seizures, weight loss and incontinence.[11, 12] Coincidentally, the initial presentation of a symptomatic CSDH may also include confusion, cognitive impairment, change in behavior and personality, memory loss, weakness and seizures.[9] The use of antiplatelet and anticoagulants are also common risk factors for CSDH in the elderly population.

Figure 2. Symptoms of mid-to-late stage AD and CSDH. There is significant overlap which includes confusion, memory loss, cognitive impairment, change in behavior, and change in personality, weakness and seizures.[2, 6]



We report this peculiar case because the initial presentation of recurrent subdural hematoma is likely to be masked by the symptoms of mid-to-late stage AD. While CSDH is treated most effectively by MMA embolization via an endovascular approach or by burr-hole evacuation, Belize, like many other developing countries currently lack the facilities and trained specialist to perform interventional neuroradiology procedures. Many of our health centers also lack neurosurgeons trained to perform the optimal lifesaving procedures.[9]

The morbidity and mortality rate in CSDH varies significantly worldwide.[1] The overall in-hospital mortality index during admission is estimated at 15.6%.[1] Overall outcome is good in patients who receive early surgical intervention with a morbidity and mortality rate about 16% and 6.5% respectively.[1] However, the morbidity, mortality, and overall prognosis in patients with comorbid AD and CSDH requires further investigation.

In conclusion, it is important for physicians to recognize signs of early recurrent CSDH in the elderly and develop protocols to effectively distinguish the condition from that of mid-to-late stage AD. Especially since both conditions are comorbid. Of significance, CSDH ultimately leads to death, and therefore must not be confused with AD, especially in patients with a past cranial surgical history. Early management is a key factor in minimizing serious complications such as recurrence, seizures, and tension pneumocephalus.[1, 8] Despite the lack of adequate neurosurgical intervention, our patient was treated conservatively and stabilized with corticosteroids, beta blockers, angiotensin-converting enzyme (ACE) inhibitors and diuretic i.e. mannitol. Our patient was then transferred to the better equipped referral trauma center in Belize City, KHMH, for further expert intervention.

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Case Report

Pulmonary Embolism Secondary to Silicone Injection

Carolyn Frances Molina,[1] Zachary Paul Retalis.[1]

Abstract

Background: The use of silicone for synthetic enhancement in cosmetic procedures has been established for decades but is questionable in safety as it is associated with a range of possible complications. Incidental injection of this polymer into the venous system is not uncommon and can result in the formation of microemboli, which can travel to the lungs. This occurrence can result in a rapid decline of respiratory function and send a patient into severe acute distress. **The Case:** This report details a female patient presenting with hemoptysis, presumed to have severe pneumonia until her history of cosmetic treatment was revealed and correlated. Her rapid respiratory decline is followed in inflammatory response markers and radiograph imaging. **Conclusion:** A unique treatment approach with prone positioning was used and may play a key role in decreasing mortality in these patients. This report draws attention to the dangers of cosmetic enhancement and raises clinical awareness for associated complications.

Key Words: Silicones, Embolism, Acute Respiratory Distress Syndrome, Cosmetic Techniques (Source: MeSH-NLM).

Introduction

Silicone is a polymer made of repeating silicon-oxygen bonds substituted with organic groups, most frequently, methyl groups. The chemical composition of these bonds gives them their waterproof and durable characteristics. It has been used for cosmetic procedures and plastic surgery since the 1960s, with a questionable safety profile, having been banned by the FDA for use in breast implants from 1992-2006 in the United States. The use of liquid silicone as an agent of augmentation has recently seen a frightening increase in women and transsexual communities. In a quest for aesthetic beauty, individuals are turning to silicone injections in areas such as the buttocks, calves, lips, and forehead in order to achieve a smooth, plump appearance. Of particular interest is the rising use of silicone injections into the buttocks, leading to complications including granulomatous reactions, acute respiratory distress syndrome (ARDS), and silicone embolism syndrome.

The inadvertent, direct injection of liquid silicone into a gluteal vein may lead to pulmonary embolism. Many of these complications are observed hours to days later in patients who are receiving their injections by unlicensed individuals using non-medical grade silicone in non-sterile environments. The trend of silicone injection use has even led to "parties", where groups of people contribute monetarily in order to receive a discounted rate on the service. That being said, often times those receiving the injections are unaware, or unperturbed by the use of these materials, sometimes resulting in disastrous consequences. This is the case seen in a 31-year-old Hispanic female who presented to the emergency department with a one-day history of worsening hemoptysis. The decline in this patient's condition resulted in rapid progression to ARDS, at which time extreme treatment measures were taken to keep her alive.

Case Report

A 31-year-old Hispanic female presented to the emergency department in the early morning hours with chief complaints of hemoptysis, shortness of breath, and acute respiratory failure. Her symptoms described on initial presentation also included chest pain with breathing, dizziness, fatigue, muscle aches, and pain in the region of her right costovertebral angle. The patient had a past medical history of asthma and recurrent pneumonia throughout her childhood. Her history of present illness described that her symptoms had begun one day prior to initial presentation. She had been to another facility approximately 15 hours prior to presentation, where she was diagnosed with pneumonia and sent home with antibiotics. From the onset of symptoms to her presentation to the emergency department in the instance described in this report she reportedly coughed up blood ten times. The patient denied any recent travel or sick contacts.

Key Points:

- Pathophysiology of silicone embolism syndrome
- Treatment with prone positioning
- Examination findings in patients with silicone embolism syndrome
- Increasing clinical awareness of complications associated with cosmetic procedures

The physical examination on initial presentation revealed lung sounds clear to auscultation with no wheezes, rales or rhonchi, and cardiac sounds including regular rate and rhythm with no murmurs, rubs or gallops. The rest of the exam was largely unremarkable except for skin findings of petechiae on her right breast, abdomen, and left buttock. At the time of presentation, a chest radiograph was performed and showed fluffy opacities of the bilateral mid-to-lower lungs with a peripheral predominance (***Figure 1***).

A chest computerized tomography (CT) without contrast on presentation also showed predominantly basilar and peripheral ground glass opacities/nodules bilaterally. A complete blood cell count taken at the same time had white blood cells within normal limits at 10.5 x 10^9/L, but an absolute neutrophil count elevated at 9.1 x 10^9/L. Arterial blood gas studies at that time were unremarkable. The patient was tested for influenza using rapid influenza diagnostic tests, infectious mononucleosis using mononuclear spot testing, and tuberculosis via acid-fast bacilli testing. All of these investigations

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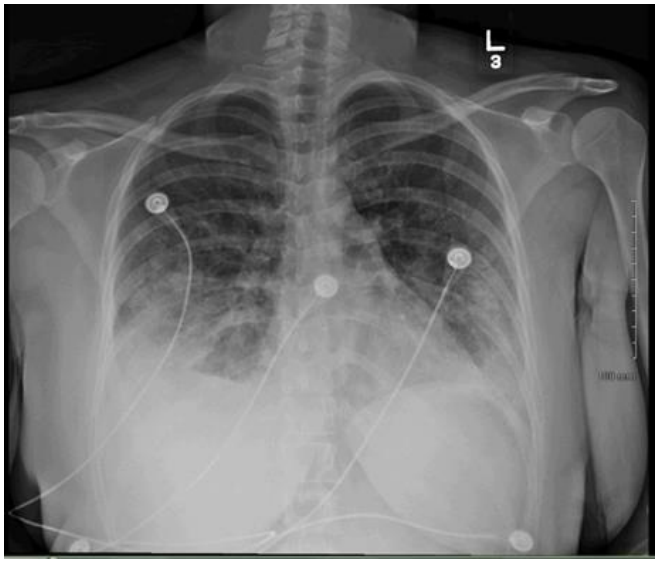
were negative. The patient was also negative for HIV and *Legionella* infection. Another significant laboratory value initially was elevated C

Figure 1. AP Chest Radiograph on Initial Presentation.



reactive protein (CRP) at 8.0 mg/L, demonstrating an inflammatory response.

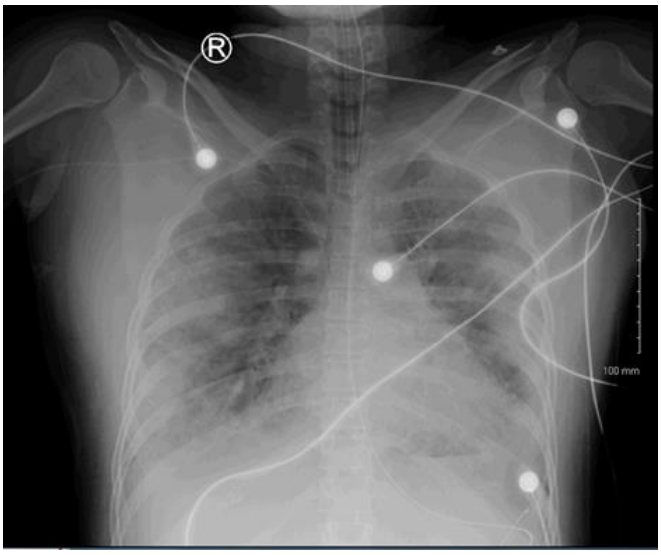
The patient was admitted to the inpatient service for workup and on day two of her hospital course, experienced worsening dyspnea and tachypnea and requested intubation fearing further decline in her breathing status. She was then transferred to the ICU for intubation and mechanical ventilation. Collateral obtained from the patient's family following her intubation revealed she received silicone injections in her buttocks bilaterally for cosmetic purposes two days prior to symptom onset. This was a procedure she had reportedly received in the past as well. It was at this time that the medical team considered the likelihood of silicone embolism syndrome versus severe pneumonia. The patient was diagnosed with silicone embolism syndrome on day two of her hospital course.

Her status continued to deteriorate over 48 hours. Serial chest radiograph demonstrated bilateral fluffy opacities representing ARDS versus focal pneumonia, only mildly worsened compared to prior exam in the emergency department (***Figure 2***). On her fifth hospital day chest radiograph showed mild interval worsening of diffuse bilateral airspace disease, not worsened in bilateral upper lungs. There was a possible small bilateral pleural effusion and the findings were determined to be likely infectious or inflammatory. White blood cell counts trended over the course of her stay showed rapid increase; from 10.5 x 10^9/L to 11.4 x 10^9/L within her first 24 hours of presentation to a critical high of 21.8 x 10^9/L on day five of her hospital course. Absolute neutrophil count also trended up from initial 9.1 x 10^9/L on day one to a critical high of 17.71 x 10^9/L on day five. CRP continued to increase from initial 8.0 mg/L, reaching 12.90 mg/L on day four of her hospital course.

On initial presentation this patient was treated with broad spectrum antibiotics based on her clinical deterioration and worsening opacities seen in her chest radiographs. Throughout her course she was treated with methylprednisolone initially at 40 mg IV every six hours. She continued to experience episodes of hemoptysis while intubated, contributing to a worsening anemia and necessitating a blood transfusion. The dose was eventually increased to 125 mg IV every six hours once she was transferred to the ICU. The patient was treated with prone positioning on her fifth hospital day while a transfer was arranged for her treatment with extracorporeal membrane oxygenation (ECMO) at a larger hospital.

After transfer and treatment with ECMO, the patient remained under the care of inpatient therapy at a hospital three months later. She

Figure 2. AP Chest Radiograph 48-Hours After Admission.



recovered and was discharged from inpatient hospital care approximately four months following her presentation to the emergency department.

Discussion

Silicone embolism syndrome is a condition that occurs when silicone injected for cosmetic or therapeutic purposes enters the systemic venous system and travels to the pulmonary vasculature. Proposed pathophysiology involves histiocytes and foreign-body giant cells migrating to the site of the micro emboli causing diffuse inflammation as well as alveolar hemorrhage.[1] This diffuse inflammation develops rapidly as was demonstrated in this patient's laboratory CRP values, leukocyte and neutrophil counts, and serial radiograph readings. Evidence of alveolar hemorrhage is provided by the patient's history of hemoptysis prior to presentation and continued hemoptysis even while on mechanical ventilation. Future investigations into this syndrome may benefit from bronchoscopy and/or serial lung biopsies to demonstrate the progression of inflammatory cell migration in alveolar capillaries.

Similar to fat embolism syndrome (FES), silicone embolism syndrome patients may present with a characteristic petechial rash, hypoxemia, dyspnea, and tachypnea. In review of this patient's hospital course, it should be noted that the patient presented with characteristic petechiae. The presence of petechial rash and respiratory decline should have prompted the question of recent trauma in consideration of fat embolism syndrome at the very least. This patient's rare case should be considered as an example of the importance of detailed history taking. Future considerations for standard of care may involve the question of foreign body contact or injection when treating a patient with cutaneous manifestations and respiratory distress.

The complication rate of silicone injections in general are estimated to be about 1-2%,[2] which includes silicone embolism to the lungs, making this syndrome particularly unusual. Given its similarity to fat embolism syndrome, guidelines for care and diagnosis are followed similarly. Both syndromes are clinical diagnoses and diagnoses of exclusion, therefore a wide differential diagnosis should be considered. The differential diagnosis for this patient included alveolar filling defects like pneumonia and ARDS, as mentioned after thoracic imaging studies. Given that the only treatment available for

silicone embolism syndrome is supportive therapy and the diagnosis is clinical, a noninvasive diagnostic approach with chest imaging is appropriate. A full diagnostic workup of a patient with silicone embolism syndrome should include coagulation panels and serial complete blood cell counts to rule out disseminated intravascular coagulation (DIC) and other hypercoagulable states like inherited thrombophilia.

As in the case of FES, presence of the characteristic manifestations of hypoxemia, fever, and a petechial rash following injection of silicone is highly suggestive of the condition. When silicone embolism syndrome is suspected, chest radiography and/or CT is performed, as seen in the case described. When compared with other case studies of silicone embolism syndrome, the presence of ground glass opacities bilaterally on chest CT in this patient is characteristic and supports the diagnosis.[3]

Because at this time there is no definitive treatment for silicone embolism syndrome, management is supportive, as mentioned previously. The standard of care is followed in the patient described as she is treated with methylprednisolone, a corticosteroid. The effects of corticosteroids in this patient and others with ARDS include inhibition of hypoxic vasoconstriction, and reduction and modulation of inflammatory mediators. The goal of corticosteroid use in these patients is to control the inflammatory response while the syndrome resolves spontaneously.

The prognosis of silicone embolism syndrome is associated with rapid clinical deterioration. Management of this condition is primarily supportive, but prone ventilation is a recruitment maneuver that may improve oxygenation. The prone ventilation treatment approach is based on the theory of redistribution of the blood so that ventilation and perfusion is better matched. Through this mechanism regional changes in ventilation will ideally improve oxygenation. Benefits of prone positioning are supported by the results of the Proning Severe ARDS (PROSEVA) study, which revealed a significantly decreased 28-day and 90-day mortality rate in patients with severe ARDS who received early treatment with prone positioning sessions of at least 16 hours when compared to patients with severe ARDS who remained in the supine position.[4] It should also be considered that the mortality benefits of prone positioning may be greatly associated with decrease in severe tissue strain and not simply increased oxygenation.[5] The mortality rate of silicone embolism syndrome has been described to be approximately 25%.[6]

In summary, the cosmetic use of silicone via injection can result in entrance of the synthetic polymer into the systemic venous system and embolization to the pulmonary vasculature. These micro emboli can lead to diffuse alveolar hemorrhage associated with rapid respiratory decline and cutaneous manifestations similar to the presentation of fat embolism syndrome. Although this presentation is rare and diagnosis is not obvious, clinicians aware of the possible complications of such cosmetic procedures can potentially screen for risk factors with a detailed history and physical exam. Increased awareness of this rare condition can improve the prognosis for patients suffering from complications.

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Case Report

Aneurysmal Subarachnoid Hemorrhage in a 68-Year-old Hyperglycemic Female Patient: Case Report and Literature Review.

Paul Marcel Morgan.[1]

Abstract

Background: While hyperglycemia is intimately associated with uncontrolled diabetes mellitus (DM), recent clinical studies have demonstrated that hyperglycemia is also present in the early acute phase of stroke and is associated with poor prognosis and increased long-term mortality. About half of patients with acute hemorrhagic stroke also present with hyperglycemia upon admission. But more than 50% of patients with acute hemorrhagic stroke develop hyperglycemia even without a previous history of DM. This sheds new light on the relationship between DM, hyperglycemia, and hemorrhagic stroke, with a pathophysiology that is perhaps more profound than is conventionally understood. **The Case:** We report a case of a 68-year-old female, with a history of DM Type 2 and stage 3 hypertension who presents to the emergency room (ER) at the Western Regional Hospital in Belmopan City, Belize, with hemorrhagic stroke and hyperglycemia. Diffuse subarachnoid hemorrhage was found in the frontal, temporal, and parietal regions. Mild intraventricular hemorrhage was also observed in the frontal horns and basal cisterns. And small areas of intraparenchymal hemorrhage were present in the frontal lobes. The patient was stabilized and treated conservatively with calcium channel blockers, and diuretics. **Conclusion:** Despite a unifying consensus that is still pending, maintaining glucose levels between 110-120 mg/dl by using continuous insulin infusions after traumatic brain injury or aneurysmal subarachnoid hemorrhage may carry some clinical benefit with slightly improved outcome.

Key Words: Intracranial Hemorrhages, Traumatic Brain Injury, Intracranial Aneurysm, Hyperglycemia, Diabetes Mellitus (Source: MeSH-NLM).

Introduction

Non-traumatic brain injury resulting in hemorrhagic stroke is a debilitating condition and one of the major complications of uncontrolled hypertension.[1] Despite hemorrhagic stroke being responsible for only 10% of all strokes, it is associated with a high morbidity and mortality index and is therefore a serious public health issue worldwide.[1, 2] However, diabetes often coexists with hypertension and more importantly both conditions are conventional risk factors for stroke.[3]

While hyperglycemia is intimately associated with uncontrolled diabetes mellitus (DM), recent clinical studies have demonstrated that hyperglycemia is also present in the early acute phase of stroke and is associated with poor prognosis and increased long-term mortality.[2] Kallikrein, a serine protease, has been recently elucidated as a crucial intermediate between hyperglycemia and profuse intracranial hemorrhage (ICH).

Kallikrein has since shed new light on the pathophysiology of hemorrhagic stroke.[4] Herein, we explore the relationship between DM and hyperglycemia and their roles in ICH. However, the clinical benefit of lowering glucose levels in ICH still remains an active subject of debate and clinical inquiry.[2] Increased efforts geared towards a consensus on hyperglycemia and hemorrhagic stroke is therefore imminent and necessary for optimal management of diabetic patients who present with profuse ICH.

The Case

A 68-year-old female patient with a history of stage 3 hypertension and inadequately controlled DM Type 2 presented to the Department of Accident and Emergency at the Western Regional Hospital in Belmopan City, Belize. The patient ailed from consciousness disturbance, poor appetite, cephalgia, emesis, dehydration, and bilateral paresis. Symptoms were most pronounced within 12 hours before admission. On admission the patient had disturbed consciousness and her Glasgow coma score was E5V3M2 (10). Vital signs in the ER revealed a temperature of 36 °C, pulse rate of 65, respiratory rate of 16, oxygen saturation 95%, and a blood pressure of 190/110. Fluid resuscitation was initiated and blood samples were taken.

ER workup revealed normal hemoglobin 13.5 g/dl (norm. 13-18 g/dl), slightly decreased haemotocrit 39 % (norm. 40-54%) and mean corpuscular volume (MCV) 81 fl (norm. 80-94 fl) without increased white *blood cells* (WBC). Differential WBC count revealed elevated neutrophils 87.3 (norm. 40-75 %) and an elevated Erythrocyte Sedimentation Rate (ESR) of 67 (norm. M 0-10/ F 0-22 mm/hr). Fasting glucose level was elevated (161 mg/dl), while the urine analysis was unremarkable. A Computerized Axial Tomography (CAT) scan was performed using a multidetector scanner Brivo CT325. Continuous helical slices of 5 mm thick sections across the entire neurocranium were performed. Reconstruction at 3 mm slices and 1.5 mm intervals were also obtained. The osseous tissues and pneumotized cavities were studied using the bone window (***Figure 1***).

Diffuse subarachnoid hemorrhage was found in the frontal, temporal, and parietal regions. Mild intraventricular hemorrhage was also observed in the frontal horns and basal cisterns. Small areas of intraparenchymal hemorrhage were also present in the frontal lobes. General effacement of the cerebral gyri was noted upon observation. The cerebellar hemispheres, vermis, brainstem, and cerebello-pontine appeared normal in density and contour. Acceptable delimitation was observed between the grey and white matter. There were no hyperdense or hypodense spaces between the lesions (***Figure 2***).

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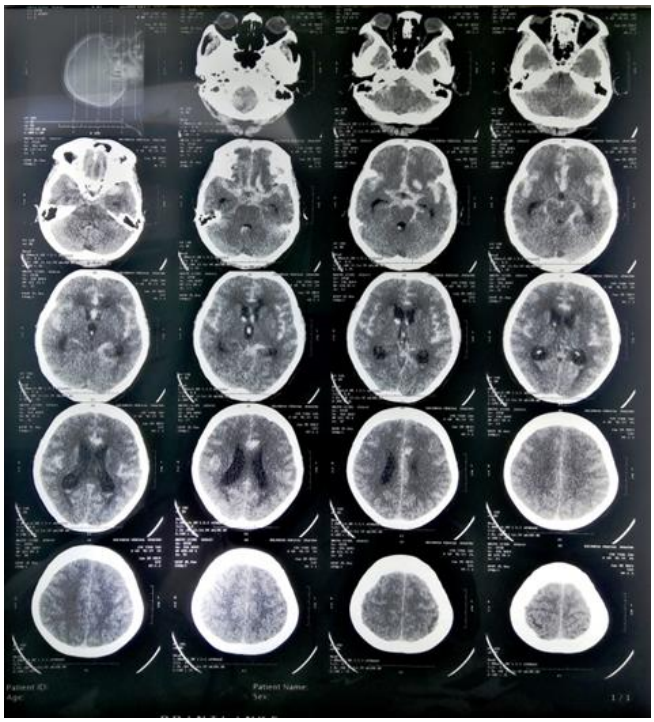
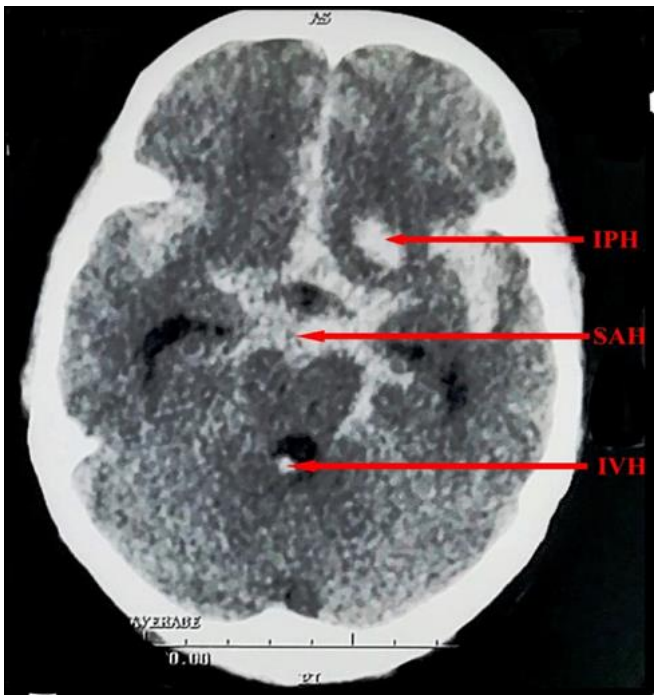
Figure 1. Non-contrast CAT scan of the entire neurocranium with 5 mm continuous helical slices and 3 mm slice reconstruction at 1.5.



The patient's fluids were maintained with 500 cc of Ringer's lactate solution and treatment was conservative with 90 mg ER PO QD nifedipine, 200mg/kg IV infused mannitol to reduce intracranial pressure associated with brain edema. A central line was established via the internal jugular vein followed by rapid sequence intubation (RSI). Despite burr-hole evacuation being the optimal choice of intervention, there are currently no neurosurgical facilities at the treatment hospital to facilitate the lifesaving intervention. Our patient was transferred to the largest equipped referral trauma center in Belize City, Karl Kushner Memorial Hospital (KHMH) for further expert intervention.

Figure 2. Axial non-contrast CAT image showing diffuse subarachnoid hemorrhage, intraparenchymal hemorrhage, and mild intraventricular hemorrhage.



Discussion

The Bondage of DM, Hemorrhagic Stroke, and Hyperglycemia

Intracranial aneurysms (IAs) occur in about 5% of the general population and are characterized by localized dilatation of cerebral arteries with a high predisposition to rupture[5]. Ruptured IAs are the leading cause of hemorrhagic stroke, and are consequently responsible for 85% of subarachnoid hemorrhages (***Figure 3***).[6]

While the pathophysiology of ischemic stroke and hemorrhagic stroke differ, hypertension, either alone or concomitant with other etiological factors is overwhelmingly the primary culprit in cases of stroke.[3] DM being a premorbid requisite for hypertension, few studies have explored the intricacy between hyperglycemia and hemorrhagic stroke. Diabetes alone quadruples the risk of intracranial hemorrhage. Several clinical studies have revealed that diabetes and hyperglycemia are associated with poor clinical outcomes flowing from ICH.[1, 2]

Nearly 50% of all acute stroke patients present with hyperglycemia upon admission as in the case of our patient.[2, 8, 9] Despite this fact, the effects of elevated glucose in a stroke patient, with or without a history of DM, and the role of DM in ICH is not fully understood.[1, 3] However, patterns of association between DM and ICH are plausible. Thus, there may be several mediating mechanisms by which hyperglycemia contributes to small vessel disease and ICH volume expansion.[10] How DM contributes to a hyperglycemic state after aneurysm rupture is therefore worth investigating.

Hemorrhagic Stroke and TBI: Smoking Gun Parallels

Traumatic Brain Injury (TBI) is classified into two main categories (i.e. primary and secondary).[9, 11-15] Primary injuries occur as a consequence of shearing and compression due to an applied physical force.[14] Secondary injury succeeds primary injury, initiates within a few hours, and terminates within a few days.[4, 10, 12, 14, 16] Secondary injury is rather complex and triggers cranial and systemic complications which are both notoriously associated with poor clinical outcomes.[4, 10, 12, 14, 16] Intracranial hypertension, cerebral edema, calcium ion toxicity, infection, and vasospasm are considered to be cranial complications while systemic complications encompass hypoxemia, hypotension, hypertension, hypoglycemia and hyperglycemia.[4, 10, 12, 14, 16] Although ischemic stroke, hemorrhagic stroke, subarachnoid hemorrhage, and intraparenchymal hemorrhage are mechanistically non-traumatic in nature, they all elicit the same hemostatic responses with cranial and systemic complications. Shi et al. reports that TBI with DM Type 2 has a much higher mortality (14%) than TBI without DM Type II (8.2%).[1, 10, 14, 15, 17] And DM Type 1 has a higher (17.1%) mortality rate than DM Type 2. It suggests that DM has the potential to be an independent predictor of poor outcome as insulin deficiency, a direct correlation to elevate glucose levels, seems to be a major contributor to increased mortality after TBI or stroke.[1, 15, 18] If so, then such a clinical pattern poses another important query; is there a glucose threshold with respect to persistent hyperglycemia?

The Hyperglycemic State

Persistent hyperglycemia can be defined as average daily blood glucose levels in excess of 149 mg/dl for the first week following TBI or stroke – cerebral vascular insult.[13] A cohort study of 834 patients found that blood glucose below 145 mg/dl significantly reduces lactate production, and results in optimal lactate/glucose and oxygen/glucose indices following a cerebral vascular insult.[13] However, the pathophysiological

and bimolecular mechanism by which aberrant glucose concentrations worsens clinical outcomes is still a subject of on-going research.[9, 13-15]

The hyperglycemic state is a consequence of a systemic inflammatory response syndrome (SIRS), which is a cascade of local deleterious mechanisms involving increase in oxidative stress, recruitment of multiple inflammatory cytokines, TNF-α, IL-6, CD11d, and an induction of excitotoxicity.[11, 19] Studies demonstrate that TNF-α regulates the role and quantity of glucose by elevating levels or pre-adipocyte genes and decreasing adipocyte specific genes ultimately resulting in hyperglycemia.[15] The inflammatory response cascade also contributes to hyperglycemia by increasing the level of corticotrophin-releasing hormone (CRH) and stimulating the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary.[15] Not surprisingly, our patient's ESR was markedly elevated, greater than 3 times above the normal range indicating active inflammation. Nevertheless, the complete relationship between SIRS and hyperglycemia needs to be further developed as well.[15, 19]

A Novel Antiplatelet Protein

A 2017 study investigated the effect of diabetes and hyperglycemia on the mechanism of acute hematoma expansion.[20] Their studies revealed that hyperglycemia increases hematoma formation and the mechanism is regulated by an osmotic-sensitive serine protease, kallikrein, which inhibits platelet aggregation.[4, 20] The authors further suggest that plasma kallikrein is activated by coagulation factor XII via a contact activation system which is crucial to the intrinsic coagulation cascade and innate inflammation.[20]

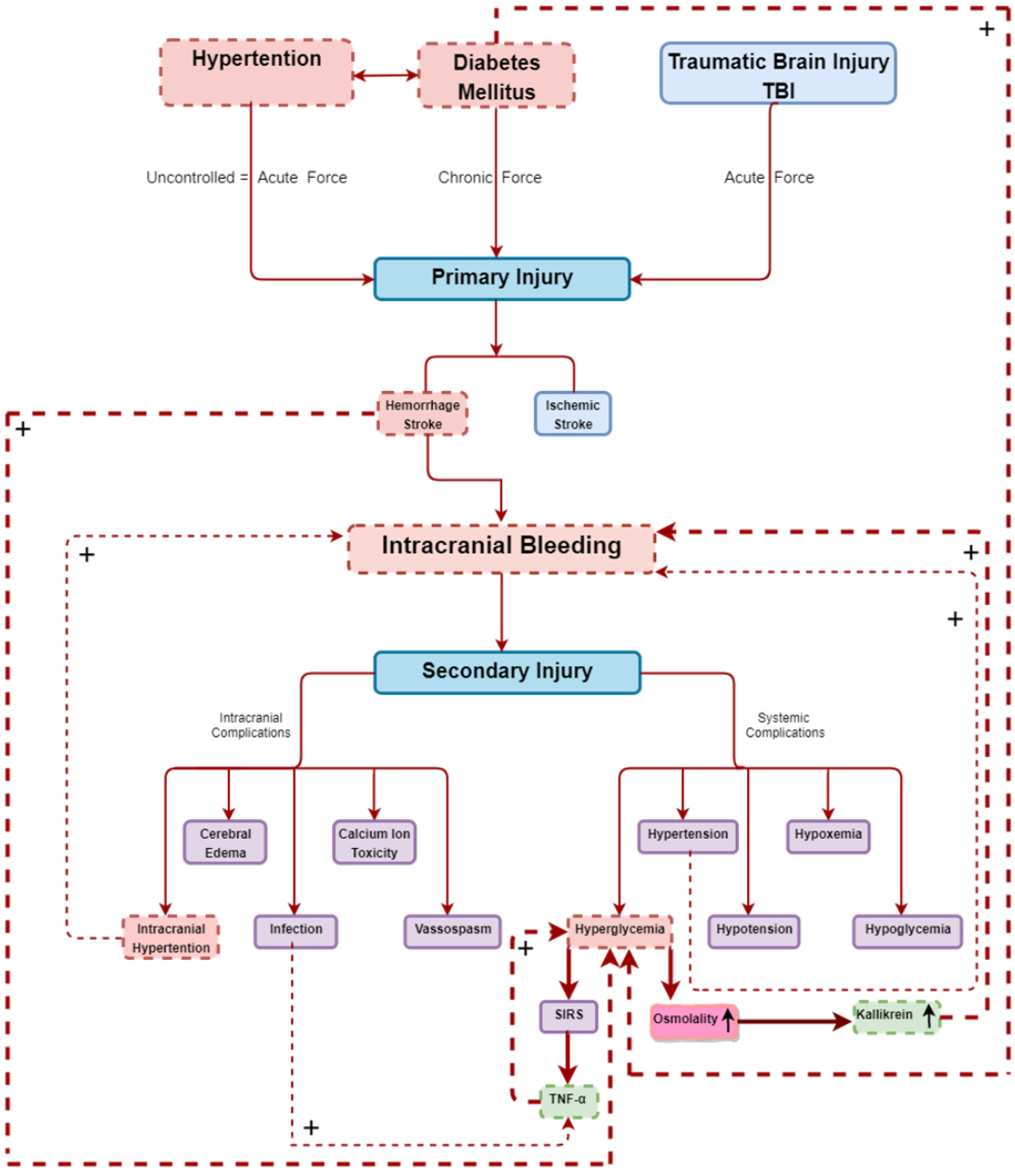
Plasma kallikrein is well known for its role in the proteolytic cleavage of kininogen which yields bradykinin leading to vascular dilation and increased permeability through bradykinin receptors 1 and 2.[4] Feener et al. results suggest that the increase in hematoma expansion associated with hyperglycemia is arbitrated by an associated increase in osmolality, which is consistent with multiple reports postulating that raised plasma osmolality on admission after acute hemorrhagic stroke increases the risk of mortality.[4, 7, 18, 20] Interestingly, the study also demonstrated that hyperosmolar mannitol and hyperosmolar salt activated plasma kallikrien in the same manner by which elevated glucose concentrations do.

Thus, hyperglycemia increases hematoma expansion in ICH and the exacerbation of hematoma expansion is mediated by kallikrein. Plasma kallikrein is therefore a potential target for controlling hematoma expansion in the setting of hyperglycemia. Currently, there are no FDA approved small molecule inhibitors for kallikrein.[21, 22] As such, small molecule inhibitors that can effectively mediate TNF-α and kallikrein levels immediately after hemorrhagic stroke may reduce cerebral bleeding, control glucose levels and significantly improve recovery, which may lead to better clinical outcomes particularly in diabetics.

Tight Glucose Control with Insulin Infusion

To determine whether elevated blood glucose levels cause or exacerbate secondary brain injury following TBI, Meng et al. conducted a prospective study of 240 adults.[2, 11] Patients with severe TBI were randomly assigned to either of two groups; a tightly regulated glucose group and a control group.[11] The glucose levels for the tightly regulated group were maintained at 80 mg/dl using continuous insulin infusion therapy throughout their stay at the hospital while the control group adhered to a conventional glucose control where insulin was given only if glucose levels exceeded 200mg/dl.[11] The results of the study revealed that significantly more patients in the intensive insulin therapy group had good outcomes - Glasgow Outcome Scale (GOS) between 4 and 5 versus that of the conventional therapy group. Interestingly, insulin therapy was also associated with significantly lower infection rates and shorter ICU stay.[11] The six month mortality outcomes in both groups were, however, similar. Despite these findings, many other clinical studies of patients with hemorrhagic stroke and TBI have found little benefit from tight glucose regulation and many propose concerns about hypoglycemia and further neuronal injury.[3, 8, 11, 13, 15, 19] In conclusion, despite the discrepancies in a unifying consensus, maintaining glucose levels between 110-120 mg/dl by using continuous insulin infusions after TBI or hemorrhagic stroke does carry some clinical benefit with slightly improved outcomes.[3, 8, 11, 13-15, 19]

Figure 3. Hypothetical pathways which explore the relationship between DM, hyperglycemia, and ICH. Uncontrolled DM contributes to a persistent hyperglycemic state. Hemorrhagic stroke also contributes to a hyperglycemic state. DM is also a major risk factor for hypertension. Uncontrolled hypertension can be equated to an acute force like that of TBI leading to cerebral insult. Hyperglycemia leads to increased osmolality which in turn up-regulates and activates plasma kallikrein.[20] Hyperglycemia also triggers SIRS which up-regulates TNF-α and, elevated TNF-α also contributes positively to the hyperglycemic state. Additionally, infection also has a positive feedback on the cytokine TNF-α.[4, 14]



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Experience

What Was the Name of That Drug? How Medical Students can Make the Most Out of Their Education

Aryan Riahi,[1] David Jung.[1]

The Experience

Information overload

As lifelong scholars, we are committed to refining our medical acumen. This is not an easy task, as medical students may be intimidated by the sheer wealth of information and the constant updates. In the beginning of our medical journey, we were also overwhelmed as learning felt like attempting to drink from fire hydrants.

Nevertheless, medical school offered learning strategies we had not experienced before, and we were encouraged to take advantage of them to maximize our learning. In hopes of sharing some of our experiences, here is a snapshot of what we found to be effective.

Case-based learning: taking an active approach to learning

In medical school, we continued to have traditional lectures similarly to our studies prior to medicine. However, they were now accompanied by a novelty called case-based learning (CBL) sessions. During CBL, a small group of students is presented with a weekly hypothesized patient case. The case aligns with lecture materials, allowing students to apply their knowledge in theoretical clinical environments. Discussions include formulating differential diagnoses, ordering investigations, and management plans once a working diagnosis was established. Facilitators are also present and guide students through self-directed clinical decision instead of serving the traditional instructional roles.

Compared to the more passive-styled learning in lectures, CBL takes an active approach requiring students to think critically. These team-based sessions began in the 1960s at McMaster University in Canada.[1] By deliberately providing students with vague patient presentations, CBL is designed to make students struggle and ponder. Oftentimes, patients would initially have nonspecific clinical presentations such as fatigue. We were forced to keep our differential diagnosis very broad and systemically rule out conditions as more information became available. This was repeated multiple times in CBL, each with a different patient. Looking back, the repetition allowed us to ingrain a systematic method in approaching patient presentations. These team-based sessions also exposed us to the collaborative working environments of healthcare institutions.

Furthermore, group learning also allows learners to identify inconsistencies in their knowledge.[2] There were times in which materials we thought we had mastered were in fact, unmastered. For instance, we would realize our gaps in the pathophysiology of diabetic ketoacidosis while attempting to explain to classmates. These gaps had been previously overlooked and prompted us to reinforce our knowledge.

It is a well-known fact that active learning produces better outcomes. Likewise, team-based learning experiences like CBL are associated with improved short- and long-term outcomes, as measured by examination results.[3] For some, CBL may require more preparation, and "risk-taking" moments, in which we present our best evidence-based opinions to our peers for discussion. Still, these are paid off by better retaining and higher learning outcomes. With CBL and similar team-based approaches already present in many schools, these sessions should be trumpeted more and not overlooked by students as opportunities to consolidate lecture materials.

Retaining information

Analogous to the benefits of active learning, active recalling is superior to its passive counterpart. Active methods of recalling information help consolidate the information much more effectively than passively restudying facts. For example, the ability to consciously recall the adverse effects of statins without the use of cues will help consolidate the list far better than passively re-reading them. Active recall would allow students to better manage the large volume of information and also retain it for long-term use in their career.

One popular form of active recall is the testing effect. While many students view tests solely as assessments, they are also an excellent way of retaining knowledge. Similarly, to having a discussion, testing ourselves allows for the identification of gaps in our knowledge. Oftentimes, it is too easy to convince ourselves that we have retained the information after passively reading the material. It may also seem intimidating to test our knowledge, in fear of recognizing our own gaps and having to return to the material. However, these gaps can only be recognized when we search for them by testing ourselves. Leaving them unattended could not only lead to lowered academic performance in the short-term but also compromised patient care in the long-term. A randomized controlled trial examined the effects of testing on the learning of residents.[4] All residents took final examinations, but certain individuals were randomized to intermittent testing while others passively reviewed the study material. At the end, groups that exposed themselves to intermittent tests had better learning outcomes. The dual role of testing can be explored by medical students for better retention and studying efficiency.

Learn for the patients

As lifelong learners, it is crucial to recognize that the objective of learning information lies beyond the successful completion of an upcoming exam. Learn for the long term. Learn for the patients.

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