Title: Windswept Deformity from pseudogout. A Diagnostic Challenge of an extreme presentation, a case report.

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Authors Contribution Statement:

Contributor Role	Role Definition	Authors 1	2	3	4	5	6
Conceptualization	Ideas; formulation or evolution of overarching research goals and aims.	X					
Data Curation	Management activities to annotate (produce metadata), scrub data, and maintain research data (including software code, where it is necessary for interpreting the data itself) for initial use and later reuse.	X					
Formal Analysis	Application of statistical, mathematical, computational, or other formal techniques to analyze or synthesize study data.	X					
Funding Acquisition	Acquisition of the financial support for the project leading to this publication.	X					
Investigation	Conducting a research and investigation process, specifically performing the experiments, or data/evidence collection.	X					
Methodology	Development or design of methodology; creation of models	X	X				

Project Administration	Management and coordination responsibility for the research activity planning and execution.	X	X
Resources	Provision of study materials, reagents, materials, patients, laboratory samples, animals, instrumentation, computing resources, or other analysis tools.	X	
Software	Programming, software development; designing computer programs; implementation of the computer code and supporting algorithms; testing of existing code components.	X	X
Supervision	Oversight and leadership responsibility for the research activity planning and execution, including mentorship external to the core team.	X	
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Visualization	Preparation, creation, and/or presentation of the published work, specifically visualization/data presentation.	X	
Writing – Original Draft Preparation	Creation and/or presentation of the published work, specifically writing the initial draft (including substantive translation).	X	X
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Highlights: This case highlights an extreme presentation in pseudogout.

- Severely destroyed knee joints can be caused by pseudogout.
- Policies in place are still not covering the extremely poor population in Malaysia.
- Transitioning countries to high-income status should reform their policies to ensure adequate health coverage.
- Companies making implants have a big role in deciding the cost of implants.

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Discussion Points:

1. A heavily destroyed joint, with radiographic evidence of osteoarthritis and chondrocalcinosis should always raise the suspicion of pseudogout. This should then be confirmed with joint aspiration and examined under compensated polarizing light microscopy.
2. In West Malaysia where access to safe and affordable surgery is readily available, it is relative to those living below the poverty line. These populations are unable to receive the care needed due to their financial status and capacity.
3. Long term policies such as access to follow-up should also be in place to provide holistic care for this population in Malaysia.

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ABSTRACT.

Background:

Twenty percent of the population globally is affected by musculoskeletal conditions. These conditions significantly impair mobility and dexterity. Pseudogout is similarly a debilitating disease that significantly increases morbidity and the disability adjusted life years. We report a case of pseudogout in its advanced stage, causing total joint destruction of the knees and shoulders, which manifested and presented as a windswept deformity.

The Case:

Our patient is a 69 year old man who complained of bilateral knee pain, shoulder pain during active flexion and an obvious knee deformity. His familial history was not significant, and there was no history of injuries, infection or congenital diseases. His knees were severely deformed, with extremely laxed collateral ligaments. Both of his shoulders had a limited range of movement with coarse crepitation on passive movement. X-ray of his knees showed a completely destroyed joint, reduced joint space, subchondral cysts and chondrocalcinosis. X-ray of his shoulder joint showed a subluxated joint, subchondral cyst and subchondral sclerosis. His joint aspirate had positive rhomboid crystals on the birefringence test, consistent with pseudogout. Joint replacement surgery is the definitive management, but the patient and caretaker were not able to afford the implants.

Conclusion:

We discussed the diagnosis of pseudogout in this patient and how the policies in place do not provide adequate coverage for these populations. This marginalizes those who need surgery and limits their access to affordable surgical care when needed.

Key Words: Pseudogout, Calcium Pyrophosphate Deposition Disease, Global Surgery

INTRODUCTION.

One in five persons globally is affected by musculoskeletal conditions.[1] These conditions significantly impair mobility and dexterity, causing early retirement and reducing the ability to participate in social activities. Pseudogout equally affects patients' quality of life. Approximately 20% of patients with osteoarthritis for total knee replacement have calcium pyrophosphate deposition (CPPD) crystals in their joints.[2] Although CPPD continues to be underdiagnosed, it is not difficult to confirm the diagnosis. Polarizing light microscopy with a red filter can accurately diagnose CPPD crystals. The hallmark of the crystal is the classical rhomboid crystal and its relation to the light source. The crystal turns blue when the light axis is parallel and turns yellow when it is perpendicular under microscopy. This contrasts with monosodium urate crystals which turns blue perpendicularly and yellow parallel to the crystal axis in relation to the light source.[3,4] The morphology of monosodium urate crystals appears as a needle like rod shape crystals.[4] We present a case of CPPD disease at its extreme stage of pathogenesis and discussed the diagnostic and social challenges in our case.

THE CASE.

A 69 year old Chinese ethnic man with underlying hypertension, presented with bilateral knee pain and windswept deformity, associated with right shoulder pain [Figure 1]. He had no history of fever, numbness, leg weakness, trauma or congenital anomaly.

The knee pain started 3 years prior to this admission and his windswept deformity progressively worsened over the past 1 year. The bilateral knee pain was sharp in nature, did not radiate and was exacerbated with walking and weightbearing. He scored his pain at 5/10. He was able to ambulate with a walking stick. His shoulder pain progressed over 8 years, and was exacerbated with movement. He was primarily concerned with the prolonged nature of the pain. He was a construction worker before the deformity severely deformed his joints.

Upon examination, there was a large boggy effusion of the shoulder joints bilaterally. The left shoulder had a reduced range of movements with gross crepitations during passive movement. Active abduction was up to 100^0 and frontal flexion up to 90^0. The right shoulder had a significantly reduced range of movements. Both active abduction and frontal flexion were up to 30^0. The pain in both shoulders was localized with a pain scale of 5/10. Biceps bilaterally presented with Popeye deformity [Figure 2]. Rotator cuff tests were abandoned due to the pain they caused.

There was an obvious windswept deformity of the knee towards the left while bearing weight. Knee flexion and extension had a full range of motion on active and passive movement. Gross crepitus was felt with passive movement bilaterally. The left knee was able to passively angle medially up to 50^0 and the right knee to passively angle laterally up to 70^0 according to his deformity as shown [Figure 1]. The knees bilaterally were tender upon performing the stress test with a pain scale of 5/10. McMurray's test bilaterally was inconclusive with the severely deformed anatomical structures.

Investigation

His full blood count, renal profile, electrolytes, liver function, coagulation profile, fasting lipid profile, cortisol and thyroid function tests were within normal ranges.

The radiographs of his shoulders and knees are described [Figures 3 and 4].

Management

This patient was initially planned for bilateral total knee replacement as the definitive treatment, but the patient decided to opt out as this is an expensive procedure. Not only was he within the low socioeconomic group, but the social welfare department was unable to fund 2 knee implants. Arthrocentesis was done over both of his shoulders and both knees for symptomatic relief. We managed to aspirate a total of 200ccs of synovial fluid from all 4 joints and immediate pain relief was reported from the patient. The fluid was immediately examined under compensated polarizing light microscopy with a red filter [Figure 5]. The diagnosis of pseudogout was made with the presence of rhomboid crystals with classical birefringence. He was discharged with Tablet

Prednisolone 20mg for once a day for 14 days and Tablet Colchicine 0.5mg for once a day for 14 days. The pain was significantly reduced and the patient was satisfied with the treatment.

The patient was followed up in the rheumatology clinic. Physical examination had similar findings from his initial presentation such as the windswept deformity, joint crepitations and laxed joints. However, his pain was significantly reduced. He has no further complaints and was happy with his current medical management plan. He was discharged with the same prescriptions of Prednisolone and Colchicine. However, he expressed his hopes for the definitive surgery and regaining basic walking function in the future if fundings are available.

DISCUSSION.

Pseudogout is caused by the deposition of CPPD which is predominantly found in the elderly over 60 years of age. Clinically the most commonly affected joints are the knees, followed by the wrist, shoulder, ankle, elbows, and hands.[4] These crystal formations are found in the extracellular matrix of the midzone chondrocytes, usually found on the surface. Multiple factors such as excessive cartilage pyrophosphate production are thought to then cause CPPD and the inhibition of basic calcium phosphate mineralization. Animal studies showed the overactivity of ectonucleotide pyrophosphatase/phosphodiesterase-1(ENPP1) catalyzes pyrophosphate production via hydrolysis of extracellular adenosine triphosphates.[12] Deficiencies of ENPP1 in mice showed increased pyrophosphate production and inhibition of basic calcium phosphate mineral formation.[13] In vitro studies have also shown transforming growth factor b-1 can overtly stimulate chondrocyte pyrophosphate production. Other factors such as increased osteopontin and cross-linking of extracellular matrix proteins with transglutaminase may increase CPPD formation.[12] Genetic factors such as the ANK gene coding for a protein ANKH, produce a transmembrane protein that facilitates the transport of pyrophosphates across cell membranes into the extracellular matrix. Mutations in this gene promote excessive pyrophosphates into chondrocytes and promote CPPD. These crystal deposits have also been found to induce the promotion of osteoclastogenesis, a cause of crystal induced joint damage.[13] Although the exact mechanism of crystal formation is still not known, the saturation of CPPD in cartilages as the cause is generally accepted. The inflammatory responses are similar to Gouty arthritis in terms of inflammatory markers and the activation of synovial mononuclear phagocytes and neutrophils. CPPD crystals as a destructive amplifying factor are likely as shown in our case. This destructive property was also evident in our patient as he presented with bilateral popeye deformity [Figure 2]. This was probably due to the destruction of his shoulder joints [Figure 3], extending to the tendons of the long head of the brachialis muscle. CPPD is usually not seen in the early stage of osteoarthritis, however, it is associated with severe progression of osteoarthritis.[13]

CPPD is commonly asymptomatic which can be observed via radiographic changes as demonstrated in our patient.[2, 3, 13] The presentation varies between acute cases and chronic cases. An acute case of pseudogout presents commonly with monoarthritis affecting the large joints, such as knees and wrists, with severe inflammation and painful swelling of the joints.[4, 11] Unlike gout, it is usually self-limiting and resolves within 10 days. Chronic cases of pseudogout clinically resemble osteoarthritis, as presented in our case, and can present with a more severe pain than similarly staged osteoarthritis.[11, 13] CPPD imitates the characteristics of gouty arthritis which increases the difficulty for clinicians to diagnose this condition. For this reason, the birefringence test of the joint aspirate examined under compensated polarizing light microscopy with a red filter to observe the rhomboid-shaped crystals is pathognomic of CPPD.[11]

This case had a particular diagnostic challenge presenting at a late stage of the disease progression. To the author's knowledge, CPPD disease causing windswept deformity has not been described in the literature. His physical examination was jarring causing additional constraints to reaching a definitive diagnosis which delayed his management plan.

Operative management of total knee replacement was considered the definitive management for this patient, however, there is no available public or private funding for this patient. Joint replacement is expensive that can risk financial catastrophe and further limit its application for the extreme poor.[6] The patient and his caretaker were unable to afford the implant as they live below the poverty line. In Malaysia, a knee replacement surgery costs approximately USD 12,000.[9] Obtaining facilities, welfare, and health care of Malaysia guidelines listed some medical conditions eligible to request financial aid. However, it can only be applied with a minimum amount of upfront payment to buy the implant.[10] This large cost for these procedures pushes the population in the lower socioeconomic status to opt out.

This family is categorized into the vulnerable poor and the aspirational poor whose families' monthly income is USD 605.91 and below.[7] This system is a great advantage for middle to upper-income earners, yet it is a conditional privilege. A new system is needed to address the lack of access for the vulnerable poor. To conclude, CPPD disease is a debilitating disease that can destroy large joints and in rare cases cause significant morbidity and deformity. With the ongoing pandemic, there is a strong need to restructure reasonable financial aid for surgical care to avert progressive disability and lifelong disability among this vulnerable group. It is integral for citizens to have complete healthcare coverage including surgical care, despite their socioeconomic status.

Potential differentials

1. Osteoarthritis
2. Milwaukee Shoulder syndrome (hemorrhagic shoulder effusions)
3. Gonarthrosis

Learning points

1. Policies should allow access to surgical care for definitive management to reduce disabilities and allow the elderly population below the poverty line to have that access.
2. An invasive procedure should be employed to further examine the underlying pathology of indeterminate joint disease. In this case, arthrocentesis was pivotal in the diagnosis and management plan.
3. Diagnosis of Calcium phosphate deposits should always be a differential in a destroyed joint.

REFERENCES.

1. World Health Organization. Musculoskeletal conditions. Available from: https://www.who.int/news-room/fact-sheets/detail/musculoskeletal-conditions. Last updated Feb 8 2021; cited Apr 30 2022.

2. Derfus BA, Kurian JB, Butler JJ, Daft LJ, Carrera GF, Ryan LM, et al. The high prevalence of pathologic calcium crystals in pre-operative knees. The J Rheumatol. 2002;29(3):570-4.

3. Rosenthal AK, Ryan LM. Calcium Pyrophosphate Deposition Disease. N Engl J Med. 2016;374(26):2575–84.

4. Loscalzo, J., Fauci, A., Kasper, D., Hauser, S., Longo, D. and Jameson, J., n.d. *Harrison's principles of internal medicine*. 20th ed. McGraw Hill.

5. Christian L, Horst S, Lena P, Uta L, Michael U and Raoul B. Distinguishing gouty arthritis from calcium pyrophosphate disease and other arthritides. The J Rheumatol. 2015;42(3):513-20.

6. Michael B, Tom B and JE Fitzgerald. What is “global surgery”? Defining the multidisciplinary interface between surgery, anaesthesia and public health. BMJ Global Health. 2019;4:e001808.

7. Shamsul AB, Sun MML, Eric SA, Thick KP, Sharifah ZSH, Korakit C, *etal.* Inclusive development for urban poor & bottom 40% communities in Malaysia. Available from: https://www.ohchr.org/Documents/Issues/Poverty/VisitsContributions/Malaysia/Malaysian_CSO_SDG_Alliance_Annex2.pdf. Last updated 2016; cited 2022 Mar 30.

8. Kumar J and Hussian K. Factors affecting medical tourism destination selection: A Malaysian perspective. International Interdisciplinary Business-Economics Advancement Journal. 2016;1(1):1-10.

9. Kementerian Kesihatan. Kerjasama Jabatan Kerja Sosial Perubatan Dengan Agensi Bantuan. Available from: http://www.myhealth.gov.my/jaringan-kerjasama-antara-jabatan-kerja-sosial-perubatan-dengan-agensi-agensi-pemberi-bantuan/ Last updated Sept 11 2017; cited Apr 30 2022.

10. Sidari A and Hill E. Diagnosis and Treatment of Gout and Pseudogout for Everyday Practice. Primary Care: Clinics in Office Practice. 2018;45(2):213–36.

11. MacMullan P and McCarthy G. Treatment and management of pseudogout: insights for the clinician. Therapeutic Advances in Musculoskeletal Disease. 2011;4(2):121–31.

12. Rosenthal AK, Gohr CM, Uzuki M, Masuda I. Osteopontin promotes pathologic mineralization in articular cartilage. Matrix Biol 2007; 26:96.

13. Rosenthal AK(2022). Pathogenesis and etiology of calcium pyrophosphate crystal deposition (CPPD) disease. In: UpToDate, Nicola D and Paul LR(Ed). Retrieved June 26, 2022, from https://www.uptodate.com/contents/pathogenesis-and-etiology-of-calcium-pyrophosphate-crystal-deposition-cppd-disease#H27474517

FIGURES

Figure 1. Knee Examination Bilaterally while Bearing Weight. Windswept Deformity towards the left of the patient.

Figure 2. Left and Right Popeye Deformity.

Figure 3.

Bilateral Shoulder Xray and Bilateral Knee Xray (non weight bearing)

Left shoulder subluxed, dislocated with a presence of subchondral cyst and subchondral sclerosis.

Right shoulder shows subchondral sclerosis and subchondral cysts.

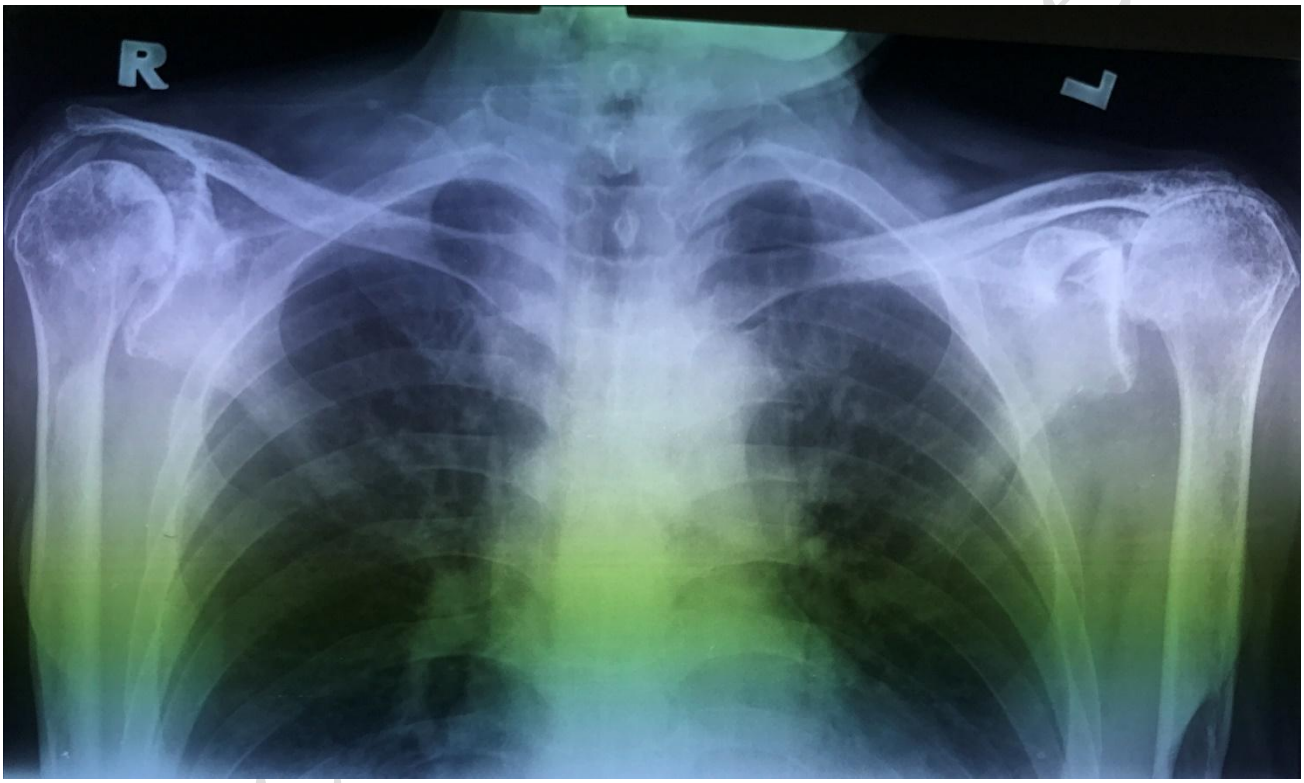
Bilateral knee Xray shows a completely destroyed knee joint with absent anatomical landmarks of the knee joint.

Black star – destroyed tibia plateau and reduce joint space.

Red arrows – variable osteophyte formation.

Black arrow – Chondrocalcinosis.

White arrow head and white arrows – Subchondral cyst



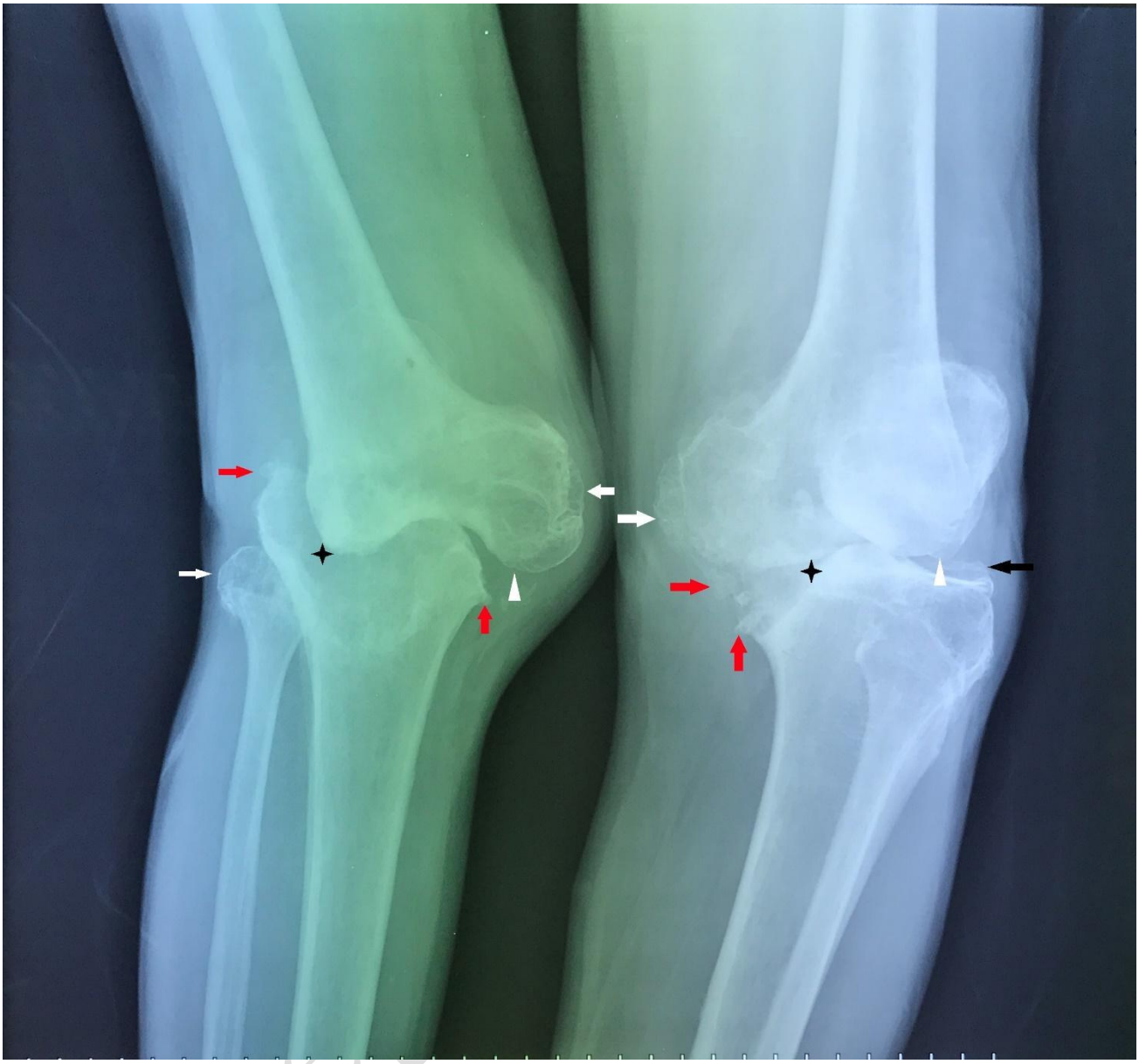
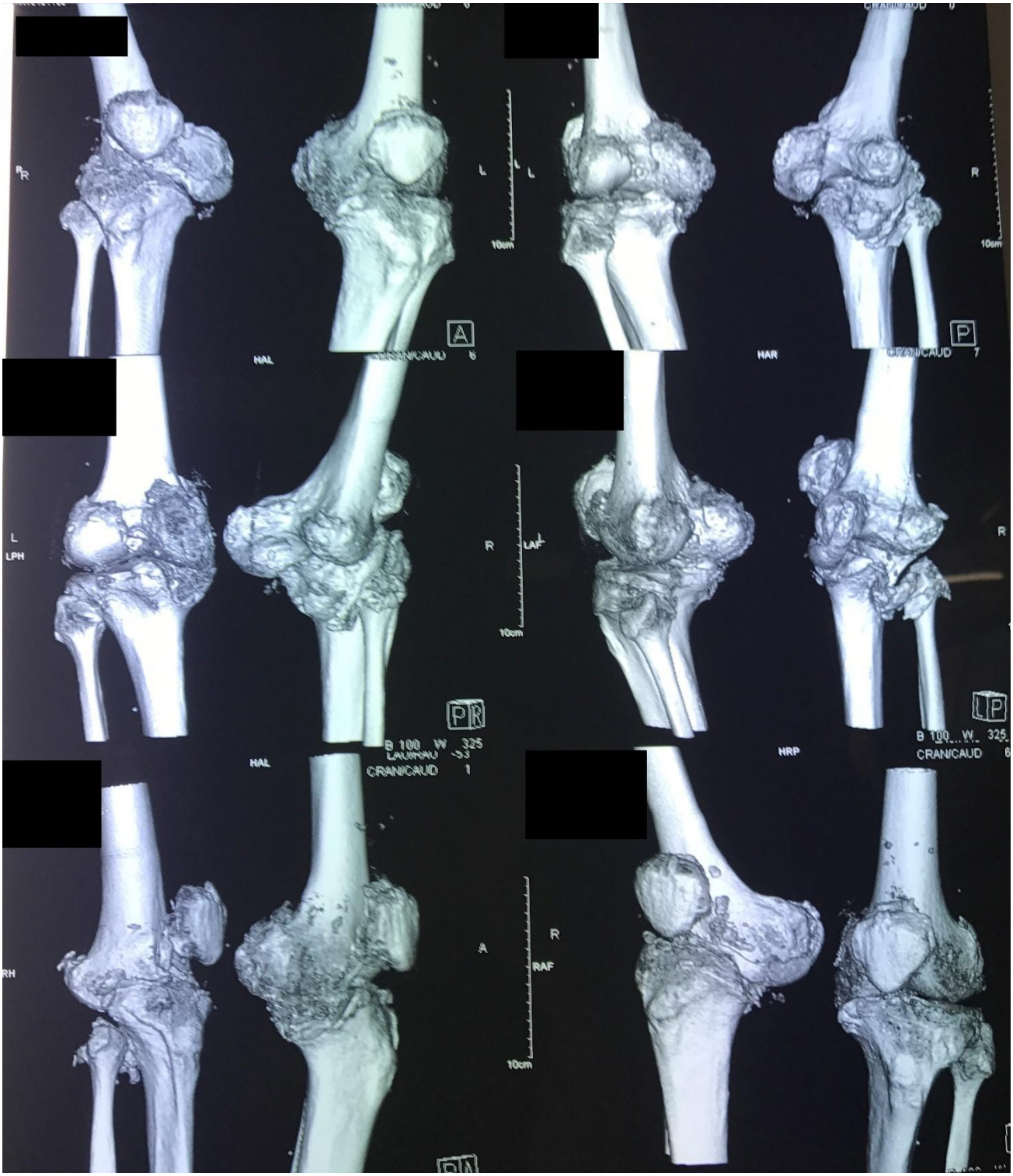


Figure 4. 3D Reconstruction CT Scan of Bilateral Knee

Findings from 3D reconstruction of bilateral knee joint suggest similar findings as the bilateral knee Xray findings. This CT scan demonstrates a completely destroyed knee joint with reduced joint space, variable osteophytes formation and subchondral cyst formation.



318 **Figure 5**. The Birefringence test of the synovial aspirate was examined under compensated polarizing light
319 microscopy with a red filter. Examination shows a rhomboid crystal.

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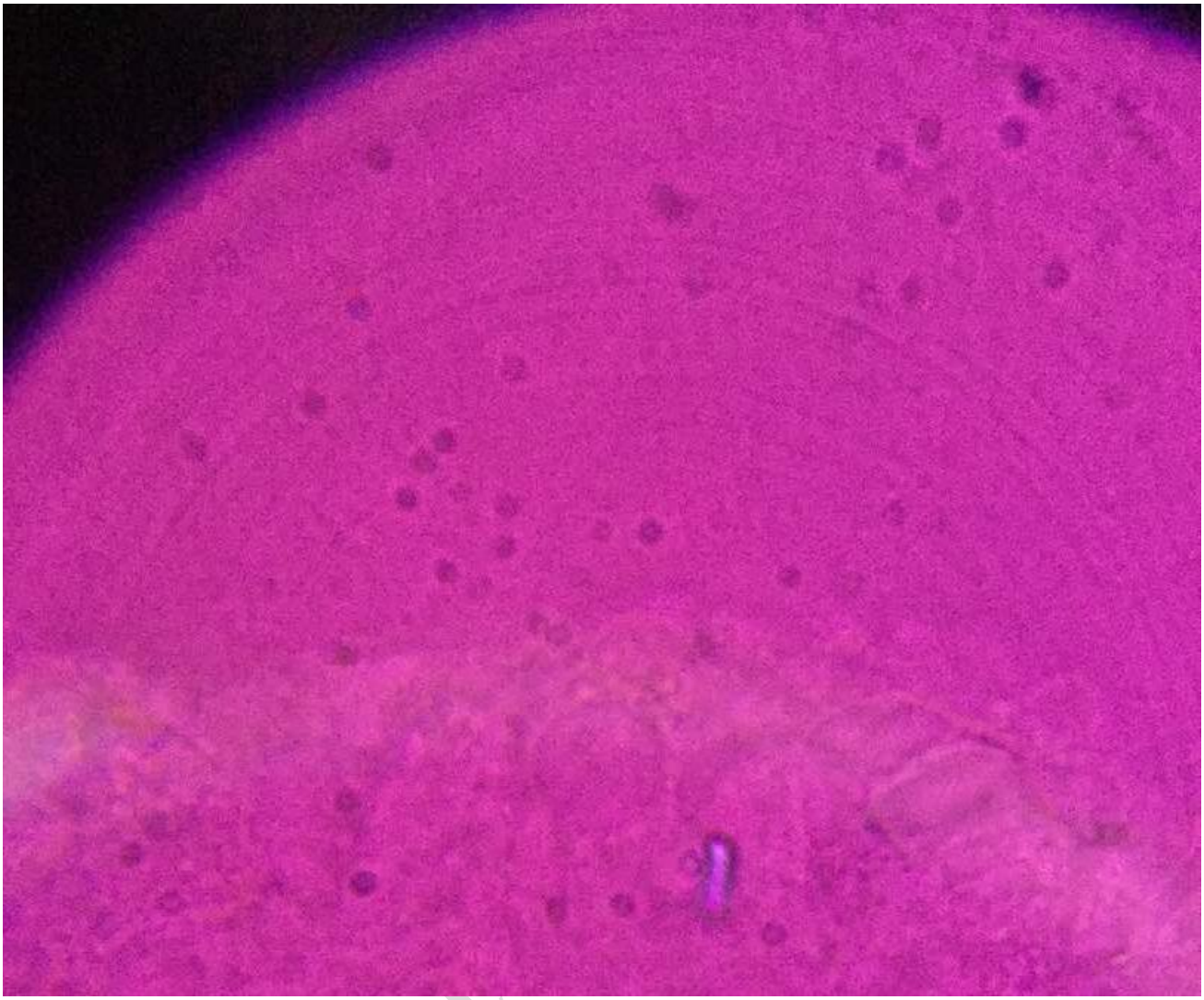

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