01. Navigating Diagnostic Uncertainty and Therapeutic Complexity in IgG4-Related Sclerosing Cholangitis: A Case Report

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Background: IgG4-related sclerosing cholangitis (IgG4-SC) is a fibroinflammatory condition that frequently mimics pancreatobiliary malignancies, contributing to its significant underdiagnosis. Critical knowledge gaps persist regarding safe diagnostic pathways when tissue biopsy is contraindicated, pharmacogenetic risk stratification for thiopurine therapy, and evidence-based rituximab maintenance strategies for high-risk phenotypes. This case addresses these gaps by validating multimodal diagnosis using the 2020 Revised Comprehensive Diagnostic (RCD) criteria in an anticoagulated patient, demonstrating the value of proactive TPMT metabolite monitoring, and providing preliminary evidence that intensified rituximab maintenance may reduce relapse in high-risk IgG4-SC.

Case Description: A 72-year-old male with a mechanical aortic valve requiring lifelong anticoagulation presented with obstructive jaundice and a pancreatic uncinate mass demonstrating superior mesenteric artery encasement, initially raising high suspicion for unresectable pancreatic adenocarcinoma. EUS-FNA was non-diagnostic due to intraprocedural bleeding despite warfarin bridging. Biliary brushings confirmed inflammatory changes without atypia, and CA19-9 was normal. Serum IgG4 was markedly elevated at 8.5 g/L (6.3× the upper limit of normal), carrying 100% specificity for IgG4-SC. Complete radiological resolution of the uncinate mass and pancreatic inflammation following corticosteroid initiation confirmed a diagnosis of Type 4 IgG4-SC with associated Type 1 autoimmune pancreatitis, per RCD criteria. Clinical relapse occurred during the corticosteroid taper, requiring repeat biliary stenting and re-induction therapy. Azathioprine was introduced as a steroid-sparing agent; however, TPMT metabolite monitoring revealed unfavorable shunting toward toxic 6-thioguanine nucleotide accumulation, prompting transition to rituximab (1000 mg IV, days 1 and 15). Following a 15-day delay in a scheduled maintenance infusion, the patient presented with acute cholangitis. Given his high-risk profile (Type 4 disease, baseline IgG4 >270 mg/dL), maintenance was intensified to five-month cycles. He remains in remission under close surveillance with longitudinal B-cell subset monitoring.

Conclusion: This case demonstrates that definitive IgG4-SC diagnosis can be safely established through convergent multimodal evidence when tissue biopsy is contraindicated, validating the real-world utility of the RCD framework. Proactive TPMT metabolite monitoring prevented life-threatening myelotoxicity and guided personalized immunosuppression. Most significantly, this case provides preliminary evidence that high-risk anatomical phenotypes warrant proactive rituximab maintenance intensification rather than reactive management, to preserve biliary integrity and prevent irreversible fibroinflammatory damage.

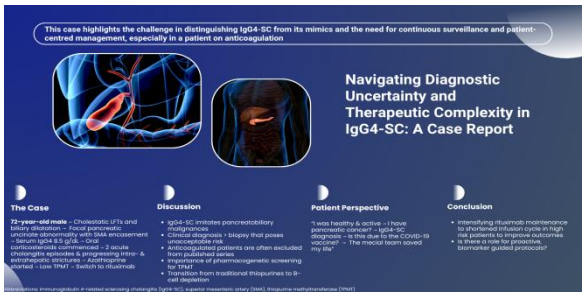

Figure 1: Graphical abstract summarizing key points of this case report.

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