CASE REPORT

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Sequential Onset of Inflammatory Myositis Following Autoimmune Pancreatitis in IgG4-Related Disease

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Abstract

Immunoglobulin G4-related disease (IgG4-RD) is a systemic fibro-inflammatory disorder that can involve multiple organs, most commonly the pancreas, biliary tree, and salivary glands. Extra-pancreatic manifestations may precede, coexist, or follow autoimmune pancreatitis (AIP), and skeletal muscle involvement is exceedingly rare. We present the case of an 80-year-old female with bronchial asthma, who was diagnosed with type 1 AIP based on clinical, biochemical, imaging, and histopathological features. Two weeks following steroid initiation, she developed proximal muscle weakness and elevated muscle enzymes, consistent with inflammatory myositis. Notably, myositis occurred despite ongoing corticosteroid therapy. This case highlights the importance of recognizing unusual organ involvement in IgG4-RD, as it may mimic or overlap with other autoimmune conditions. To our knowledge, IgG4-related myositis as a sequential manifestation after AIP has rarely been reported in literature.

Introduction

IgG4-related disease (IgG4-RD) is a chronic, immune-mediated condition characterised by tumefactive lesions, storiform fibrosis, obliterative phlebitis, and lymphoplasmacytic infiltration rich in IgG4-positive plasma cells and mimics many inflammatory and malignant conditions[1]. First recognised in the context of autoimmune pancreatitis (AIP), it is now understood as a multisystem disorder affecting the pancreas, hepatobiliary tract, salivary glands, retroperitoneum, kidneys, lungs, and rarely, skeletal muscle[2].

Autoimmune pancreatitis is the prototypical manifestation of IgG4-RD, with diagnostic features including characteristic imaging (diffuse or focal pancreatic enlargement with ductal narrowing), elevated serum IgG4 levels, histology, and response to corticosteroids[3,4]. While extrapancreatic involvement is common, muscular manifestations are extremely rare. Only a handful of case reports have described IgG4-related myositis[5,6].

We report an unusual case of an elderly woman, with biopsy-proven AIP, who subsequently developed inflammatory myositis despite corticosteroid therapy, emphasizing the diagnostic and therapeutic challenges in managing multi-organ IgG4-RD.

Case Presentation

An 80-year-old woman, known case of bronchial asthma, presented in July 2025 with complaints of dull aching epigastric pain, radiating to the back, without any aggravating factors or relieving factors and vomiting for 3 days. She also developed progressive jaundice. There was no history of fever, hematemesis, or melena. On examination, she was icteric, with epigastric tenderness but no palpable organomegaly.

Baseline investigations revealed predominantly conjugated hyperbilirubinaemia with mild elevation of transaminases and alkaline phosphatase, along with baseline renal dysfunction. Serial trends are shown in Table I.

Fine Needle Aspiration biopsy of a pancreatic mass revealed dense lymphoplasmacytic infiltrate with storiform fibrosis and abundant IgG4-positive plasma cells, consistent with IgG4-related autoimmune pancreatitis (type 1 AIP). ERCP was performed and biliary stent was placed to relieve the cholestasis.

The pattern was consistent with predominantly conjugated hyperbilirubinaemia, mild transaminitis with ALP elevation, biochemical features of mixed hepatocellular – cholestatic injury eventually improved by day 4 after ERCP. She was started on oral corticosteroids (prednisolone 40 mg/day) and discharged home.

Second episode

Two weeks later, she re-presented with acute-onset severe myalgia, initially in proximal lower limbs, rapidly progressing to involve hip girdle, trunk, and neck flexors, causing difficulty rising from sitting, squatting, and ambulating

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without support. There was no diplopia, dysphagia, respiratory difficulty, skin rash, sensory loss, or bowel/bladder involvement. On clinical examination, she had Medical Research Council (MRC) grade 2/5 proximal muscle power with preserved distal strength and intact reflexes and sensation.

Investigations revealed marked elevation of serum creatine phosphokinase (>10,000 U/L) and leukocytosis, while repeat lever function tests showed worsening transaminases (Table II). Myositis panel was positive for Mi-2β antibody, while viral serology and thyroid profile were normal. MRI thigh was not performed due to logistic limitations. Muscle biopsy demonstrated inflammatory infiltrates without IgG4-positive plasma cells, raising the possibility of autoimmune myositis coexisting with IgG4-RD rather than direct IgG4-mediated myopathy.

Given the severity of muscle involvement and unsatisfactory steroid response, she was started on pulse intravenous methylprednisolone 1 g/day for 7 days, followed by oral prednisolone 50 mg/day and mycophenolate mofetil as a steroid-sparing agent. Over the next two weeks, pain resolved, CK levels reduced, and she regained ambulatory ability with minimal support. She remained clinically stable at follow-up, with ongoing physiotherapy and slow steroid taper.

Table I: Laboratory parameters during first episode (July 2025).

Date	Hb/TLC/Plt (×10y /L)	Na/K (mmol/L)	TB/DB (mg/dL)	SGOT/SGPT (U/L)	ALP (U/L)	TP/Alb/Glob/A:G (g/dL)	Creatinine (mg/dL)	PT INR	Comment
07/07/25	11.8 / 7780 / 3.5	138/4.0	6.19 / 4.95	128 / 96	242	8.2 / 3.1 / 5.1 / 0.6	2.3	1.5	Predominantly conjugated hyperbilirubinaemia, mixed hepatocellular – cholestatic picture, mild coagulopathy
08/07/25	11.3 / 4990 / 3.5	–	4.87 / 3.91	210 / 162	217	6.8 / 2.8 / 4 / 0.70	2.24	–	Bilirubin improving, but worsening transaminitis, possible inflammatory flare
09/07/25	11 / 11,990 / 4.79	–	4.97 / 4.04	223 / 182	237	6.6 / 3 / 3.6 / 0.83	–	–	Bilirubin plateaued, persistent hepatocellular injury, leukocytosis suggestive of secondary inflammation
11/07/25	10.4 / 8170 / 3.2	–	4.01 / 2.95	94 / 39	242	6 / 2.5 / 3.5 / 0.71	2.13	–	Improvement in bilirubin and creatinine

Table II: Laboratory parameters during second episode (July-August 2025).

Date	Hb/TLC/Plt (×10y /L)	Na/K (mmol/L)	TB/DB (mg/dL)	SGOT/SGPT (U/L)	ALP (U/L)	TP/Alb/Glob/A:G (g/dL)	Creatinine (mg/dL)	PT INR	Comment
24/07/25	11.9 / 12160 / 1.74	134/3.5	2.32 / 1.55	348 / 336	311	5.3 / 2.6 / 2.7 / 0.9	0.7	1.13	Raised transaminases and Alkaline phosphatase correlates with Inflammatory Myositis
06/08/25	12.4 / 13840 / 4.5	137/3.2	2.1 / 1.14	71 / 158	146	5.1 / 2.6 / 2.5 / 1.1	0.7	–	Investigations post pulse steroid therapy showing reduction in transaminases and alkaline phosphatase

Discussion

IgG4-related disease (IgG4-RD) is a fibroinflammatory disorder that can involve virtually any organ, with autoimmune pancreatitis (AIP) type 1 being its pancreatic manifestation. Skeletal muscle involvement, however, remains exceedingly rare, with only a handful of cases reported in the literature. In our patient, myositis developed within two weeks of an episode of IgG4-related pancreatitis, despite corticosteroid therapy, making the chronology unusual and noteworthy.

Hart *et al* (2015) reviewed the systemic spectrum of IgG4-RD and emphasized pancreaticobiliary disease, but did not identify skeletal muscle as a frequent site of involvement[3]. Similarly, the International Consensus Diagnostic Criteria (ICDC) for AIP established by Shimosegawa *et al* (2011) do not list skeletal muscle among common extrapancreatic sites[4]. Thus, our case expands the known spectrum of IgG4-RD.

Inoue *et al* (2015), in a cohort of 235 patients with IgG4-RD, found salivary glands, kidneys, lungs, and retroperitoneum to be commonly affected, but no cases of myositis were described[5]. This discrepancy underlines the rarity of skeletal muscle involvement and suggests either under-recognition or misclassification of myositis in IgG4-RD patients.

Casteleyn *et al* (2019) reported one of the few detailed descriptions of IgG4-related myositis, with biopsy-proven IgG4-positive plasma cell infiltration of skeletal muscle[6]. Unlike their case, our patient's muscle biopsy did not demonstrate IgG4-positive cells.

The possible explanation of the absence of IgG4-positive cells on biopsy in our case may be patchy disease involvement, as IgG4-related disease often shows focal lesions leading to potential sampling error; by the prior use of corticosteroids for pancreatitis, which could have suppressed IgG4-positive cell infiltration at the time of muscle biopsy; or by an immune overlap, wherein the

presence of anti-mi-2β antibody suggests that autoimmune myositis in this patient may represent a secondary autoimmune process ("second hit") triggered in the setting of IgG4-related disease rather than direct IgG4-mediated involvement.

An additional point of interest is that our patient developed myositis despite being on corticosteroids. Steroid-refractory or steroid-breakthrough manifestations in IgG4-RD are unusual but have been described. Inoue *et al* also reported that 30 - 40% of patients with IgG4-RD relapse after steroid tapering[5]. It is plausible that skeletal muscle disease may be more resistant to glucocorticoids, or that the concurrent autoimmune myositis pathway (indicated by Mi-2β positivity) required additional immunosuppression.

Finally, the age and co-morbidities of our patient (80 years and asthma) make this case distinctive, as most reported IgG4-RD series include elderly men with relatively lesser systemic involvement.

Taken together, our case illustrates the possibility of sequential organ involvement in IgG4-RD, the diagnostic challenge when biopsy is negative for IgG4-positive cells, and the potential overlap with other autoimmune myositis syndromes. It emphasizes the importance of considering IgG4-RD in atypical presentations of myositis, especially when there is a recent history of IgG4-related pancreatitis.

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