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Case Report

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Immunoglobulin G - 4(IgG4)-Related Disease: A Case of Retroperitoneal Disease with Mass Formation

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ABSTRACT

IgG4-related disease is a rare cause of retroperitoneal fibrosis with mass formation. A 46-year-old female presented with lower back pain. She had an on-and-off mild fever and constitutional symptoms with evidence of tenderness over the lower back. Investigations revealed high inflammatory markers. Magnetic resonance imaging revealed an ill-defined signal area in the left paraspinal area. Histology revealed fibromuscular tissue with scattered plasma cells showing positivity for immunoglobulin-G-4 (IgG4). The immunomorphological features are suggestive of IgG4-related-retroperitoneal fibrosis. She was commenced on glucocorticoids. It is imperative to consider unusual diagnoses such as IgG4-related disease in a patient with retroperitoneal disease with evidence of mass formation.

Keywords: Immunoglobulin G 4 (IgGG4) – related disease, retroperitoneal fibrosis, mass formation, pseudotumor

INTRODUCTION

Immunoglobulin G – 4 (IgG4) related disease is an immune-mediated fibro-inflammatory disorder. It is a recently recognized disease entity which can affect any organ [1]. It has been known to affect the salivary gland, lacrimal gland, orbital cavity, pancreas leading to pancreatitis, kidney leading to interstitial nephritis and the retroperitoneum leading to retroperitoneal fibrosis [2]. An incidence of 0.28–1.08/100 000 inhabitants/year, with a prevalence of about 1/600 000 inhabitants has been shown in a few studies conducted among the Japanese. No other studies describe the incidence of the above in different regions of the world [1]. It is characterised by the presence of a high percentage of IgG4-bearing plasma cells, abundant storiform fibrosis, dense lymphoplasmacytic infiltrate, obliterative phlebitis and tissue eosinophilia [3]. It leads to the development of sclerotic like mass lesions of varying sizes in almost any organ. Patients diagnosed with IgG4-related disease have increased levels of serum IgG4 concentration. Among the patients who are diagnosed to have IgG4-related disease about 30–50% show normal IgG4 serum levels [4]. Very few

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cases of patients with IgG4-related disease have been described in Sri Lanka [5]. We present a female patient in her forties with evidence of IgG4-related retroperitoneal disease.

CASE REPORT

A 46-year-old female fitness instructor mother of two, presented with pain over the back, buttock, and inguinal region. She had on-and-off mild fever with constitutional symptoms with loss of appetite and loss of weight of four kilogrammes throughout the one-month duration, no nausea and vomiting, arthralgia, and myalgia, generalized body aches, there was no evidence of joint swelling, headache, backache, chest pain, any other neurological, gastrointestinal, dermatological, or genitourinary symptoms. She denied a significant travel history, recent change in diet, history of contact with exotic pets or any other considerable childhood illness.

There was no critical past medical or surgical history. She was a mother of two children with a previously uncomplicated obstetric history. On examination, she was afebrile with evidence of tenderness over the lumbar, inguinal and buttock region. There were no significant findings on cardiovascular, respiratory, and neurological examination. Her haematological and biochemical investigations, imaging, and histology are shown in Table 1 and Figure 1. She was initially treated with intravenous antibiotics. Due to the hyper-endemic nature of tuberculosis in Sri Lanka, as well as psoas muscle involvement empirical therapy with anti-tuberculous therapy (ATT) was commenced. Despite the treatment, there was no improvement in the symptoms. However, a repeat lesion biopsy revealed evidence of IgG4-related retroperitoneal disease. The symptoms improved following a trial of steroids.

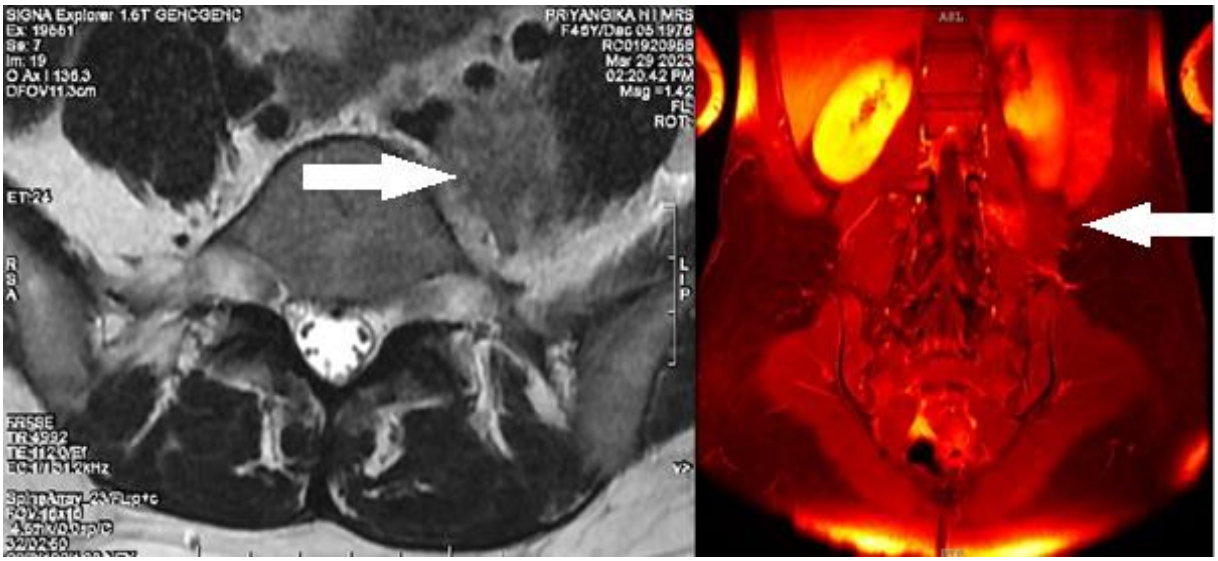

Figure 1: MRI imaging of the patient showing mass formation and muscle infiltration of the left psoas muscle as indicated by the solid arrows.

Table 1: A summary of the haematological, biochemical, and imaging findings of the patient.

Investigation	Result	Reference range
WBC	8.2 x10^9/L	4.5-11x 10^9/L
N	5.3 x10^9/L	2.0-7.5 x10^9/L
L	1.8 x10^9/L	1.5-4.5 x10^9/L
M	0.6 x10^9/L	0.2-0.8 x10^9/L
E	0.5 x10^9/L	0.04-0.4 x10^9/L
B	0.0 x10^9/L	<0.1 x10^9/L

Haemoglobin	11.4 g/dL	11-16 g/dL
Platelet	303 x 10^9/L	150-450 x10^9/L
Blood picture	Neutrophilia with marked rouleaux formation and mild normochromic normocytic anaemia	
LDH	331 IU/L	100-190 IU/L
Amylase	54 U/L	1-130 U/L
Urea	18.3 mg/dL	7-30 mg/dL
S. Cr	0.84 mg/dL	0.7-1.2 mg/dL
Na	134 mmol/L	130-145 mmol/L
K	3.8 mmol/L	3.5 – 4.5 mmol/L
Cl	116 mmol/L	98-108 mmol/L
Ca	8.4 mg/dL	8-14 mg/dL
PO43-	3.2 mmol/L	2-3.3 mmol/L
Uric acid	3 mg/dL	2.4-5.7 mg/dL
CRP	120 – 84 – 120 – 100 mg/dL	< 6 mg/dL
ESR	74 – 100 – 120 mm/Hour	<20 mm/Hour
Brucella culture and Ab	Negative	
SPEP	No monoclonal band	
USS	There is an oval-shaped hypodense lesion measuring 2.8 x 2.4cm just medial to the left common iliac vessels—no para-aortic lymphadenopathy.	
CT	The hypodense lesion was posteromedial to the left psoas muscle, impressing upon the left common iliac and external iliac vein with fat stranding to the surrounding area. Definite continuation to the spinal cord canal is not demonstrated.	
MRI	Ill-defined signal area in the left paraspinal area in contact with the L5 vertebral body posterior to the iliac vessels inflammatory lesion. There is a thick enhancing wall with a non-enhancing possible cystic area within. There was fat stranding in the surrounding area, with several lymph nodes in the adjacent para-aortic area.	
Pyogenic culture and ABST	Negative	
Fungal culture and ABST/ Stain	Negative	
TB PCR	Negative	
TB culture	Negative	
IgG4 level	0.4 g/L	0.052-1.250 g/L
Histology	All three cores of tissues are composed of fibromuscular tissue containing a dense mixed inflammatory cell infiltrate composed of neutrophils, lymphocytes, plasma cells, histiocytes and eosinophils with degranulation. The inflammatory infiltrate focally extends into the skeletal muscle. There were areas of fibrosis and small, small foci of necrosis. There is no evidence of storiform pattern of fibrosis, obliterative phlebitis, granulomata, multinucleated giant cells, atypical cells or fungal elements. Scattered plasma cells show positivity for IgG4 with a maximum count	

	of 26 per hpf. The scanty amount of tissue is negative for ALK1 immunostain. The immunomorphological features are suggestive of IgG4-related retroperitoneal fibrosis.	

DISCUSSION

IgG4-related disease is an uncommon condition in Sri Lanka, and only a handful of cases have been described among Sri Lankans. Based on our literature search, only one patient with IgG4-related retroperitoneal disease has been published in Sri Lanka, causing parametrial disease [5]. We describe a patient with IgG4-related disease, causing fibro-inflammatory retroperitoneal disease and mass formation.

There are numerous causes of retroperitoneal fibrosis, such as malignancy (sarcomas), infections (TB, fungal infections), radiation therapy for malignancies, retroperitoneal haemorrhage and surgery [6]. The other conditions which can have similar presentations include Sjögren syndrome, multicentric Castleman disease, secondary retroperitoneal fibrosis, sarcoidosis, eosinophilic granulomatosis with polyangiitis however our patient did not meet sufficient clinical or imaging classification criteria for consideration of the above diagnosis. Due to the high prevalence of tuberculosis in Sri Lanka, we need to conclusively rule out evidence of it via both microbiological and histological investigations, which we carried out and were shown to be absent as it is a well-known cause of retroperitoneal fibrosis [7, 8].

Our patient had high inflammatory markers with negative pyogenic, fungal and mycobacterial cultures, so infective causes became unlikely. Her imaging revealed evidence of an inflammatory lesion with a thick enhancing wall with a non-enhancing possible cystic area within and surrounding fat stranding showing mass/pseudotumor formation. Her IGG4 level was normal. Among the patients who are diagnosed to have IgG4-related disease about 30–50% show normal IgG4 serum levels [1, 4]. Our patient did not have the typical histological features, such as the obliterative phlebitis and storiform pattern of fibrosis [9]. However, she had lymphoplasmacytic infiltration with fibrosis extending into the skeletal muscle. Considering the 2020 revised comprehensive diagnostic classification criteria for the diagnosis of IgG4-related disease, she had the clinical, imaging and some of the histological criteria but without serological criteria, which makes it a probable diagnosis of IgG4-related disease [4, 10].This case report highlights the importance of considering unusual diagnoses such as IgG4-related disease despite their rarity if the clinical, imaging and histological criteria are met. However, it is imperative to conclusively exclude common conditions which can give rise to similar presentations.

CONCLUSIONS

Hence, in a patient with retroperitoneal pseudotumor or mass formation, it is imperative to consider unusual diagnoses such as IgG4-related disease when conventional diagnoses turn out to be negative on routine investigations.

Author declaration

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Study concept and design, acquisition of data, analysis and interpretation of data: B.S. and M.S.
Drafting of the manuscript: B.S., M.S., and U.D.
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