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Thymoma-Associated Paraneoplastic Syndromes: Concurrent Inflammatory Myopathy and Guillain–Barré Syndrome Complicated by Reverse Takotsubo Cardiomyopathy

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Case Report

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Abstract

Background:

Thymoma is associated with a range of paraneoplastic and immune-mediated conditions, most commonly myasthenia gravis and less frequently inflammatory myopathy or Guillain-Barré Syndrome (GBS). The co-occurrence of GBS and inflammatory myopathy in the setting of thymoma is extremely rare. Additionally, reverse Takotsubo cardiomyopathy, a stress-induced cardiac dysfunction, has not been reported in association with this combination.

Case presentation:

We report a 48-year-old Indian male who presented with subacute proximal limb weakness, followed by acute ascending paralysis. Investigations revealed elevated muscle enzymes, MRI features of myositis, and nerve conduction studies suggestive of the Acute Motor and Sensory Axonal Neuropathy (AMSAN) variant of GBS. Cerebrospinal Fluid (CSF) analysis showed albumin-cytologic dissociation, and muscle biopsy was suggestive of inflammatory myopathy. Imaging identified an anterior mediastinal mass, confirmed as Type A thymoma. The patient also developed chest pain, with elevated troponin levels and echocardiographic findings consistent with reverse Takotsubo cardiomyopathy, despite normal coronary angiography. He was treated with high-dose corticosteroids and plasmapheresis, followed by immunosuppressive therapy, resulting in gradual neurological improvement.

Conclusion:

This case discusses a rare combination of GBS, inflammatory myopathy, and thymoma, complicated by reverse Takotsubo cardiomyopathy in the absence of myasthenia gravis, and highlights the importance of evaluating for paraneoplastic etiologies in atypical neuromuscular presentations.

BACKGROUND

Inflammatory myopathies are a heterogeneous group of chronic autoimmune disorders, affecting approximately 2–5 individuals per million annually [1]. Among thymoma patients, 25–40% develop myasthenia gravis, and 0.5–9% develop myopathy, often in combination [2]. Guillain-Barré Syndrome (GBS) is one of the most common acute neuropathies in adults, with an incidence of 1.3 per 100,000 [3]. Its pathogenesis involves molecular mimicry, where antibodies targeting pathogens cross-react with peripheral nerve gangliosides (e.g., GM1, GD1b), resulting in demyelination or axonal injury [4]. While GBS has been reported with thymoma in the context of myasthenia gravis [5], its co-occurrence with acute myositis is rare, with isolated reports linked to Mycoplasma pneumoniae, cytomegalovirus, and dengue virus [3,6,7]. However, GBS in a patient with thymoma in the absence of myasthenia gravis is exceedingly rare, with very limited reports in the literature.

Takotsubo cardiomyopathy is a non-ischemic, stress-induced cardiomyopathy characterized by transient left ventricular systolic dysfunction, often mimicking myocardial infarction [8]. The reverse variant, involving basal rather than apical ballooning, accounts for 1%–23% of cases [8]. While typically attributed to catecholamine surges, thymoma-associated paraneoplastic inflammation or autonomic dysfunction may also contribute to myocardial stunning. We report a rare case of GBS with concurrent myositis in a patient with thymoma and reverse Takotsubo cardiomyopathy, a triad not previously described in the literature.

CASE PRESENTATION

A 48-year-old Indian male construction worker from a semi-urban area presented with progressive weakness of the trunk and proximal limbs over three months. Ten days prior to admission, he developed retrosternal chest pain, and eight days prior, he had multiple episodes of diarrhea lasting 3–4 days. Two days before admission, he experienced sudden-onset bilateral lower limb weakness, followed by upper limb weakness on the day of admission. He also reported an unintentional weight loss of 15–20 kg over the past year. At presentation, the patient was hemodynamically stable, and general physical examination was unremarkable. Neurologically, he was alert (GCS: E4V5M6), with intact cranial nerves. He had hypotonia in all four limbs, absent deep tendon reflexes, and mute plantar responses. Muscle power was 2/5 in the lower limbs and 4/5 in the upper limbs, which deteriorated to 2/5 in the upper limbs by evening. Sensory examination revealed reduced fine touch and temperature sensation below the wrists and ankles bilaterally, with absent joint position sense in both great toes. Cerebellar function was intact. Laboratory investigations showed neutrophilic leukocytosis (total leukocyte count: 15.18 x 10^9/L), normal hemoglobin (13.1 g/dL), a platelet count of 272 × 10^9/L, elevated transaminases (AST 424 IU/L, ALT 162 IU/L), C-reactive protein (CRP) 3.88 mg/L, erythrocyte sedimentation rate (ESR) 5 mm/hr, elevated creatine phosphokinase (CK) (6207 IU/L), and lactate dehydrogenase (LDH) (875 U/L) (Table 1). Thyroid function tests were normal. Based on clinical and laboratory findings, the initial differential diagnoses included inflammatory myopathy, viral myositis, vasculitis, Behçet’s disease, sarcoidosis, and porphyria.

Table 1
Baseline laboratory investigations

Investigation	Result	Unit	Reference Range
COMPLETE BLOOD COUNT (CBC)			
Hemoglobin	13.13	g/dl	12–16
Total Leukocyte Count	15.18	$x10^9/L$	4–11
Platelet Count	272.0	$x10^9/L$	150–450
KIDNEY FUNCTION TESTS (KFT)			
Urea	25.0	mg/dl	10–50
Creatinine	0.66	mg/dl	0.6–1.3
LIVER FUNCTION TESTS (LFT)			
Total Bilirubin	1.6	mg/dl	0.1–1.2
Direct Bilirubin	0.29	mg/dl	< 0.3
AST	424.0	U/L	< 40
ALT	162.0	U/L	< 40
ALP	80.0	U/L	30–120
Total Protein	5.63	g/dl	6.0–8.0
Albumin	3.06	g/dl	3.5-5.0
Globulin	2.57	g/dl	2.0-3.5
INFLAMMATORY MARKERS			
C-Reactive Protein	3.88	mg/L	5
Erythrocyte Sedimentation Rate	5.0	mm/hr	< 20
CEREBROSPINAL FLUID (CSF)			
WBC (Microscopy)	10 cells/mm^3	-	< 5
RBC	Nil		
Glucose	54	mg/dl	40–70
Protein	65	mg/dl	20–40

A viral panel for CMV, EBV, HCV, HIV, HBsAg, and dengue along with blood and urine cultures were negative. Lyme serology, ANA, c-ANCA, and p-ANCA were also negative. 24-hour urinary porphobilinogen levels were within normal limits. A comprehensive myositis antibody panel, including TIF1γ, MDA5,

NXP2, SAE1, Ku, Mi-2α/β, PM-Scl100/75, Jo-1, SRP, PL-7, PL-12, EJ, OJ, and Ro-52, was negative. Magnetic resonance imaging (MRI) of bilateral thighs showed findings consistent with myositis involving bilateral paraspinal, iliopsoas, pelvic girdle, thigh, and leg muscles. Due to rapid worsening of limb power and areflexia, acute inflammatory demyelinating polyneuropathy was suspected. Nerve conduction studies revealed sensorimotor axonal polyneuropathy, consistent with the AMSAN variant of GBS. CSF analysis showed mild pleocytosis with elevated protein (Table 1), supporting the diagnosis. Muscle biopsy demonstrated mild-to-moderate endomysial inflammatory infiltrates composed predominantly of lymphocytes and histiocytes, along with scattered necrotic and regenerating myofibers. CD8 immunostaining highlighted few lymphocytes. No mitochondrial abnormalities, inclusion bodies, rimmed vacuoles, perimysial vasculitis, or fibrosis were identified. While these findings were interpreted as suggestive of inflammatory myopathy, they are not specific and mandate correlation with clinical, electrophysiological, and biochemical parameters (Fig. 1). Contrast-enhanced CT of the thorax and abdomen, done for malignancy screening, revealed a lobulated, heterogeneously enhancing anterior mediastinal mass (Fig. 2.) Whole-body positron emission tomography–computed tomography (PET-CT) showed a mildly FDG-avid anterior mediastinal lesion, likely thymoma, with no evidence of metastasis. CT-guided biopsy confirmed Type A thymoma (Fig. 3.). High-sensitivity troponin I was markedly elevated (2222.1 pg/mL). Echocardiography revealed basal and mid-left ventricular (LV) hypokinesia with preserved apical function, consistent with reverse Takotsubo cardiomyopathy.

The patient was treated with high-dose intravenous (IV) methylprednisolone (1 g/day for 3 days) and five sessions of plasmapheresis, followed by oral prednisolone 50 mg/day (1 mg/kg) tapered biweekly. Significant clinical improvement was noted by Day 8, with motor power improving to 3/5 in lower limbs and 4-/5 in upper limbs. Liver enzymes, CK, and LDH showed a declining trend. Patient was advised for thymectomy but denied for the procedure. The patient was discharged on oral prednisolone 40 mg with tapering plan and methotrexate 15 mg/week. At 2-month follow-up, he could walk with support, with motor power of 4-/5 in lower limbs and 5/5 in upper limbs.

DISCUSSION

Guillain-Barré Syndrome (GBS) is the most common cause of acute flaccid paralysis worldwide and can lead to respiratory failure in severe cases. The patient’s rapidly progressive muscle weakness, absent deep tendon reflexes, and sensory deficits were strongly suggestive of acute motor and sensory axonal neuropathy (AMSAN), a rare and severe GBS variant [9]. Concurrently, chronic proximal limb weakness, movement-related pain, elevated CK, LDH, and AST, along with MRI findings and muscle biopsy showing features supportive of inflammatory myopathy, supported the diagnosis of inflammatory myopathy coexisting with GBS. Distinguishing between GBS and inflammatory myopathy can be challenging, as both may present with generalized muscle weakness, involving both proximal and distal muscle groups.

We acknowledge that endomysial inflammatory infiltrates on H&E staining are not specific and may be seen in neurogenic conditions such as GBS; however, the presence of myofiber necrosis and

regeneration, elevated muscle enzymes, and MRI evidence of myositis favored a concomitant myopathic process rather than purely neurogenic pathology.

Thymomas are the most common anterior mediastinal epithelial tumors, often asymptomatic and detected incidentally on imaging. They are frequently associated with autoimmune and paraneoplastic syndromes, including myasthenia gravis, pure red cell aplasia, and other neuromuscular disorders [10]. In a review by Yuan et al. [11], 15 cases of coexisting GBS and MG were analyzed, of which four had associated thymoma. It was hypothesized that thymoma-induced multi-organ autoimmunity may contribute to the development of GBS. Similarly, Cao et al. [5] suggested that thymic abnormalities, including thymoma or hyperplasia in MG patients, may predispose to other autoimmune diseases. External triggers such as infections may further activate the immune system, leading to a surge in pathogenic autoantibodies and unmasking clinical features of both GBS and MG [5].

Huang et al. reported thymic abnormalities in most cases of MG–inflammatory myopathy overlap, all of whom were anti-AChR antibody positive, suggesting a link between thymoma and broader autoimmune activation [12]. Similarly, Garibaldi et al. found that among 441 MG patients, 13 had coexisting inflammatory myopathy, and 10 of these had thymoma [13]. It is proposed that thymoma may facilitate the escape of autoreactive T cells and promote the production of anti-striational antibodies (e.g., titin, RyR1), which are implicated in the pathogenesis of inflammatory myopathies [13].

In this case, to investigate potential paraneoplastic causes of inflammatory myopathy, a contrast-enhanced computed tomography (CECT) of the thorax and a whole-body PET scan were performed. These imaging and subsequent biopsy confirmed the diagnosis of type A thymoma. Repetitive nerve stimulation testing was performed alongside assessment of anti-acetylcholine receptor (AChR) antibody levels, both of which were negative in our patient. The co-occurrence of inflammatory myopathy and GBS in the absence of thymoma has been reported only once, by Chabcoub et al. [14], suggesting that virus-induced immune responses, possibly via molecular mimicry, may play a role in the pathogenesis [14].

The literature suggests that thymoma is commonly associated with both MG and GBS as well as MG and inflammatory myopathy overlap syndromes, supporting a possible link in our case of GBS and inflammatory myopathy overlap. Proposed mechanisms such as thymoma-induced autoimmune activation, escape of autoreactive T cells, and production of striational antibodies may underlie the pathogenesis. Additionally, infectious triggers are known to initiate or exacerbate autoimmune responses. In our patient, multiple episodes of diarrhea eight days prior to admission may have acted as a precipitating event for both GBS and inflammatory myopathy.

Reverse Takotsubo cardiomyopathy (rTTC), a variant of stress-induced cardiomyopathy, was identified in this patient. It is characterized by basal hypokinesia with apical hyperkinesia and typically mimics acute coronary syndrome, presenting with chest pain, diaphoresis, and elevated cardiac troponins [10]. In this case, the patient had retrosternal chest pain for 10 days, elevated high-sensitivity troponin, and echocardiography showed an ejection fraction of 35–40% with basal hypokinesia, consistent with rTTC, with subsequent improvement on follow-up. A CT coronary angiogram ruled out obstructive coronary

artery disease. Cardiomyopathy associated with thymoma is rare and typically occurs in the setting of myasthenia gravis (MG) [15]. MG itself has been linked to stress-induced cardiomyopathy, including Takotsubo cardiomyopathy (TTC) [16]. However, when thymoma presents with cardiomyopathy in the absence of MG, the mechanism remains unclear. Lim et al. proposed that mediastinal irritation from thymoma may provoke arrhythmias, leading to tachycardia-induced cardiomyopathy (TIC) as a possible explanation [16]. To date, there are no reported cases in the English literature describing reverse Takotsubo cardiomyopathy in association with either GBS or inflammatory myopathy.

This case highlights a rare combination of Guillain-Barré Syndrome and inflammatory myopathy associated with thymoma, complicated by reverse Takotsubo cardiomyopathy, in the absence of myasthenia gravis. It underscores the importance of considering paraneoplastic and immune-mediated mechanisms in patients presenting with overlapping neuromuscular and cardiac manifestations.

Overall, this case represents a rare clinicopathological overlap of Guillain–Barré syndrome and inflammatory myopathy associated with thymoma, complicated by reverse Takotsubo cardiomyopathy, emphasizing the need for a multidisciplinary diagnostic approach in atypical neuromuscular presentations.

This case report has been prepared in accordance with the CARE guidelines.

Abbreviations

GBS
Guillain–Barré syndrome
AMSAN
Acute motor and sensory axonal neuropathy
CK
Creatine kinase
LDH
Lactate dehydrogenase
MRI
Magnetic resonance imaging
CSF
Cerebrospinal fluid
PET
CT–Positron emission tomography–computed tomography
MG
Myasthenia gravis
rTTC
Reverse Takotsubo cardiomyopathy

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent for publication of this case report and accompanying images was obtained from the patient.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

RG and DSM managed the patient and drafted the manuscript. AM, NL, ST, and AM contributed to clinical care and data collection. PS and RB revised the manuscript and collected patient data. SK provided pathological interpretation. GKB supervised patient management and manuscript writing and critically revised the manuscript. All authors read and approved the final manuscript.

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Figures

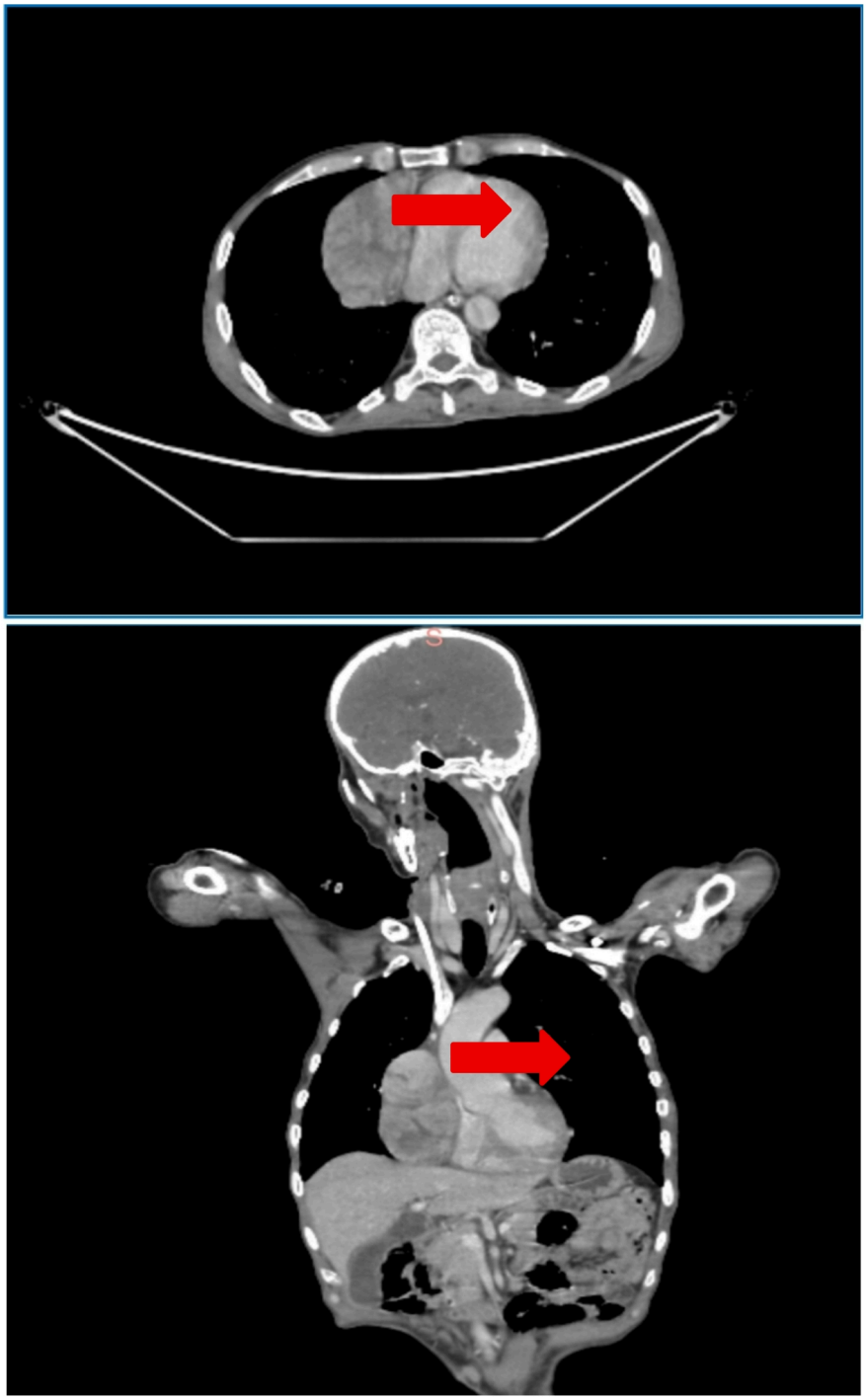


Figure 1

Axial and coronal section of Contrast enhance computed tomography showing lobulated, heterogeneously enhancing anterior mediastinal mass

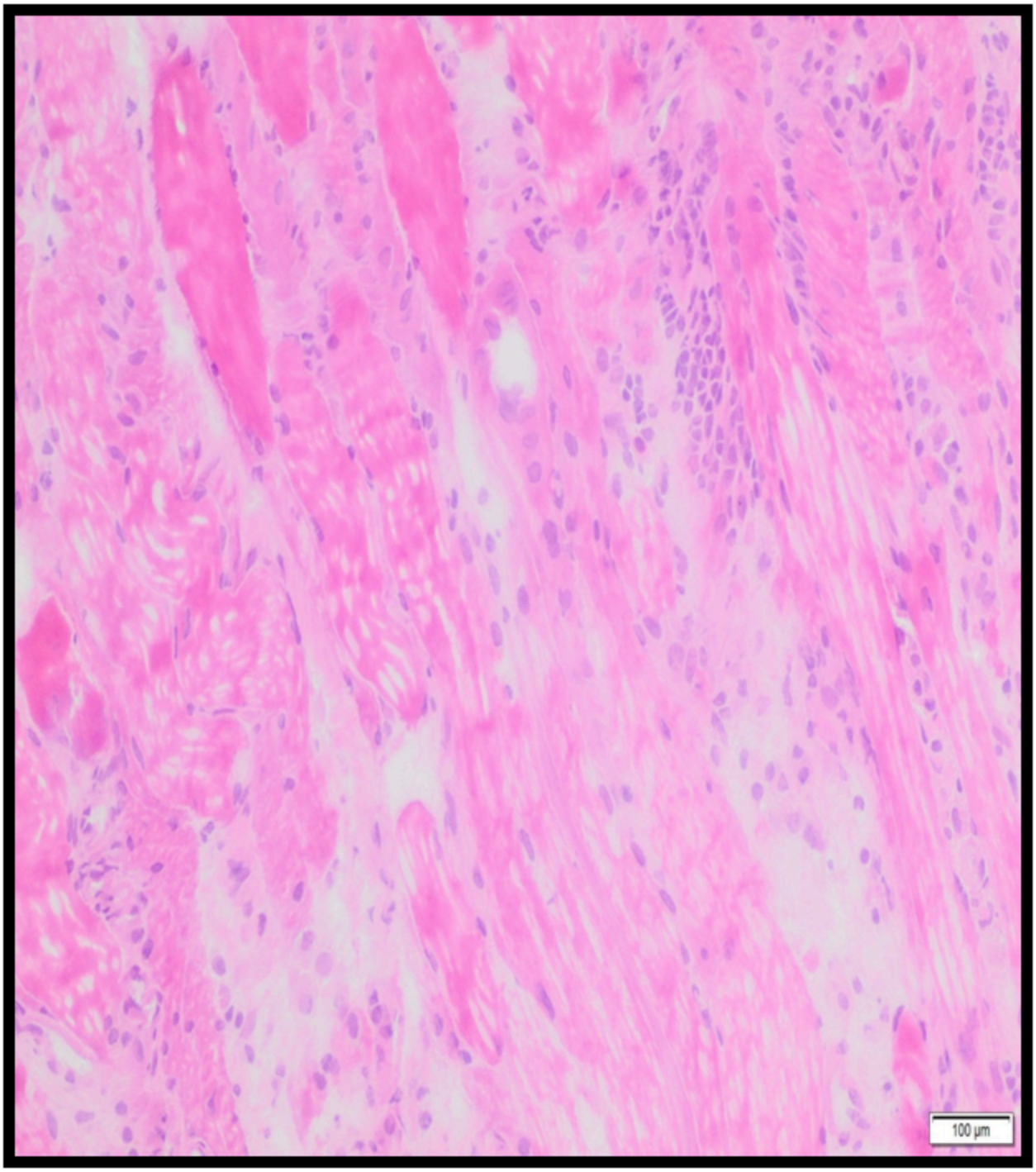


Figure 2

H&E stain, 100×: Muscle biopsy from the left semimembranosus shows mild-to-moderate endomysial inflammatory infiltrates composed of lymphocytes and histiocytes, with scattered necrotic and regenerating muscle fibers and mild variation in fiber size.

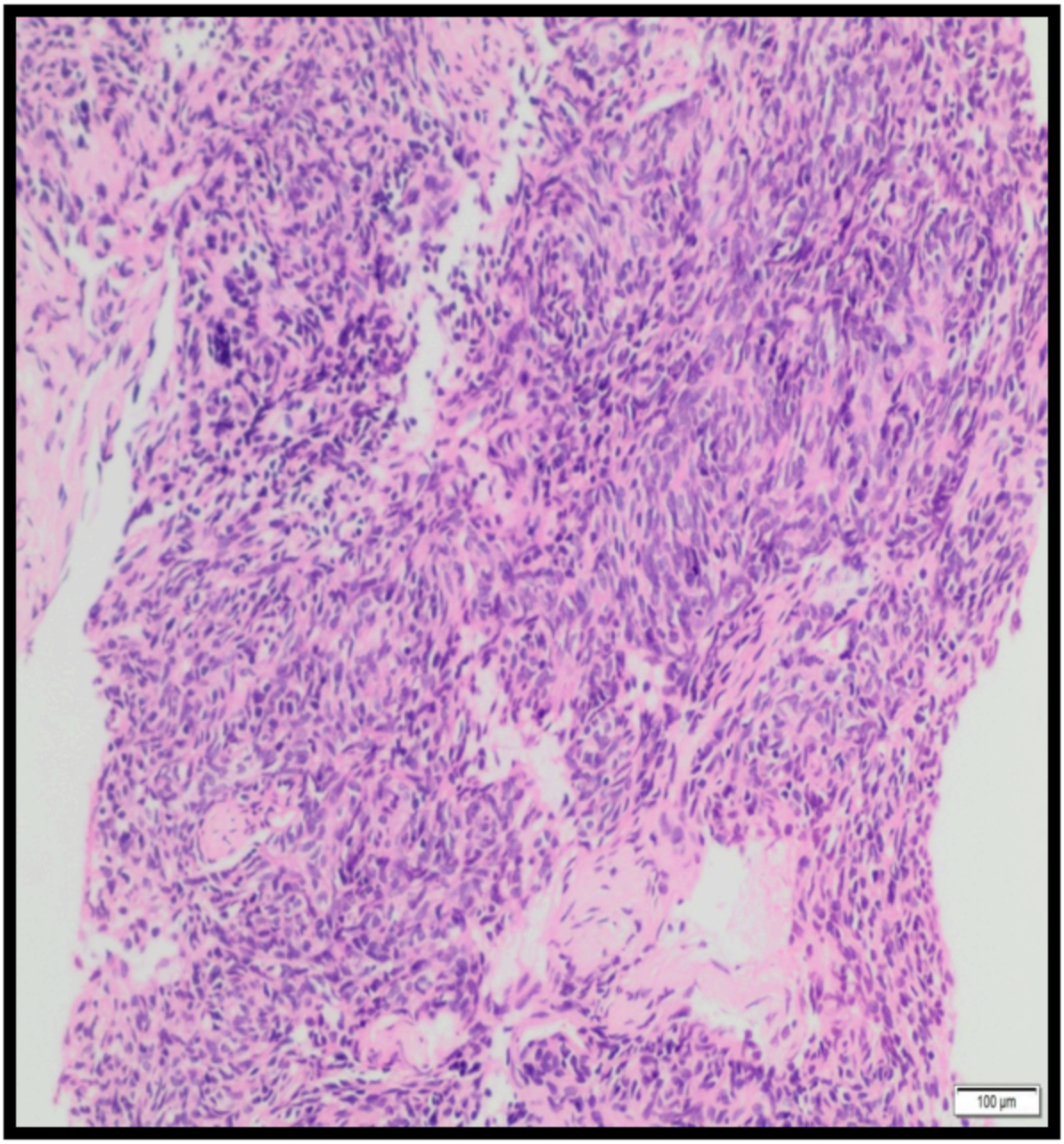


Figure 3

HPE showing Thymoma- H&E, 100x: Section shows a lesion composed of spindle shaped cells admixed with few scattered lymphocytic cells