CASE REPORT

OVERLAP AXONAL POLYNEUROPATHY WITH IMMUNE MEDIATED NECROTISING MYOPATHY

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Immune mediated necrotising myopathy (IMNM) is a rare autoimmune disease of the muscles belonging to the subset of the idiopathic inflammatory myopathies (IIM). This disease entity has classically been associated with myositis specific antibodies. The hallmark feature in clinching the diagnosis of IMNM would be a muscle biopsy showing muscle necrosis and regeneration in the absence of significant inflammatory infiltrates, interpreted in an appropriate clinical context. The term 'neuromyositis' was previously coined in the year 1893 to describe a concomitant polyneuropathy in patients with polymyositis or dermatomyositis. However, a combined polyneuropathy with IMNM has never been reported in previous literature. We describe a case of a 35-year-old gentleman who presented with a 5-day history of symmetrical bilateral lower limb pain and weakness. Despite a negative autoimmune work-up, his muscle biopsy was suggestive of IMNM. A nerve conduction study done had also revealed a superimposed non-length dependant axonal polyneuropathy. The patient had responded well to steroids and is now under remission. This case serves to highlight a rare entity of seronegative IMNM superimposed with an axonal polyneuropathy.

Keywords: Immune mediated necrotising myopathy; Neuromyositis; Axonal polyneuropathy

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INTRODUCTION

The idiopathic inflammatory myopathies (IIM) are a diverse group of pathologies classically presenting with proximal muscle weakness, elevated muscle enzymes, with positive muscle specific antibodies. The most commonly described diseases under this umbrella term are polymyositis (PM), dermatomyositis (DM), the anti-synthetase syndrome and sporadic inclusion body myositis (sIBM).[1] Prominent inflammatory infiltrates on muscle biopsy are almost always seen universally in the above spectrum, which is unsurprising given the inflammatory nature of these diseases.[2]

Over the past 20 years, it has been acknowledged that muscle biopsies from some patients with myositis have significant myofiber necrosis but with minimal, if any, inflammatory infiltrates.[3] These patients are now widely recognized to have immune-mediated necrotizing myopathy (IMNM), which has been included in the IIM nomenclature.[4] IMNM has a prevalence of approximately 7 to 11 per 100,000 people per year in the United States.[5] In Malaysia itself, a study in 2021 revealed that the age of onset of IMNM was 37.1 years on the average with a female predominance. A vast majority of these patients have positive myositis specific antibodies.[6]

By convention, diseases of the musculoskeletal and the peripheral nervous system are usually viewed as mutually exclusive entities. Myopathies usually present with proximal muscle weakness, while diseases of the peripheral nervous system present with distal weakness and/or numbness. However, our patient has shown evidence that muscle and nerve disorders may overlap and possibly confound the initial clinical presentation. Our patient was eventually diagnosed with IMNM based on his muscle biopsy and also an axonal polyneuropathy from the nerve conduction study.

CASE REPORT

A 32-year-old Malaysian gentleman presented to the emergency department with a two-day history of proximal thigh muscle pain. He had denied any strenuous physical activities leading to the presentation. The patient had also denied any preceding fever or constitutional symptoms. Coincidentally, he had also complained of a symmetrical glove and stocking sensory loss over the bilateral lower limbs. This was also associated with predominant distal weakness and bilateral foot drop.

Figure-1: Bilateral foot drop on presentation

Physical examination revealed a normal built gentleman who was saturating under ambient air His vital signs were otherwise unremarkable. Of note, power was reduced over the distal bilateral lower limbs with hypotonia and areflexia. There was glove and stocking sensory loss up to the midshin. There was otherwise no spinal sensory level. Cranial nerve examination and the cerebellar system were also unremarkable. No vasculitic skin rashes were identified as well. The patient had also denied any history of trauma.

The patient's serum creatine kinase CK was only marginally raised at 373 units/litre. Serum electrolytes, B12, folate and thyroid function tests were normal. He also had a negative hepatitis and retroviral test. Lumbar puncture revealed only a raised protein level of 0.6g/L, however there were no detectable leucocytes on the cell count. Cultures of the cerebrospinal fluid (CSF) were also negative. In light of these available investigations and given the acute presentation, he was treated for an acute Guillain Barre syndrome and was commenced on intravenous immunoglobulin 2g/kg over 5 days and was therefore admitted to the general medical ward.

Interestingly, the patient developed severe abdominal discomfort and metabolic acidosis on the second day of admission which necessitated admission into the intensive care unit. He had also required mechanical ventilation. The metabolic acidosis was not in keeping with the initial diagnosis of Guillain Barre syndrome. This new development led to further workup as to other potential diagnoses.

A computed tomography of the thorax, abdomen and pelvis (CT TAP) done to further delineate the abdominal pain was otherwise unremarkable. Porphyria work-up was also negative. The patient was eventually nursed in the intensive care unit for approximately two months. Due to limited resources, a nerve conduction study (NCS) and electromyography (EMG) was only done after two months into admission. The NCS revealed a non-length dependant axonal polyneuropathy, while the EMG showed complex repetitive discharges at the proximal muscles of the thigh.

The patient eventually had a muscle biopsy which revealed scattered atrophic, regenerating and necrotic fibres with no mononuclear cell infiltrates seen. There were also no endomysial mononuclear cells or perifascicular atrophy seen to suggest polymyositis and dermatomyositis. The muscle biopsy was consistent with immune mediated necrotising myopathy (IMNM). His myopathy antibody panel was also negative.

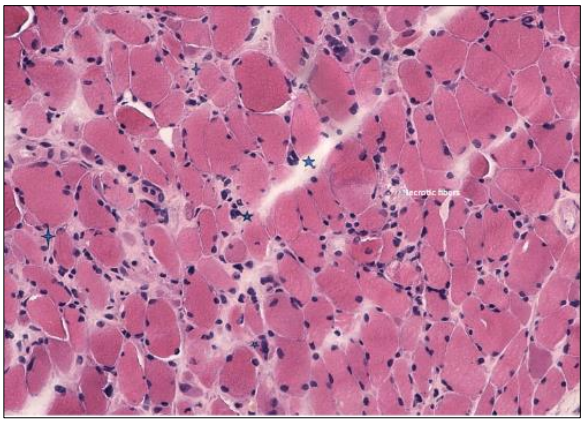

Figure-2: H&Ex100: Marked fiber size variation with scattered atrophic and regenerating fibers (*)

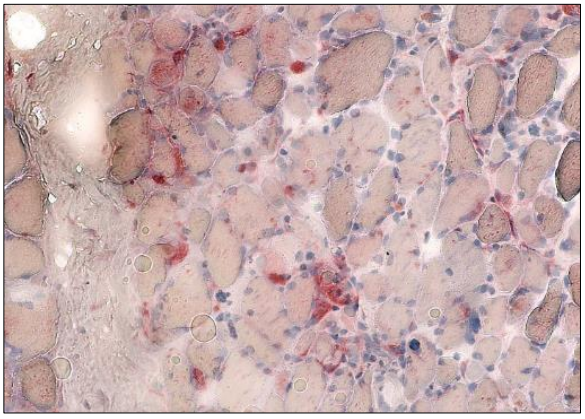

Figure-3: Acid Phosphatase: Increased enzymatic activity in necrotic fibers

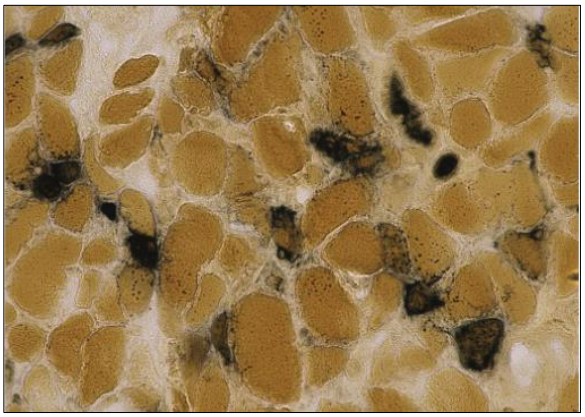

Figure-4: Alkaline phosphatase: Increased enzymatic activity in necrotic and regenerating fibers

Tying the presentation of proximal muscle thigh pain, with a compatible EMG/ NCS and muscle biopsy, the patient was diagnosed with immune mediated necrotising myopathy with overlap axonal polyneuropathy.

The patient made a good recovery and is under rehabilitation follow-up. He was put on oral Azathioprine 100mg daily. During the most recent review one month post discharge, he was making positive progress under rehabilitation and is now ambulating.

DISCUSSION

The term neuromyositis was first described by Senator *et al* in 1893 which described a concomitant involvement of the peripheral nervous system with superimposed dermatomyositis or polymyositis.[7] On the contrary IMNM was only distinguished as a separate entity from polymyositis in 2004.[8] In keeping with the objective evidence of necrotising myopathy from the muscle biopsy and also a nerve conduction study showing an axonal polyneuropathy, we postulate that our patient could be having neuromyositis.

At present, there are only scarce reports of a combined polyneuropathy and proximal myopathy. Literature search with the terminology of neuromyositis only revealed isolated case reports, similar to our patient's presentation.

Our patient had presented with a combined symmetrical distal weakness and numbness, with superimposed proximal muscle pain. Due to the rapid and acute presentation, he was initially treated for Guillain-Barre syndrome and was commenced on intravenous immunoglobulin on admission. However, within the first 2 days, he developed severe metabolic acidosis which confounded the diagnosis of Guillain Barre syndrome. Retrospectively, the severe metabolic acidosis could have been due to rhabdomyolysis from the superimposed myopathy from presentation.

The muscle biopsy however needs to be interpreted in the appropriate clinical context. In our patient, the biopsy was done only after approximately one month into admission. He spent a significant amount of time in the intensive care unit prior to the muscle biopsy being done. The authors would like to acknowledge that critical illness myopathy would also show the same muscle biopsy result[9]. It could therefore be possible that the muscle biopsy would have in fact been due to critical illness myopathy. Furthermore, his muscle specific antibodies had been negative. However, his first initial presentation of proximal muscle pain still places IMNM as the most possible explanation of the muscle biopsy results.

This case raises a significant learning point. There is a need to acknowledge that a combined myopathy and polyneuropathy may co-exist during initial presentation and therefore should not be looked as just separate entities. This is especially true if the clinical presentation is suggestive of a combined distal and proximal weakness accompanied by muscle pain. It is important to be able to diagnose a combined myopathy and polyneuropathy as the management principle differs.

In the case of a pure polyneuropathy such as Guillain Barre syndrome, there would be no need for long term immunosuppressive therapy as it is a self-limiting disease. However, if there is a combined myopathy involved, long term immunosuppressive therapy will be the backbone of treatment. An under-diagnosis may therefore deprive patients from immunosuppressive therapy.

CONCLUSION

Although a combined polyneuropathy and myopathy on initial presentation is a rare entity, there is a need to recognise this clinical overlap syndrome. Although the acute management may be the same of an isolated polyneuropathy and isolated myopathy may be the same with possibly high dose steroids or intravenous immunoglobulin, however prognosis and subsequent therapies differ between the two.

A combined polyneuropathy and myopathy will require long term immunosuppressive therapy. This case therefore serves to highlight the need to recognize this rare phenomenon. More case reports are required to further establish the overlap between a combined polyneuropathy and myopathy.

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Conflicts of Interest: None

AUTHORS' CONTRIBUTION

EJK: Conceptualization, literature search and write up.
MLC: Literature search, write up and proof reading.
NAAA: Pathology slides reporting, write up and proof reading

REFERENCES

1. Malik A, Hayat G, Kalia JS, Guzman MA. Idiopathic inflammatory myopathies: Clinical approach and management. Front Neurol 2016;7:64.
2. Vattemi G, Mirabella M, Guglielmi V, Lucchini M, Tomelleri G, Ghirardello A, *et al*. Muscle biopsy features of idiopathic inflammatory myopathies and differential diagnosis. Auto Immun Highlights 2014;5(3):77–85.
3. Verma R, Paliwal V. Idiopathic inflammatory myopathy: From muscle biopsy to serology. Indian J Rheumatol 2020;15(Suppl 2):S123–30.

4. Pinal-Fernandez I, Casal-Dominguez M, Mammen AL. Immune-mediated necrotizing myopathy. Curr Rheumatol Rep 2018;20(4):21.
5. Anim-Koranteng C, Akpoigbe O, Miller M, Averbukh Y. From studio to rehab: A debilitating form of anti-HMGCR myopathy. Cureus 2023;15(6):e40825.
6. Alenzi F. Myositis specific autoantibodies: A clinical perspective. Open Access Rheumatol 2020;12:9–14.
7. Park CK, Yoo SJ, Yoo IS, Kim J, Shim SC, Kang SW. Neuromyositis: A rare extramuscular manifestation of dermatomyositis. J Rheum Dis 2019;26(3):211.
8. Allenbach Y, Benveniste O, Stenzel W, Boyer O. Immune-mediated necrotizing myopathy: clinical features and pathogenesis. Nat Rev Rheumatol 2020;16(12):689–701.
9. Shepherd S, Batra A, Lerner DP. Review of critical illness myopathy and neuropathy. Neurohospitalist 2017;7(1):41–8.

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