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RESEARCH ARTICLE

AN UNUSUAL ASSOCIATION OF CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY: A CASE REPORT

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Abstract

Distal Acquired Demyelinating Polyneuropathy (DADS), a variant of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is rarely associated with Monoclonal Gammopathy of Undetermined Significance. A case of quadriparesis is reported here, who was found to have DADS in background of MGUS IgA lambda. He was treated with intravenous Immunoglobulin and Azathioprine and showed good response. We report this case to sensitize the medical fraternity about the unusual association of CIDP with plasma cell dyscrasia.

Introduction:-

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a disorder of the peripheral nerves and nerve roots causing limb weakness and sensory deficits. Demyelinating symmetric polyneuropathies are classified by the pattern of weakness into (1) CIDP characterized by proximal as well as distal weakness, and (2) distal acquired demyelinating symmetric polyneuropathy (DADS). DADS may present with length-dependent sensory features or with predominantly distal motor symptoms[1]. DADS is further sub-divided into DADS-M (with M band on protein electrophoresis) and DADS-I (indeterminate type, without M protein), with DADS-M patients being older, more predominantly male, and less responsive to immunologic treatment than those with DADS-I or with other sub-types of CIDP. We present a case of DADS-I variant with MGUS association.

Case report:

A 35 year old married, male, Hindu, by profession a salesman, presented with low back pain and weakness of both lower limb for past 8 months, along with weakness of both upper limbs and sensory loss over all four limbs for the last 4 months. He had no major medical or surgical milestones and was not addicted to tobacco or alcohol. His family history was non-contributory.

Clinical examination revealed an alert and well oriented patient with normal built and vital parameters. Neurological examination documented symmetric flaccid quadriparesis with power 2/5 in all limbs. The patient had bilateral foot drop but no involuntary movements in any limb. All modalities of sensation were diminished over all four limbs. CBC, KFT, LFT and electrolytes were unremarkable, except for globulin 5.6g/L (2.0 – 3.5 g/L) and serum Calcium 10.2 mg/dL (8 - 10 mg/dL). Urine examination showed moderate proteinuria. The CSF study revealed albumino-cytological dissociation, with 5 cells (all lymphocytes) and a CSF protein of 142g/dL, with no RBC and normal

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glucose level. The right and left kidneys were 94mm and 96mm in longitudinal dimension, with well – maintained cortico – medullary differentiation on Ultrasound. Nerve conduction velocity testing reported bilateral distal symmetrical demyelinating and axonal polyneuropathy with predominantly motor involvement (Fig 1).

We proceeded for serum protein electrophoresis which demonstrated a monoclonal IgA lamda peak, with no M spike (Fig 2). Bone marrow histopathology was normal without any preponderance of plasma cells (<5%). X-ray of spine showed osteolytic lesions spread over multiple dorsal and lumbar vertebrae. The skull X-ray was normal. Search for malignancy was unrewarding and tumour markers (PSA, CEA, CA 19.9 and AFP) were negative. Assimilating the above, we made a diagnosis of IgA associated DADS-I variant of CIDP.

The patient was treated in consultation with Neurology colleagues and received IVIg at 400mg/kg/day for 5 days, during which substantial neurological improvement was achieved. This was followed by oral maintenance therapy with tablet prednisolone 60mg/day (1mg/kg), and tablet Azathioprine 50mg/day. He is now functionally independent and has been on monthly cycles of IVIg for the past three months and the steroid dose has been tapered to 30mg day. We plan to complete six cycles of IVIg and maintain him indefinitely on Azathioprine 50 mg/day and tablet prednisolone 10mg/day, thereafter.

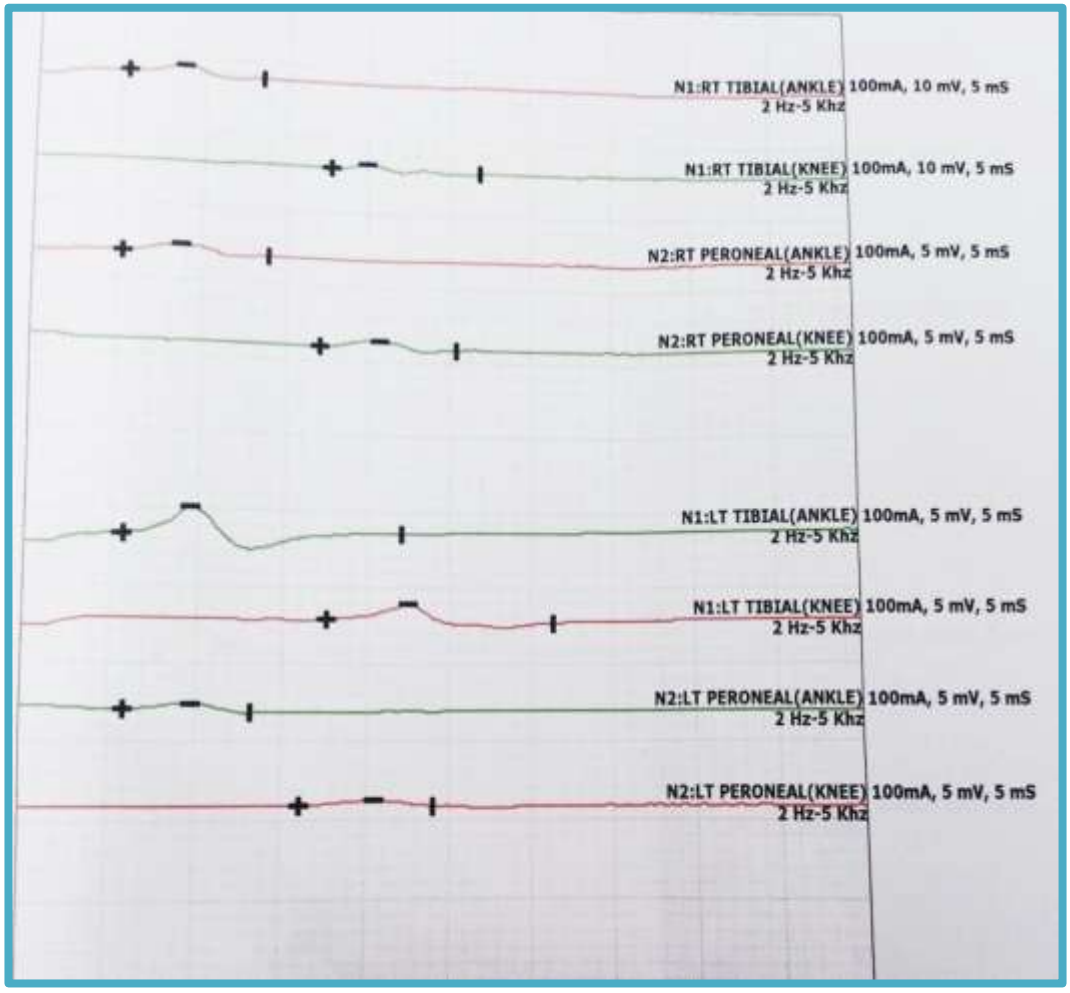
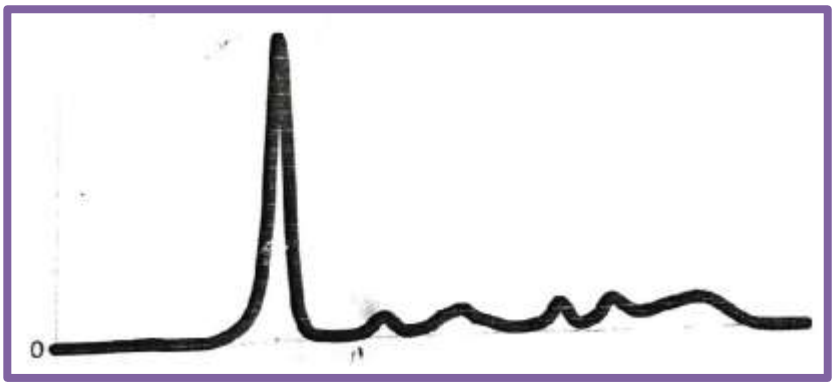


Fig 1:- NCV showing features (tibial and peroneal tracings) suggestive of distal symmetrical demyelinating and axonal polyneuropathy.

A



B

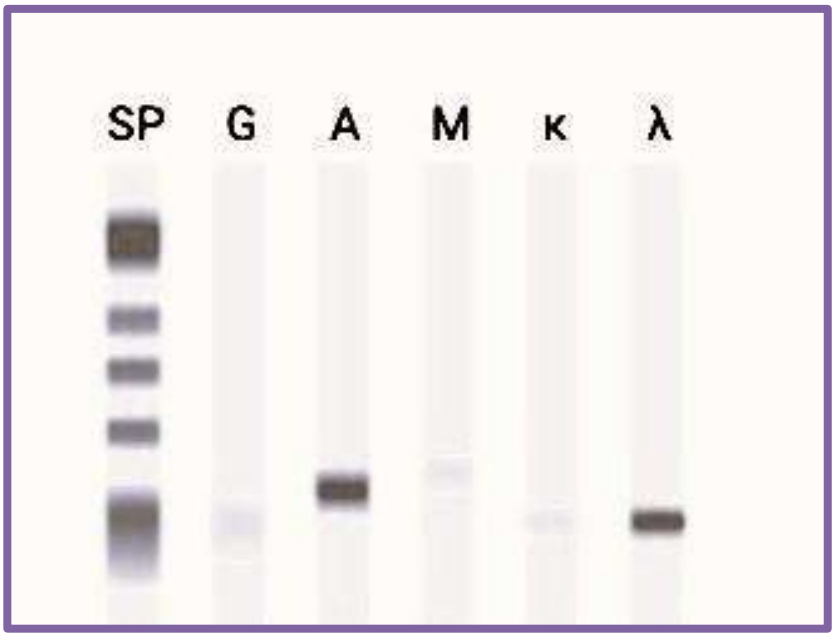


Fig 2:- A and 2B: Serum protein electrophoresis showing IgA lambda peak.

Discussion:-

Diabetes, IgG or IgA monoclonal gammopathy of unknown significance, IgM monoclonal gammopathy without anti-MAG (myelin associated glycoprotein) antibodies, connective tissue diseases, and HIV infection have all been associated with CIDP.[2] DADS polyneuropathy is a variant of CIDP with the phenotype of symmetric, demyelinating sensory, length dependent polyneuropathy, and is frequently associated with paraproteinemia and anti-myelin associated glycoprotein (anti-MAG) antibody.[3] We could not test for anti-MAG antibody as the patient could not afford this out – of – pocket expense.

Antiganglioside antibodies are associated with chronic demyelinating neuropathies and IgM monoclonal gammopathy.[4] A third of DADS cases may be negative for anti-MAG antibodies, suggesting the antibody is a marker for disease, rather than being pathognomonic[1]. However, haematological associations are common, with a case series reporting an associated haematological diagnosis in 9 out of 10 cases of anti-MAG negative DADS neuropathy.[5]

Our case demonstrates an association of DADS neuropathy with MGUS, having an IgA lambda peak. However, the association between IgA paraprotein and neuropathy is not as strong as that of IgM, in which pathogenic activity of IgM antibodies against myelin associated glycoprotein (MAG), gangliosides, and glycosphingolipids has been established.[6]

IVIg, corticosteroids, plasma exchange, and more recently subcutaneous immunoglobulin (SCIG) are the first line therapies of CIDP.[7] However, more than 20% patients respond poorly and immunosuppressive agents in the form of

azathioprine, cyclophosphamide, cyclosporin, mycophenolate mofetil, and rituximab have all been used, when first line treatment was ineffective or intolerable.[8] In CIDP – MGUS patients, steroids, immunosuppressive agents, plasma electrophoresis (PE), or IVIG, alone or in combination, are established therapeutic options.[9]

Our patient with IgA MGUS associated DADS responded well to IVIg therapy used in combination with azathioprine and glucocorticoids. Literature suggests that the efficacy of IVIG in patients with IgG/IgA MGUS is better than that in patients with IgM MGUS. Patients with axonal damages have a poorer response to immunotherapy.[8]

We report this case to highlight the varied presentations and diverse associations seen in the broad spectrum of CIDP, as well as to underline DADS as a variant of CIDP. We feel that clinicians must be sensitized to the less common variants of paraprotein associated peripheral neuropathies.

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