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A Rare Case of Polyneuropathy with an Underlying Paraprotienemic Origin

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Abstract: ***Introduction: Monoclonal gammopathies consist of a spectrum of clonal plasma cell disorders that includes Monoclonal Gammopathy of Undetermined Significance (MGUS), multiple myeloma (MM) and Waldenstrom Macroglobulinemia (WM). Peripheral neuropathy is a well-recognized complication of monoclonal gammopathies, and a difficult clinical problem in terms of diagnosis and treatment. Case Report: 54 year old male presented with symmetrical chronic progressive LMN type quadriparesis (distal> proximal) lower limb predominant with wasting, fasciculations, hypotonia and hyporeflexia, with both small and large fibre sensory involvement with skin changes with cachexia. Materials And Methods: We have done following investigations: CBC, RFT, LFT, serum electrolytes– within normal limits, NCS shown Bilateral severe sensori - motor demyelinating poly radiculoneuropathy with secondary axonal changes, CSF Analysis: TC-4 cells, DC-mostly lymphocytes; no RBC, Protein-144mg/dL, sugar-74mg/dL; Serum protein electrophoresis: non discrete protein band in gamma globulin region, possibly monoclonal gammopathy. Advised immunotyping which has shown Very faint? M spike in gamma globulin region of igG and kappa lane. Final Diagnosis: Paraproteinemic neuropathy- Monoclonal Gammopathy of undetermined significance (MGUS). Discussion: The most common presentation is a symmetrical sensorimotor polyneuropathy, one of three more common subtypes: 1) CIDP phenotype, 2) Distal acquired demyelinating symmetric (DADS) neuropathy, or 3. an axonal sensorimotor peripheral polyneuropathy. Conclusion: Approximately 10% of patients with idiopathic peripheral neuropathy have an associated monoclonal gammopathy. Patients undergoing evaluation for chronic peripheral neuropathy should be screened for the presence of a monoclonal protein (M protein).***

Keywords: MGUS- Monoclonal Gammopathy of Undetermined Significance, MM-multiple myeloma, WM- Waldenstrom Macroglobulinemia, IVIG-Intravenous Immunoglobulin

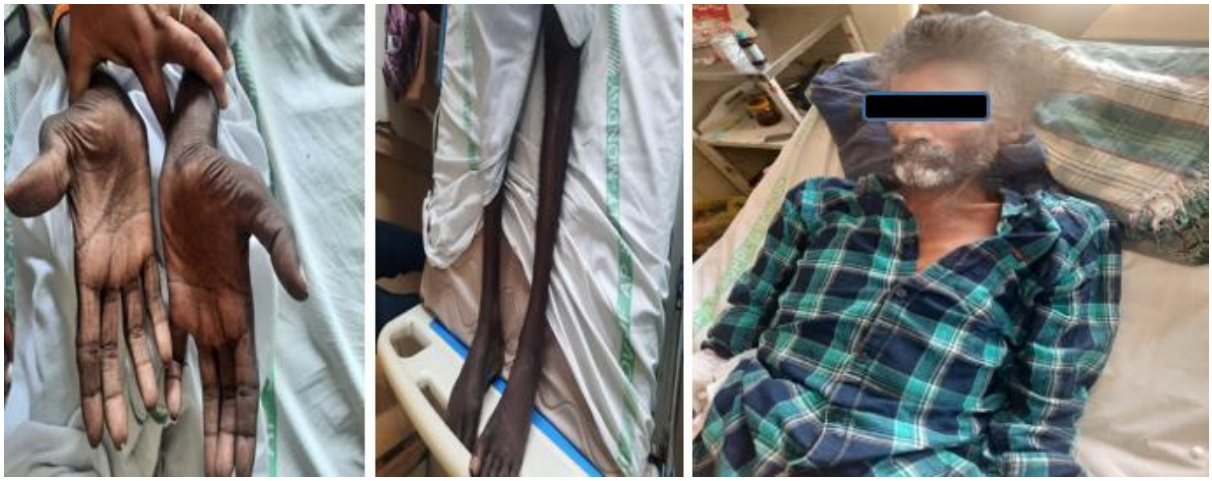
1. Introduction

Monoclonal gammopathies consist of a spectrum of clonal plasma cell disorders that includes monoclonal gammopathy of undetermined significance (MGUS), multiple myeloma (MM) and Waldenstrom Macroglobulinemia (WM). Peripheral neuropathy is a well-recognized complication of monoclonal gammopathies, and a difficult clinical problem in terms of diagnosis and treatment. [1]

2. Case Report

This is a 54- year old male chronic alcoholic, smoker, farmer by occupation. Since 1 year he stopped going to work due to this present illness. He came with chief complaints of: 1) Weakness with tingling and numbness of both lower limbs since 1&1/2 year. 2) Weakness with tingling and numbness of both upper limbs since 4 months. **History of present illness:** Patient was apparently alright 1&1/2 year ago to start with he has developed asymmetrical onset chronic progressive symmetrical Lower motor neuron type of quadriparesis (distal > proximal) lower limb predominant with wasting and fasciculations, with hypotonia and hyporeflexia with both small and large fibre sensory involvement with skin changes, with significant weight loss with no cranial nerve involvement with no cerebellar or autonomic symptoms with no cognitive or extrapyramidal dysfunction ,no features of raised ICT, no seizures. With this history and examination findings, our differential diagnosis were:

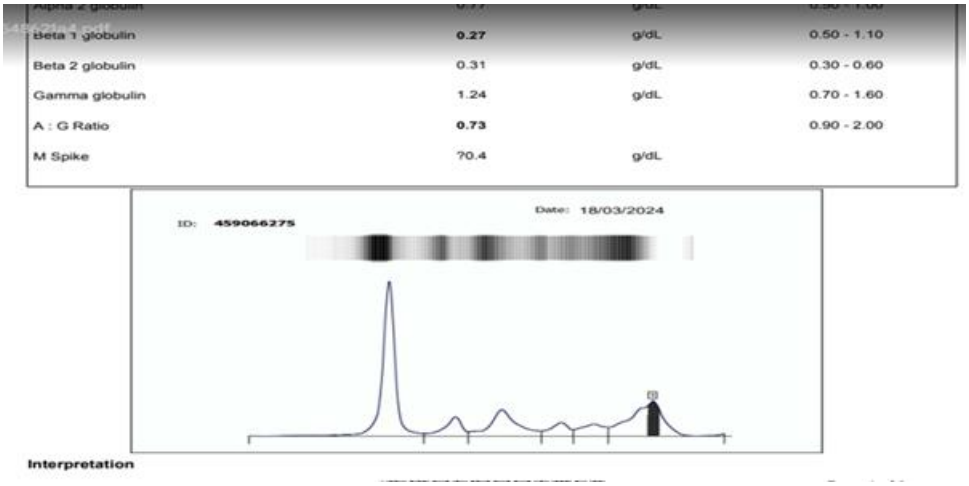
1) Paraproteinemic neuropathy.
2) Paraneoplastic neuropathy.
3) Vasculitic neuropathy.



3. Materials and Methods

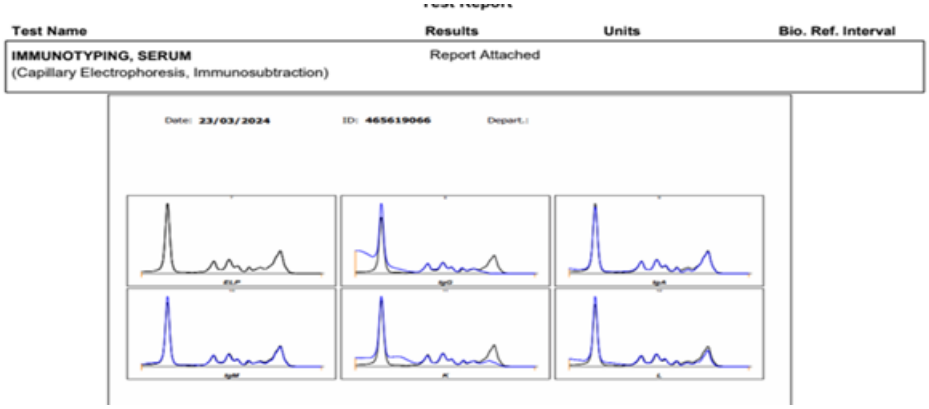
We have proceeded for further evaluation with following Investigations: CBC, RFT, LFT, serum electrolytes are within normal limits, Nerve conduction studies: bilateral severe sensori - motor demyelinating poly radiculoneuropathy (sensory predominant) With secondary axonal changes, **CSF Analysis**: TC-4 cells, DC-mostly lymphocytes; no RBC, Protein-144mg/dL, sugar-74mg/dL. Urine Bence jones proteins-negative, ANA profile and ANCA profile were negative. Peripheral smear -normal. **Serum protein electrophoresis**: serum total protein 5.1g/dL, **M spike**: 0.4g/dL, non-discrete protein band in gamma globulin region, possibly monoclonal gammopathy was observed. Immunotyping has shown faint non discrete protein band in gamma globulin region of igG and kappa lane corresponding to? M spike, (planned to repeat the test after 8 weeks in follow up.)

Serum Protein Electrophoresis:



Beta 1 globulin	0.27	g/dL	0.50 - 1.10
Beta 2 globulin	0.31	g/dL	0.30 - 0.60
Gamma globulin	1.24	g/dL	0.70 - 1.60
A : G Ratio	0.73		0.90 - 2.00
M Spike	?0.4	g/dL	

Immunotyping:



Test Name	Results	Units	Bio. Ref. Interval
IMMUNOTYPING, SERUM (Capillary Electrophoresis, Immunosubtraction)	Report Attached		

Final diagnosis: **Paraproteinemic neuropathy**: secondary to Monoclonal Gammopathy of undetermined significance (MGUS).

4. Treatment

He was treated with pulse dose of steroids followed by Intravenous Immunoglobulin (IVIG) course over 5 days, with

which he had moderate improvement of his sensory symptoms and weakness.

After 20 days of admission he has developed myocardial infarction for which CAG was done, which shown recanalized LAD and kept on medical management.

Later he developed cardiogenic shock and he was on inotrope support for 20 days, finally stabilized and sent home. Skeletal survey did not show any bone lesions. Bone marrow aspiration shown normal plasma cells. He was on follow up for monthly IVIG administration for 3 months. He later succumbed to a myocardial infarction at home.

5. Discussion

Monoclonal Gammopathy of Undetermined Significance (MGUS) is a premalignant plasma cell disorder characterized by the presence of a monoclonal (M) protein in the blood, produced by a small clone of cells. [3] The M protein is named according to the class of heavy chain (IgG, IgM, IgA, IgD, and IgE) and type of light chain, κ (kappa) or λ (lambda). In two-thirds of patients with a monoclonal protein, no detectable underlying disease is found, and they are described as having MGUS (monoclonal gammopathy of unknown significance).

Peripheral neuropathy is a well-recognized complication of monoclonal gammopathies, and a difficult clinical problem in terms of diagnosis and treatment. [3] The vast majority of such patients does not have any evidence of overt malignancy such as MM or WM, but rather are at the premalignant MGUS stage in terms of plasma cell biology. MGUS is present in 1%–3% of the population, mostly elderly. MGUS has replaced the term benign monoclonal gammopathy because up to one-fourth of patients go on to develop malignant plasma cell dyscrasias in long-term follow-up.

Characteristic Findings of MGUS:
Common monoclonal type IgM, IgG, IgA
Common light chain κ
Quantity <3 g/dL
Urine light chains Rare
Marrow plasma cells <5%
Skeletal lesions Absent
Complete blood cell count Normal
Organomegaly, lymphadenopathy Absent

The most common neurological presentation is a symmetrical sensorimotor polyneuropathy which may be one of three more common subtypes:
1) CIDP phenotype,
2) Distal acquired demyelinating symmetric (DADS) neuropathy, or
3) An axonal sensorimotor peripheral polyneuropathy.

A predominantly sensory neuropathy may be seen in up to 20% of patients. Cranial nerves and autonomic functions are preserved. Sensory impairment can be prominent. Muscle stretch reflexes are universally diminished or absent. The lower limbs are involved earlier and to a greater extent than the upper. Patients with MGUS may improve with IVIG treatment. If not improved, we shall go for more aggressive immunosuppression like cyclophosphamide or rituximab and plasmapheresis may help in some cases.[6]

Patients with MGUS had a 39% higher risk of Acute Myocardial Infarction and a trend for higher risk of CAD, at least 6 months after the time of screening than those without MGUS.[5]

6. Conclusion

Approximately 10% of patients with idiopathic peripheral neuropathy have an associated monoclonal gammopathy. Patients undergoing evaluation for chronic peripheral neuropathy should be screened for the presence of a monoclonal protein (M protein). [4]

Ethical Considerations:
Written informed consent of the patient has been taken during his hospital stay to use this clinical data related to him and to use the photographs of him relevant to this case report publication.

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