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A Case of IgM Multiple Myeloma with Symptomatic Anemia and Extensive Lymphadenopathy

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Abstract **Case Report**

Immunoglobulin M multiple myeloma (IgM MM) is a rare variant of multiple myeloma (MM) accounting for less than 1% of all MM cases. In contrast, the majority of patients with MM demonstrate monoclonal IgG (52%) or IgA (21%) in their serum and urine. The clinical presentation of IgM MM can overlap with that of Waldenstrom's macroglobulinemia (WM), making it challenging to establish an accurate differential diagnosis. In this report, we present a case of IgM multiple myeloma in a patient who exhibited symptomatic anemia, extensive lymphadenopathy, and cytogenetic abnormalities commonly associated with this subtype. We provide a detailed account of the diagnostic evaluation, treatment approach, and subsequent response observed in this patient.

Keywords: IgM multiple myeloma, Waldenstrom's macroglobulinemia (WM), lymphadenopathy.

INTRODUCTION

Multiple myeloma is a plasma cell disorder characterized by clonal proliferation of malignant plasma cells in the bone marrow, leading to monoclonal gammopathy and various clinical features [1]. IgG and IgA are the most common immunoglobulin isotypes found in multiple myeloma, with IgM being a rare subtype. IgM multiple myeloma presents as a distinct clinical entity, posing a diagnostic challenge due to its rarity and varied clinical presentation [2-3]. IgM multiple myeloma accounts for less than 1% of all cases of multiple myeloma and has been reported to have a more indolent clinical course compared to other subtypes.

The diagnosis of IgM multiple myeloma is further complicated by the fact that it can present with nonspecific laboratory findings, such as elevated serum viscosity and serum protein electrophoresis (SPEP) patterns that are not typical of other multiple myeloma subtypes [4-5]. The purpose of this case report is to present a rare case of IgM MM and to address the diagnostic subtleties and treatment strategies associated with this subtype of MM.

CASE PRESENTATION

The case presented here is that of a 43-year-old woman who consulted her primary care physician with complaints of increasing fatigue and a cervical tumor that was progressively enlarging over a 6-month period. Physical examination revealed palpable lymph nodes in the neck, axillae, and groin, as well as splenomegaly. Laboratory examinations revealed a monoclonal peak in the gamma region on serum protein electrophoresis (SPE), with a concentration of 60 g/L. Subsequent immunofixation confirmed the presence of a monoclonal antibody in the gamma region. Subsequent immunofixation confirmed the presence of a cervical tumor. Subsequent immunofixation confirmed the presence of a monoclonal IgM protein. The patient's hemoglobin level was 8 g/dl, and blood calcium, renal, and liver function tests were within normal limits. Urine protein electrophoresis was negative.

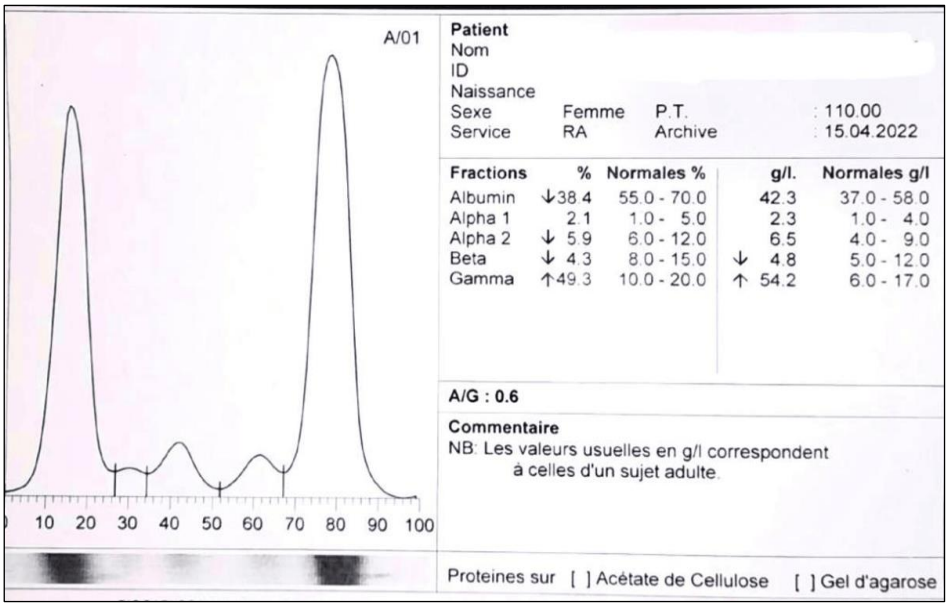

Figure 1: electrophoretic profile at diagnostic with a monoclonal peak at 60g/l

Initially, the patient's condition was suspected to be consistent with Waldenstrom's macroglobulinemia. However, further evaluation, including bone marrow biopsy with immunohistochemistry, revealed a 30% plasma cell infiltration with monoclonal IgM lambda protein. The malignant cells also showed positivity for CD138 and MUM1, consistent with a diagnosis of plasma cell neoplasm. Cytogenetic analysis identified common chromosomal abnormalities associated with IgM multiple myeloma, including a translocation (4;14), a deletion of the P53 locus (17p13), and a trisomy of the CKS1B locus at 1q21. A CT scan of the chest, abdomen, and pelvis demonstrated lymph node enlargement in multiple regions, involving the cervical, hilomedastinal, axillary, intraperitoneal, retroperitoneal, iliac, and inguinal lymphatic chains, and macronodular splenomegaly.

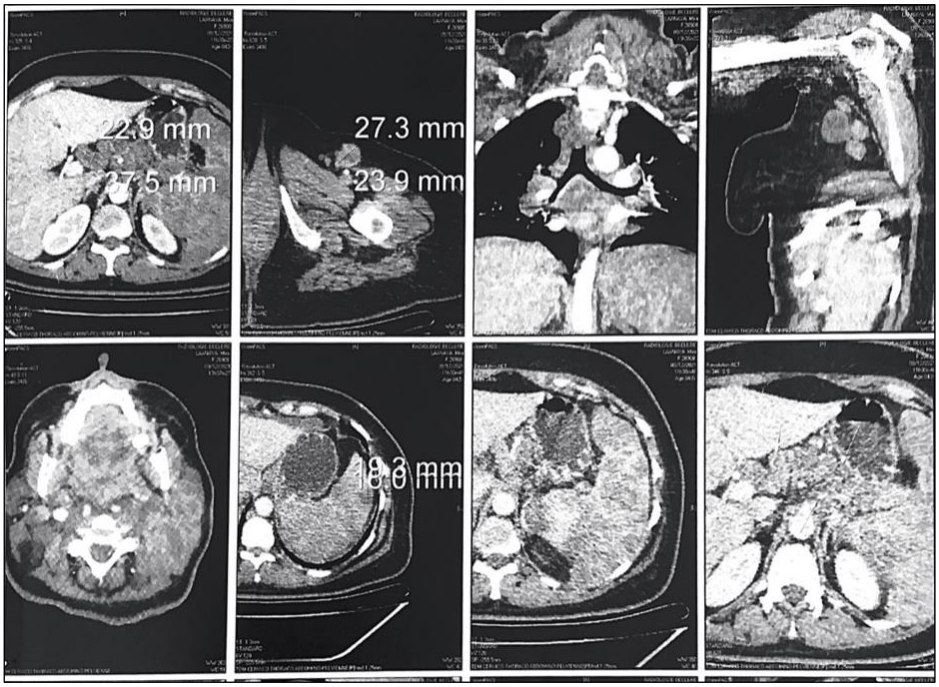

Figure 2: CTAP scan of our patient with adenopathy above and below the diaphragm with splenomegaly

Based on these clinical and laboratory findings, the patient was diagnosed with IgM multiple myeloma, with the monoclonal peak of 60 g/L being symptomatic of the anemia. Of note, there was no evidence of hyperviscosity syndrome despite the presence of a monoclonal IgM peak. Treatment options for IgM multiple myeloma are similar to those for other subtypes of multiple myeloma and include

chemotherapy, immunomodulatory drugs, and stem cell transplantation. In this particular case, the patient received treatment with bortezomib, thalidomide, and dexamethasone, followed by hematopoietic stem cell autotransplantation, resulting in a complete response characterized by disappearance of the monoclonal peak and negative immunofixation at the end of treatment. To maintain this response, the patient is currently receiving subcutaneous injections of Velcade (bortezomib) at a dose of 1.3 mg/m2 every 2 weeks.

DISCUSSION

IgM multiple myeloma is a rare subtype of multiple myeloma that presents a diagnostic challenge. Diagnostic criteria have been developed to facilitate the diagnosis of this rare disease, which includes the presence of monoclonal IgM protein in the serum or urine, more than 10% clonal plasma cells in the bone marrow, and evidence of end-organ damage related to plasma cell disease. Early recognition of IgM multiple myeloma is essential as this disease has a more aggressive clinical course compared to other types of multiple myeloma [6]. The clinical presentation of IgM multiple myeloma can vary widely, with patients presenting with symptoms ranging from anemia, bone pain, and renal dysfunction to neurological symptoms such as peripheral neuropathy and cranial nerve palsies. In some cases, IgM multiple myeloma may be asymptomatic, and diagnosis may be incidental. The diverse clinical presentation of this disease makes it difficult to diagnose and manage [7].

Treatment of IgM multiple myeloma is challenging due to its rarity and lack of standard treatment options. The choice of treatment modality is based on the patient's clinical presentation, stage of disease, and comorbidities. Current treatment strategies for IgM multiple myeloma include chemotherapy, immunomodulatory agents, and stem cell transplantation. However, there is no consensus on the optimal treatment approach for IgM multiple myeloma due to the rarity of the disease and limited data on the efficacy of different treatment regimens [6, 7]. Recent studies have shed light on the pathogenesis of IgM multiple myeloma, revealing that it is due to activating mutations in the MYD88 gene, which is involved in Toll-like receptor signaling pathways. MYD88 mutations are also commonly found in other B-cell lymphoproliferative disorders, including Waldenstrom macroglobulinemia (WM). This genetic similarity between WM and IgM multiple myeloma has led to the exploration of the use of WM therapies, such as the Bruton's tyrosine kinase (BTK) inhibitor ibrutinib, in the treatment of IgM multiple myeloma. Ibrutinib has shown promising results in early clinical trials and has been approved by the US Food and Drug Administration (FDA) for the treatment of WM [8, 9].

CONCLUSION

The diagnosis of IgM MM is particularly challenging because it shares many clinical and laboratory features with other hematologic malignancies, such as WM. However, distinct molecular and genetic abnormalities help differentiate it from other subtypes of MM. MYD88 mutations are frequently found in IgM multiple myeloma and WM, and the use of MYD88-targeted therapies, such as ibrutinib, is a promising therapeutic approach. Further studies are needed to establish the optimal therapeutic approach for IgM multiple myeloma and improve outcomes for patients with this rare disease.

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