Case report

Extramedullary Jaw Mass and Multiple Myeloma: Resource Limitation and its Effect on Diagnostic and Therapeutic Efforts

.

ABSTRACT

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| Non-Hodgkin lymphoma and extramedullary plasmacytoma are some diseases which are known to cause swellings in the head and neck region of the body. Making diagnosis and distinguishing both conditions require biopsy of the tissue for immunohistochemistry, and where immunohistochemistry is unavailable, it presents a diagnostic dilemma.We report the case of jaw swelling in an elderly man; swelling was thought to be non-Hodgkin lymphoma, but patient subsequently had bone marrow aspiration showing multiple myeloma, suggesting the possibility that the jaw swelling was an extramedullary plasmacytoma. The histologic composition of the swelling was not confirmed due to inability to have immunohistochemistry done, however, patient’s swelling reduced significantly following treatment of the multiple myeloma. |

*Keywords: Multiple myeloma, non-Hodgkin lymphoma, immunohistochemistry, extramedullary plasmacytoma, jaw swelling*

1. INTRODUCTION

Plasma cells, which are the primary population of cells that produce immunoglobulins, are terminally differentiated lymphocytes;1 they arise from lymphocytes after the processes of somatic hypermutation and/or perhaps class-switch recombination.2 Due to this singularity in progeny of the plasma cells and lymphocytes, diseases of both cells could be described phenotypically as lymphoplasmacytic, with entities like lymphomas and plasma cell dyscrasias making up this category, and this may cause for confusion in their morphologic diagnosis under light microscopy;3 this is especially true for oral lesions4 in which even immunohistochemistry may not be able to clearly distinguish them.

Multiple myeloma is quite common to haematology practice in this part of the world and predominantly affects elderly patients.5 It belongs in the spectrum of diseases referred to as plasma cell dyscrasias and can be defined by established criteria of biopsy-proven plasmacytoma of bone or soft tissue. Plasmacytoma could be solitary plasmacytoma of bone, SPB or extramedullary plasmacytoma, EMP; though EMPs are quite rare,6 they have been known to mimic lymphomas and it has demonstrated that they involve lymph nodes in 10 – 15% of cases.7 Other criteria for diagnosing MM include monoclonal marrow plasmacytosis of at least 60%, or monoclonal plasmacytosis of at least 10% in the presence of at least 1 of CRAB or SLiM parameters.

2. case report

[(Arial, normal, 10 font, justified) Our patient is a 72 years old retired civil servant who presented to the dental centre of our facility on account of left jaw swelling of 6 months duration; there was also history of episodes of body weakness which necessitated blood transfusions in peripheral facilities, and waist pains. Patient first noticed pain in a tooth in the lower jaw, however, pain resolved followed by swelling, increasing in size in a few months. Histological examination of sections of the mass by the oral pathologists showed proliferating typical lymphocytes arranged in sheets, with sparse intervening fibrous connective tissue; tumour cells were pleomorphic and showed hyperchromic nuclei, increased nucleo-cytoplasmic ratio and frequent mitotic figures. A diagnosis of diffuse non-Hodgkin lymphoma (NHL) was made, and the haematologists were invited. On examination, he was an elderly man who was not in distress, afebrile, not pale, had no palpable peripheral lymphadenopathy, and no pedal oedema; patient however had a firm to soft, nontender, left jaw mass, measuring 10cm x 16cm x 16cm in the widest diameters, with the superior border provided by the lower lips and an imaginary line extending from the angle of the mouth to the lobe of the ear, and the inferior border made by the mass as it extends below the lower edge of the mandible. He was to commence chemotherapy with CHOP pending the result of requested immunohistochemistry to confirm NHL; however, he was unable to provide chemotherapy at this time and also could not have IHC done. Ten days later, he presented with weakness and waist pains, and had urgent full blood count (FBC) which showed Hb of 6.8g/dL; other parameters were within range but platelet count was 96 x 109/L. Peripheral blood film (PBF) findings were significant for microcytic and hypochromic cells which were markedly sparsely distributed. Plan was to optimize the Hb to ≥ 10g/dL and to commence chemotherapy, but patient declined admission, only to represent four days after with complaints of episodes of bleeding per mouth and history of having received 3 units of blood transfusion in a peripheral facility. Urgent FBC done showed Hb of 10.5g/dL and platelets of 27 x 109/L; kidney function test, liver function test plus lactate dehydrogenase measurement were within normal limits; patient was admitted and transfused on two separate days with platelet-rich plasma extracted from 3 donors. He also had a bone marrow aspiration done which showed plasmacytosis making > 90% of marrow nucleated cells, binucleated plasma cells, and mott cells as shown in the figures below.



Figure 1: Wright/Giemsa-stained marrow BMA slide of patient on oil immersion showing numerous plasma cells making >90% marrow nucleated elements



Figure 2: Wright/Giemsa-stained BMA slide of patient on oil immersion showing a binucleated and other plasma cell



Figure 3: Wright/Giemsa-stained BMA slide of patient on oil immersion showing a Mott cell at the 3 o’clock position.

Baseline FLC showed elevated kappa (κ) light chains at 2800mg/L, lambda (λ) chains of 73.2mg/L, with κ/λ of 38.36, while SPE showed components within normal range but an M-protein at 32.4g/dL. Total protein was elevated at 95g/l and albumin was reduced at 28g/L. IHC on the jaw mass tissue for CD138 and CD38 was requested but the patient was also unable to have it done. ECG done showed sinus rhythm, and he was seronegative to HCV, HIV 1&2, HBsAg, and VDRL. He commenced chemotherapy with VRD (Velcade at 2mg on days 1, 8, 15, 22; Revlimid at 25mg on days 1 – 21, Dexamethasone at 40mg on days 1 – 4) 6 days later due to inability to provide the meds earlier, along with tabs allopurinol 300mg daily, tabs Elthrombopag 50mg daily, and tabs Dabigatran 110mg daily. The clinical course of his disease was dotted with numerous episodes of thrombocytopaenia, anaemia, and neutropaenia which were treated at different times with fresh whole blood (FWB) transfusions, platelet-rich plasma (PRP), and neupogen 300mcg daily; he also had intermittent doses of subcutaneous Dabopoietin 65mcg together with iron sucrose 200mg in 250mls of normal saline. He defaulted severally on his chemotherapy and other medications because of financial difficulties; at the time of this report, 2 years since the diagnosis of MM, he has only been able to complete 10 cycles of VRD but with a lot of missed doses of Velcade and Revlimid. Serial FLC in this time has shown reducing κ/λ ratio of 4.28, 1.9, and 3.3, and the jaw mass has reduced in size to 7cm x 5cm in the widest diameters.

3. discussion

[(D Most cases of MM occur in patients who are elderly, with the bulk of these patients being above 65 years of age at time of diagnosis.8 Patients with NHL also fall within this age range. Our patient was 72 at the time of diagnosis, and is the age for most of MM diagnoses. He was referred from anther dental clinic with history of left jaw mass, and also history of waist pains and recurrent blood transfusions for episodes of weakness. Anaemia and osteolytic bone disease are the most common presenting features of MM9 and though the history was not stated, it is likely that index patient had these episodes of weakness and pains in the lumbar region even before the onset of the jaw swelling. Although not quite common but EMP has been documented to be a presenting manifestation of MM in a sizable number of patients, with the incidence differing based on whether a PET/CT scan was done or not.10, 11 Because as many as 15% of cases of EMPs involve the lymph nodes,7 especially in the head, neck, face regions of the body,12 which is the part of the body the swelling was located in index case, there is high likelihood that the mass is an EMP; however, because IHC for CD138 and CD38 has not been done at the time of documentation, we can never be sure.

Lymphomas in the face, head and neck regions of the body are more common in males, and show highest incidence at over 65 years of age,13 as it is in this case. NHL makes about 5% of all tumours in the head and neck region;14 the rapid increase in size, as well as the absence of involvement of any groups of lymph nodes, also support this likelihood, as extranodal NHL makes about 25% of NHL.14 However, patient’s recurrent anaemia is highly unlikely in an individual with isolated extranodal NHL. Some mechanisms by which lymphomas cause anaemia are immune destruction of RBCs, infiltration of the bone marrow in advanced disease, and increase release of inflammatory mediators which cause disturbances in erythropoiesis.15 In this case in which PBF did not show microspherocytes or schistocytes, LDH which was within normal range, as well as the absence of splenomegaly or hepatomegaly, an immune-component to the anaemia is unlikely; we did not request a direct antiglobulin test as patient has been multiply transfused. Marrow infiltration as the cause of the anaemia was also unlikely in this patient who had isolated jaw mass and no organomegaly, if NHL were to be the cause of the marrow failure. However, marrow infiltration with plasma cells, as was confirmed by the BMA that showed plasmacytosis of over 90% of marrow cellular elements, is the plausible cause of failure of the marrow, manifesting as thrombocytopaenia, and anaemia, even before commencement of chemotherapy. Though spontaneous bleeding is unexpected at platelet count of 27 x 109/l, it is most likely that the function of these platelets was disturbed by the paraproteins in his serum.16

Ordinarily, a history of recurrent anaemia necessitating multiple blood transfusions would warrant quick bone marrow aspiration and biopsy, however, this patient presented with histology report that suggested the mass was diffuse NHL, and this made the haematologist not to consider immediate BMA/BMB until there was the episode of mouth bleeds. While difficulty in distinguishing plasma cells from lymphocytes using light microscopy has been documented,3 especially for oral lesions, an IHC which would have made for easier distinction was not done. For same reason, he was only able to receive 10 cycles of VRD after about 20 months, what he should have received in about 10 months. In spite of these challenges, the patient made significant improvement as evidenced by reduction in k/l ratio from 38.38, 4.8 to 1.9 before the 3.3 at the last check, and his less dependence on blood product support, and on neupogen use.

Although bortezomib has shown activity against some diffuse large B cell lymphomas, DLBCL, this activity is not significant enough to improve the survival of such patients when compared with standard R-CHOP regimen;17 similarly, lenalidomide has been demonstrated to have apoptotic activity against follicular lymphoma and mantle cell lymphoma cells,18 and this activity is improved when used in combination with other medications. It therefore follows that VRD regimen, which is traditionally used in the treatment of MM, may have some effect in reducing the size of NHL, however, the significant reduction in size of the swelling in this patient is more likely in a plasma cell-based tumour than in NHL.

4. Conclusion

Extramedullary plasmacytoma (EMP) is a rare presentation of multiple myeloma and can be difficult to diagnose because of its similarities to other conditions like lymphomas. This report highlights the importance of a comprehensively diagnostic workup, including IHC, to differentiate EMP from other conditions. In a resource-limited setting, diagnosing EMP can be difficult, however, histopathological examination and BMA remain essential in making accurate diagnosis.

Ethical approval

Patient details were treated with utmost confidentiality.

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