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Case Report

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Central Nervous System Involvement: A Rare Detour for Myeloma Cells-Case Report of an Usual Presentation!

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Abstract:

Extramedullary involvement in multiple myeloma (MM) is seen in 7%–18% of cases. The common organs involved are skin and upper respiratory tract. The uncommon organs involved include the liver, spleen, kidney, pleura, lymph nodes, and soft tissue. Central nervous system (CNS) involvement is extremely rare and occurs in only about 1% of patients. We present an interesting case of nonsecretory MM (NSMM) with atypical involvement of the liver, spleen and CNS. An elderly female patient initially presented with low backache. Skeletal survey showed multiple lytic bony lesions. An initial diagnosis of plasma cell neoplasm was made based on the biopsy of the sacral lytic lesion. No monoclonal gammopathy was found in the serum or urine electrophoresis. A diagnosis of NSMM was made and the patient was started on bortezomib, dexamethasone, lenalidomide (VRD regime). However, over the next 2 months or so, the patient was found to have involvement of liver, spleen, and meninges on imaging despite chemotherapy. The plasmablastic lesions were confirmed on liver biopsy, bone marrow, and cerebral spinal fluid study. Patient showed remarkable clinical improvement on addition of daratumumab to the VRD regime and is currently under maintenance therapy. Repeat imaging shows the reduction in lytic lesions. This case is reported as a rare combination of NSMM with CNS involvement.

Keywords:

Central nervous system, extramedullary, multiple myeloma, nonsecretory, plasmacytoma

Introduction

Multiple myeloma (MM) is malignant proliferation of plasma cells primarily in their native abode, i.e., bone marrow (BM). The most common manifestation of bone involvement is in the form of osteolytic lesions.[1] A total of 7%–18% of MM cases are associated with extramedullary (EM) involvement, which may be discovered at baseline, during disease, or at relapse.[2] EM plasmacytoma can occur in any tissue or organ, however, the common sites include skin, nasal cavity, paranasal sinus, nasopharynx, oropharynx, and larynx.[3] Other less common sites of involvement include the liver, spleen, kidney, pleura, lymph nodes, soft tissue.[4] Rarely, central nervous system (CNS) involvement has also been reported but is seen in only about 1% of patients.[5] Our case here is a rare combination of nonsecretory MM (NSMM) with the atypical spread in an elderly female. NSMM cases are noted to have better outcomes and better responses to chemotherapy due to a lack of secretory immunoglobulins.[6] However, our patient behaved differently and was found to be refractory to first-line chemotherapy leading to the continued spread of disease to the liver, spleen, and CNS. The case is reported for its unique presentation and rarity.

Case Report

A 59-year-old female, known case of type 2 diabetes mellitus, presented with pain in left gluteal region, low backache and

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numbness of left thigh for past 2–3 months. She was evaluated at her native place and her initial laboratory results revealed a hemoglobin of 8.8 g/dL, with normal leukocyte and platelet count (4.8×10^3/μL and 192×10^3/μL, respectively). Peripheral blood smear showed normocytic normochromic anemia, normal differential, and no significant rouleaux formation or background staining. Other relevant investigations were – erythrocyte sedimentation rate of 39 mm in 1st h, blood urea nitrogen - 12.2 mg/dL, creatinine - 1.2 mg/dL. Total protein - 6.4 g/dL, albumin 1.89 g/dL, serum calcium - 10.8 mg/dL (corrected - 12.1 mg/dL) and lactate dehydrogenase - 262 U/L. Further evaluation at our center with magnetic resonance imaging (MRI) scan revealed multiple irregulars homogenously enhancing lytic lesion with associated soft tissue component involving the left side of S2, S3, S4 vertebra with encasement of nerve roots and presence of similar lytic lesions in the bilateral sacrum, iliac bones, ischium, and lumbar vertebral bodies. A tru-cut biopsy was done from sacral lytic lesion which showed diffuse sheet of plasma cells. The same was confirmed on immunohistochemistry (IHC) (CD 20 negative, CD 38 Positive, CD 138 positive with lambda restriction). The myeloma panel revealed no M spike on urine/serum electrophoresis or immunofixation. Free kappa and lambda light chains in serum were 15.1 mg/L and 62.7 mg/L respectively with a kappa/lambda ratio of 0.241. The patient was labeled as NSMM (multiple lytic lesions with biopsy-proven plasmacytoma in absence of M spike) and was started on bortezomib, dexamethasone, lenalidomide (VRD regimen). Prognostic markers included beta 2 microglobulin of 3.178 mg/L and normal cytogenetic studies (Negative for translocation t (4:14), t (11:14), t (14,16), 13qdel, 17p del and TP53).

After about 1.5 months of starting chemotherapy, she started complaining of right frontal headache, decreased sensation on the right side of the face and angle of the mouth, and double vision. A positron emission tomography scan done at this juncture showed multiple metabolically active lytic lesions in the liver, spleen, and lungs. MRI brain done showed meningeal involvement with dural deposits. Such atypical organ involvement raised suspicion of epithelial malignancy (? Concurrent). Blood counts at this stage showed Hb of 7.2 g/dL, leukocyte count of 2.1×10^3/μL and platelet count of 75×10^3/μL. PBS showed pancytopenia with 6 nucleated red blood cell/100 white blood cell (WBC). No plasma cells or rouleaux seen on the smear. An urgent cerebral spinal fluid (CSF) tap, liver biopsy, and BM biopsy were done to reconfirm the primary diagnosis and to rule out any other concurrent pathology if any. BM was hypercellular and showed sheets of markedly pleomorphic cells which looked like plasmablasts [Figure 1]. Liver biopsy showed multiple foci of similar sheets of plasmablastic cells along with normal preserved hepatocytes [Figure 2a]. IHC was performed individually on BM and liver biopsy which confirmed plasma cell origin and ruled out suspicion of any concurrent epithelial lesion (CD 38/138 positive with lambda restriction and negative for PanCK, EMA, CD20, vimentin, CD99, Synaptophysin, melan A) [Figure 2b-e]. CSF study showed cellular fluid with WBC count of 250 cells per microlitre. Many atypical large plasmablasts with similar morphology as in BM were noted [Figure 3]. Cellblock was prepared from residual fluid which confirms plasmablastic morphology. Flowcytometry and IHC could not be done on CSF fluid. A final diagnosis of highly aggressive NSMM with EM involvement (liver, spleen, and CNS) was made, following which daratumumab (anti CD38 monoclonal Ab) was added to the VRD regime. The patient started responding to the treatment slowly over the next 2 months. Repeat imaging showed reduction in lytic lesions. She is currently under treatment and regular follow-up at our center.

Discussion

NSMM is a diagnostic challenge for pathologists due to the absence of biochemical markers. The final diagnosis relies on morphology, IHC or multiparametric flowcytometry in such cases.[6] The diagnosis may get further complicated by factors like inadequate BM sampling, atypical morphology of plasma cells or if uncommon organs are involved as it was seen in our case detailed above. Dissemination of plasma cells through the hematogenous route may lead to the involvement of practically any organ (liver, spleen, kidney, lungs, and nervous system) in the body.[7] CNS involvement is defined as the presence of plasma cells in cerebrospinal fluid and/or leptomeninges, duramater, or intraparenchymal involvement as confirmed by imaging or histopathology.[7] We demonstrated the presence of plasmablastic cells in CSF in our case. Imaging studies also corroborated with morphological findings.

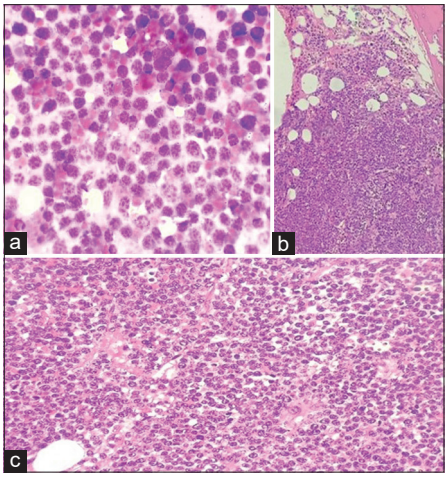

Figure 1: (a) Leishman Giemsa (×100) stained bone marrow imprint smears showing complete replacement by sheets of markedly pleomorphic plasmablastic cells. (b and c) hematoxylin and eosin stained (×10 and × 40) microphotograph depicting hypercellular bone marrow with complete replacement with plasmablastic cells

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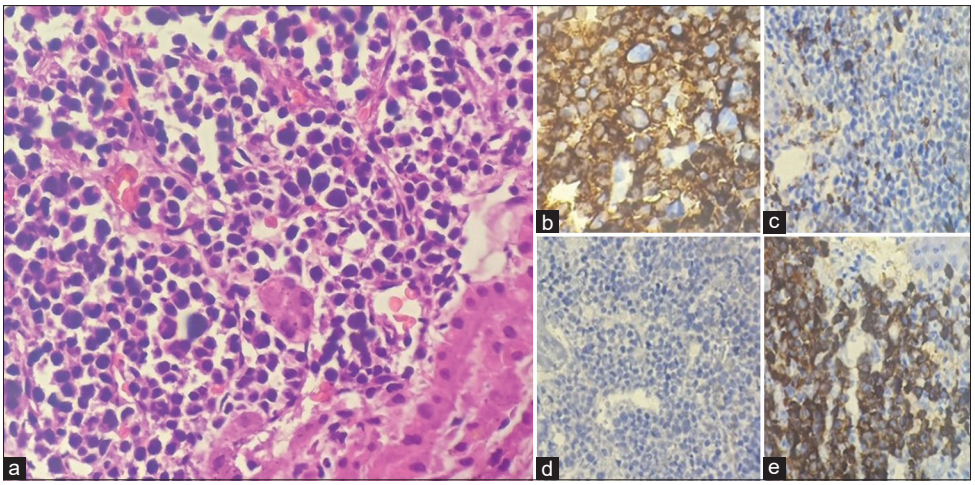

Figure 2: (a) H and E (×40) microphotograph of liver biopsy depicting infiltration by plasmablastic cells. Normal residual hepatocytes can be seen at right bottom. (b-e) Immunohistochemistry on liver biopsy shows cells to be positive for CD 138 (b) with lambda restriction-(c), CD 45 (e) and kappa (d) are negative

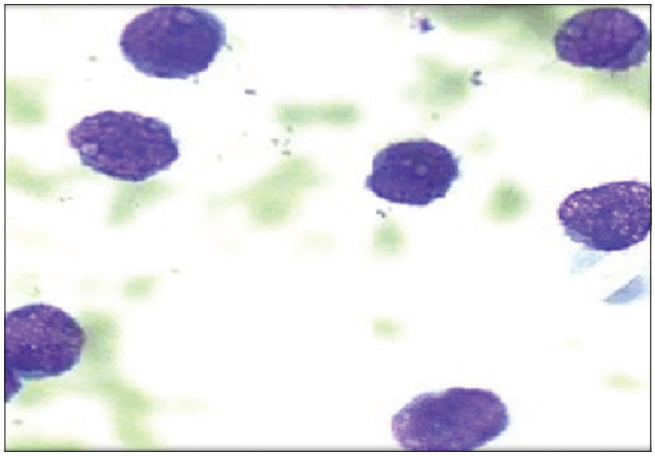

Figure 3: Leishman Giemsa stained (×100) microphotograph of cerebral spinal fluid deposit showing cellular smears with atypical plasmablastic cells in cerebral spinal fluid

Given the rarity of NSMM in the overall MM population, its clinical course and prognosis are still not thoroughly characterized. Added CNS involvement makes it further doomed for poor survival.[8] Current therapeutic approaches appear to be largely ineffective for this subset of patients with MM, however, targeted therapy in the form of novel agents (e.g., daratumumab) have recently shown promising results.[9] The dilemma in this subset of patients continues during monitoring of response too, due to the absence of measurable biochemical markers. Serial imaging studies or BM studies could be the gold standard, but the cost, time, and patient discomfort associated make them less desirable.[10]

Conclusion

NSMM with uncommon organ involvement poses a diagnostic dilemma owing to its low incidence and scant supporting biochemical markers. It is essential for clinicians to keep an open mind for atypical presentations in such cases. Imaging and IHC are cornerstones in diagnosing such challenging cases.

Ethical approval

Written informed consent of patient in case obtained.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Bladé J, Fernández de Larrea C, Rosiñol L, Cibeira MT, Jiménez R, Powles R. Soft-tissue plasmacytomas in multiple myeloma: Incidence, mechanisms of extramedullary spread, and treatment approach. J Clin Oncol 2011;29:3805-12.
2. Usmani SZ, Heuck C, Mitchell A, Szymonifka J, Nair B, Hoering A, *et al*. Extramedullary disease portends poor prognosis in multiple myeloma and is over-represented in highrisk disease even in the era of novel agents. Haematologica 2012;97:1761-7.
3. Castro EB, Lewis JS, Strong EW. Plasmacytoma of paranasal sinuses and nasal cavity. Arch Otolaryngol 1973;97:326-9.
4. Varettoni M, Corso A, Pica G, Mangiacavalli S, Pascutto C, Lazzarino M. Incidence, presenting features and outcome of extramedullary disease in multiple myeloma: A longitudinal study on 1003 consecutive patients. Ann Oncol 2010;21:325-30.
5. Fassas AB, Ward S, Muwalla F, Van Hemert R, Schluterman K, Harik S, *et al*. Myeloma of the central nervous system: Strong association with unfavorable chromosomal abnormalities and other high-risk disease features. Leuk Lymphoma 2004;45:291-300.

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6. Low SF, Mohd Tap NH, Kew TY, Ngiu CS, Sridharan R. Non secretory multiple myeloma with extensive extramedullary plasmacytoma: A diagnostic dilemma. Iran J Radiol 2015;12:e11760.
7. Paludo J, Painuly U, Kumar S, Gonsalves WI, Rajkumar V, Buadi F, *et al.* Myelomatous involvement of the central nervous system. Clin Lymphoma Myeloma Leuk 2016;16:644-54.
8. Avet-loiseau H, Garand R, Lodé L, Harousseau J, Bataille R, Dc W, *et al.* Nonsecretory multiple myeloma variants Brief report Translocation t (11 ; 14)(q13 ; q32) is the hallmark of IgM , IgE , and nonsecretory multiple myeloma variants. Blood 2013;101:1570-1.
9. Katodritou E, Terpos E, Kastritis E, Delimpasis S, Symeonidis AS, Repousis P, *et al.* Lack of survival improvement with novel anti-myeloma agents for patients with multiple myeloma and central nervous system involvement: The Greek Myeloma Study Group experience. Ann Hematol 2015;94:2033-40.
10. Corso A, Mangiacavalli S. Non-secretory myeloma: Ready for a new definition? Mediterr J Hematol Infect Dis 2017;9:1-7.