CASE REPORT

Clear Cell Myeloma - A Rare Histopathological Variant of a Common Disease

Neha Agarwal, T. Mitila, Ganthimathy Sekhar

Abstract:
Multiple myeloma (MM) is characterized by neoplastic proliferation of plasma cells and monoclonal immunoglobulin production. Clear-cell myeloma is an exceptionally rare histopathological variant of MM, with only ten cases reported worldwide. We present one such case in a 67-year-old female, presenting as a soft tissue osteolytic lesion in the thoracic vertebrae. The final diagnosis was made with the help of histopathological examination, immunohistochemical and hematological features, along with protein electrophoresis and serum free light chain assay. We aim to emphasize its importance as a differential diagnosis for clear cell neoplasms, as timely chemotherapeutic intervention improves the survival rate.

Keywords:
Clear-cell myeloma, Multiple myeloma

Introduction

Clear cell myeloma (CCM) is a rare histopathological variant of multiple myeloma (MM) first reported by Chen et al in 1985.[1] MM is characterized by neoplastic proliferation of plasma cells and monoclonal immunoglobulin production.[2] Most MMsare composed of plasma cells with characteristic cytomorphology easily recognizable on microscopic examination. Rarely, they may present with an aberrant cytomorphology posing a diagnostic challenge.[3]

Case Presentation

A female in her sixties presented with complaints of pain in the mid-back for the past six months. There was no history of radiating pain, heaviness, tingling, numbness/ paraesthesia in bilateral upper or lower limbs. No history of evening rise of temperature, loss of weight or appetite, cough with expectoration, early morning stiffness, urge/ stress incontinence was elicited from the patient. The patient had a past history of a slip and fall, five years ago, due to which she sustained a D6 burst fracture for which she underwent posterior stabilization with instrumental fusion. She is a diabetic on treatment for the last six years. On local examination, kyphosis and a healthy, healed surgical scar was noted. On palpation, there was no swelling felt but diffuse tenderness was elicited over the D4-D8 vetebrae. Distal pulses were felt. The range of movement and power of the bilateral lower limbs were 5/5. Straight leg raising test was negative and sensations were intact in both the lower limbs.

Investigations

Patientwas mildly anaemic with a haemoglobin of 11.4g/ dl. The peripheral smear examination showed the presence of predominantly microcytic hypochromic red blood cells and increased rouleaux formation (Fig.1A). The platelet and total leukocyte count were within normal limits. Patient had elevated levels of ESR (120 mm at the end of 1 hour) and CRP (66.08mg/l). Random Blood Sugar was 367mg/dl and HbA1C was 16.5%. Renal function test showed elevated S.Urea levels of 40mg/dl. Levels of S.Creatinine, electrolytes, liver function tests and coagulation profile were within normal limits. Patient underwent a whole spine MRI with contrast (Fig.1B) and PET-CT (Fig.1C) which showed a soft tissue mass

Department of Pathology, Saveetha Medical College, Chennai, Tamil Nadu, India

Correspondence to: Dr. T. Mitila, Postgraduate, Department of Pathology, Saveetha Medical College, Chennai,Tamil Nadu, India

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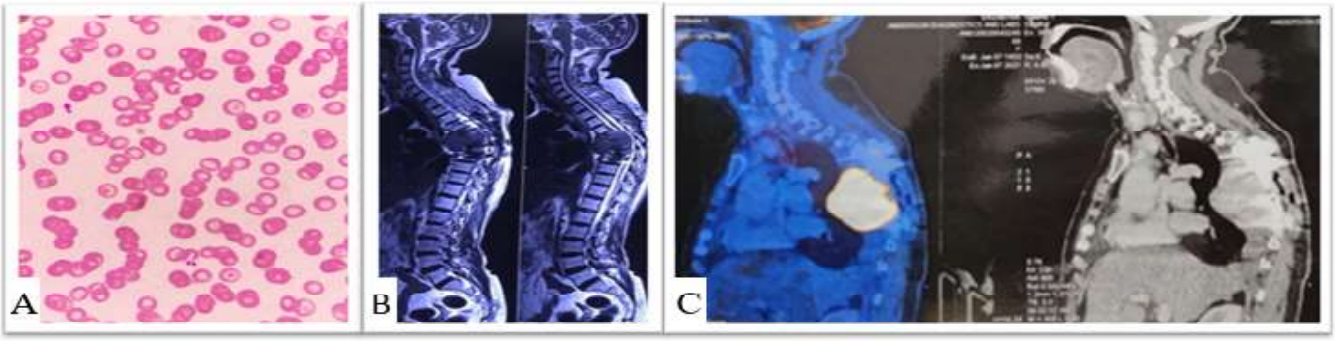

Fig.1 (A) Peripheral smear showing predominantly microcytic hypochromic RBCs with increased rouleaux formation. (B) MRI with contrast showing a hetero-intense soft tissue lesion causing destruction of D4,D5,D6 vertebrae. (C) PET CT showing a soft tissue mass causing destruction of the mid dorsal vertebrae.

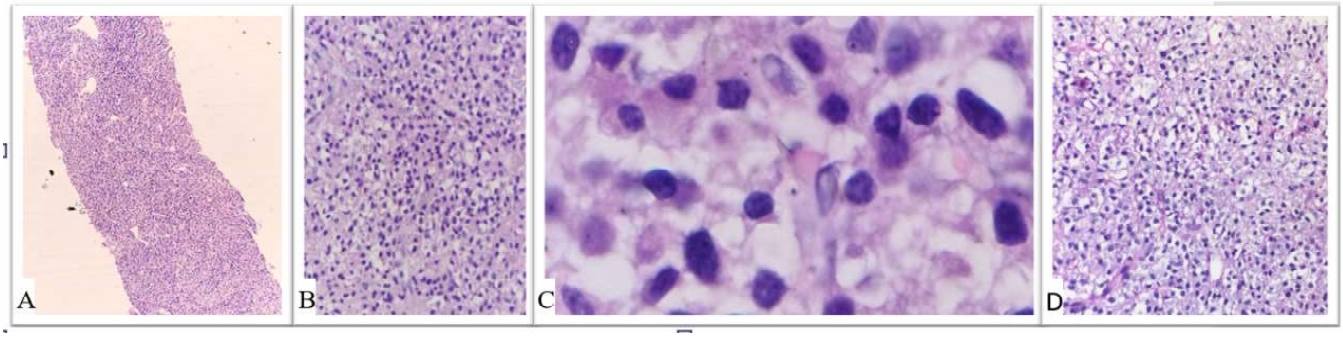

Fig.2 (A) H&E 4x B) H&E40x Vague lobular and diffuse sheets of polygonal cells with moderate amount of clear cytoplasm and round to oval centrally located nuclei with clumped chromatin. (C) H&E 100x Few binucleate cells and occasional hyaline globules were seen. (D) PAS 40x Clear cells were not stained.

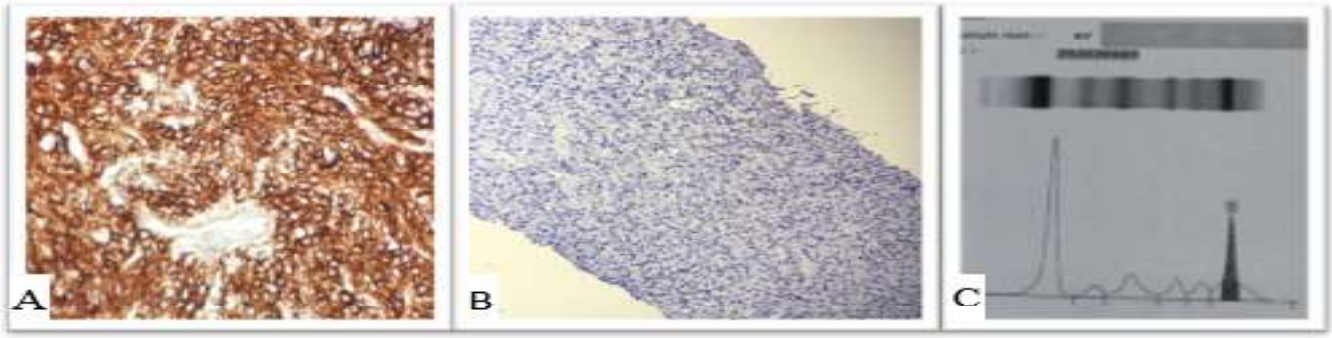

Fig.3 (A) Strong cytoplasmic membrane positivity for CD 138 in 90% of cells. (B) panCk – Negative (C) "M" Spike in ã-globulin region of serum protein electrophoresis.

causing destruction of the mid-dorsal vertebrae with features highly suggestive of a malignant neoplastic lesion. A biopsy was taken from the same and sent for microbiological and histopathological examination (HPE). Culture-sensitivity of the tissue elicited no growth of either acid-fast bacilli or fungal elements. HPE of the biopsy specimen showed vague lobular and diffuse sheets (*Fig.2A*) of polygonal cells with moderate amount of clear cytoplasm and round to oval centrally located nuclei with clumped chromatin (*Fig.2B*). Few binucleate cells and occasional hyaline globules were present (*Fig.2C*). No areas of necrosis or hemorrhage were seen in the specimen received. Staining with Periodic acid-Schiff (PAS) was negative (*Fig.2D*). Based on the above findings, the differential diagnoses considered were metastatic clear cell neoplasm and clear cell variant of MM. Immunohistochemicalstaining showed strong cytoplasmic membrane positivity in 90% cells for CD138 (*Fig.3A*) and faint patchy focal positivity for SMA. However, staining for panCK (Fig.3B), CK7, CK20,

CD45, S100, p63, Synaptophysin, Chromogranin, HMB45 and CD34 was negative. Nuclear positivity for Ki-67 was seen in 10-12% cells. Serum protein electrophoresis was done and showed a "M"spike (*Fig. 3C*) in the gamma-globulin region, with elevated M protein levels of 150g/l. Serum free light chain (SFLC) assay revealed elevated levels of Kappa free light chain of 7.30g/l and an involved-to-uninvolved SFLC ratio of 470. Based on the above biochemical, histopathological and IHC results; along with elevated levels of serum M protein and kappa free light chain, osteolytic bone lesions in MRI and PET-CT and the absence of a renal mass on USG, a diagnosis of CCM was made. We also did a retrospective analysis of the duration and concentration of reagents used for tissue processing in this case to eliminate the possibility of an artefactual change due to underfixation by formalin asreported by Kotru M et al and Pandey V *et al*.[4,5]. This artefactual clearing can further be ruled out by a strong positivity on staining with ubiquitin and a high alkaline phosphatase score as reported by Svec *et al*.[6]

Discussion

Most MMs are composed of plasma cells with characteristic cytomorphology easily recognizable on microscopic examination.[3,7] Rarely, they may present with an aberrant cytomorphology and/or architecture posing a diagnostic challenge, leading to an imprecise diagnosis.[3,5,7]. The spectrum of of MM variants reported in literature include a polymorphous variant with an aggressive clinical course having cleaved, multilobated monocytoid cells; a pleomorphic variant which mimics anaplastic carcinoma/anaplastic large cell lymphoma and a blastic variant composed of plasma-blasts or cells resembling those in large cell non-hodgkin's lymphoma.[3,7-8] The cytomorphological variations seen in the plasma cells of MM consist of clear cells, signet ring cells, small cell type, histiocytoid cells, spindle cells, cells with oncocytic change and one case where the neoplastic cells seemed to resemble erythrocyte laden macrophages.[3,5] The clear cell variant of MM was first reported by Chen *et al*. in 1985 who initially misdiagnosed it as liposarcoma.[1] An extensive literature review revealed only 10 other reports of cases of MM with clear cell change and one case report of MGUS with vacuolar change.[1,5,6,9,10] Including the current case only 2 cases of CCM have been reported in females and 10 cases have been diagnosed in males to date.[1,5,6,9] All the cases including the current case were reported in individuals above 50 yrs of age except for 1 case published by Eyden BP *et al*. in 1990 which was reported in a 44-year-old male.[9] Elevated M-protein levels were seen in majority of the cases and all the cases exhibited serum free light chain restriction.[1,5,6,9] Three of the reported cases were stained with acid phosphatase and were found to be positive indicating that misfolded proteins were responsible for the clear cell change seen and that it was not an artefact.[6]

Conclusion

CCM is an extremely rare variant of MM that needs to be kept in mind whenever we encounter a tumor composed of clear cells. Its rarity emphasizes the importance of ruling out metastatic clear cell neoplasms especially clear cell renal cell carcinoma and eliminating the possibility of artefactual cytoplasmic clearing due to under fixation by formalin during tissue processing by doing ubiquitin and alkaline phosphatase staining prior to making a diagnosis of CCM.

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Conflicts of Interest

There are no conflicts of interest.

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