



Multiple Myeloma with Cutaneous Amyloidosis: A Case Report

Authors

Dr Harsha¹, Dr Shama Prakash K²

¹Junior Resident, Department of Medicine, K S Hegde Medical Academy

²Associate Professor, Department of Medicine, K S Hegde Medical Academy

Abstract

Multiple myeloma is a plasma cell disorder characterized by clonal proliferation and monoclonal immunoglobulin production. The disease manifestations are secondary to direct invasion of plasma cells and excessive light chain production. AL amyloidosis is seen in Multiple myeloma due to light chain deposition. Here we report a case of elderly male presented with multiple swellings and dark pigmentation around both eyes and progressive weakness and stiffness in both limbs diagnosed to have Multiple myeloma with cutaneous and systemic amyloidosis.

Keywords: Multiple myeloma, AL amyloidosis, Cutaneous amyloidosis.

Introduction

Multiple myeloma (MM) is a plasma cell disorder characterized by malignant clonal proliferation of plasma cells producing monoclonal immunoglobulins. MM forms 1% of all the malignancies and 10% of all hematological malignancies. The global age standardized incidence rate is 2.1 per million at 95% CI¹. Raising incidence and prevalence of MM can be attributed to better diagnostic techniques and treatment. It is slightly more common in men than woman with approximately 1.4:1 ratio. Median age of diagnosis is 66 years and only 10% are less than 50 years and 2% less than 40 years of age^{2,3}. Most of the symptoms of MM are due to infiltration of plasma cells and excess light chains. Immunoglobulin light chain (AL) amyloidosis where in monoclonal light chains deposit in various organs can be seen in patients with MM. Here we report a case of Multiple myeloma with cutaneous and systemic amyloidosis.

Case Report

A 58 year old gentleman with no previous comorbidities presented to us with multiple round swellings over both eyelids since 6 months and progressive weakness in both lower limbs and stiffness with pain in both hips and knees since 3 months. On examination he was moderately built and poorly nourished, conscious and oriented. He was pale, no lymphadenopathy, no edema. There were multiple nodulopapular swellings on both eye lids which were non tender non pruritic. Conjunctivae were congested with mucopurulent discharge and left eye corneal ulcer. Bilateral knee fixed flexion deformity of 50°, contracture of the hamstring muscles, power in both upper limbs was normal, lower limbs was 4/5, deep tendon reflexes in both lower limbs were sluggish, sensations intact. Abdominal examination revealed no hepatosplenomegaly. Respiratory system cardiovascular system examinations were unremarkable.

Laboratory Investigations: Severe Anemia with Hemoglobin of 7.7 g/dL, Total Leucocyte Count of 6300 per cubic millimeter with 86% neutrophils, 13% lymphocytes and 1% eosinophils, Platelet count of 214000 per cubic millimeter and an elevated ESR of 80 millimeters in the first hour. Peripheral blood smear showed, predominantly microcytic hypochromic RBCs with mild anisopoikilocytosis and short rouleaux formations, WBCs were normal in number, with neutrophilic predominance, platelets were adequate and no abnormal cells or hemoparasites. Serum total protein was 8g/dL, Albumin: 3.2g/dL, Globulin: 4.8g/dL, Albumin/Globulin ratio: 0.67, Total Bilirubin: 0.9 mg/dL, Direct Bilirubin 0.37 mg/dL, AST 61 U/L, ALT 15 U/L and ALP 127 U/L. Blood Urea 103.2 mg/dL, Creatinine 3.29 mg/dL, Uric Acid 13.9 mg/dL, Sodium 128 mmol/L, Potassium 4.25 mmol/L, Serum Calcium 18.5 mg/dL, Urine Analysis showed trace protein, No RBCs, 4-6 WBCs. Serology for HIV, HBsAg and HCV were negative. LDH was 137 U/L and Beta-2 Microglobulin 10.84 mg/L (0.8-2.2). Parathormone was 3.61 pg/ml (12-88 pg/ml) and Thyroid Stimulating Hormone was 6.39 uIU/mL. Serum Protein Electrophoresis: Albumin level was normal, and there was significant increase in gamma globulin levels, M spike was noted in gamma region with M band on the electrophoretogram.

Fluorescence in situ hybridization (FISH) analysis of bone marrow aspirate: Negative for Del 17p (TP53), IgH Gene rearrangement, FGFR3-IGH/t(4;14), IGH/MAFB/t(14;20) and IGH-MAF/t(14;16)

Bone Marrow Aspiration cytology showed features of erythroid hyperplasia and multiple myeloma, with 15% plasma cells. Bone Marrow Biopsy showed features of MM with collections of plasma cells with interstitial pattern of infiltration, along with few binucleated plasma cells and occasional plasma blasts.

MRI Lumbosacral spine with pelvis showed diffuse heterogeneously altered signal intensity involving multiple vertebral bodies. Left

paracentral disc extrusion at L4-L5 level indenting the thecal sac and compressing on the left traversing/ exiting nerve root. Disc extrusion with inferior migration at L5-S1 indenting the thecal sac and compressing on the right traversing nerve root. Thickening of bilateral hip joint capsule. Ill defined altered signal intensity focus was noted in head and neck of the left femur measuring around 3.5x2.5cm, which was hypointense on T2 weighted sequences and hyperintense on STIR sequences. Ill defined hyperintensity was also noted in the neck of right femur. Loculated fluid signal intensity collection measuring 3x2.7cm in the left iliopsoas and another measuring 1cm in the right iliacus muscle and ill defined STIR hyperintense signal noted in bilateral iliacus and gluteus muscle.

Eye lid lesion biopsy showed normal epidermis, edematous dermis with multiple epidermal inclusion cysts lined by stratified squamous epithelium containing accumulation of laminated keratin with Congo red positive deposit.

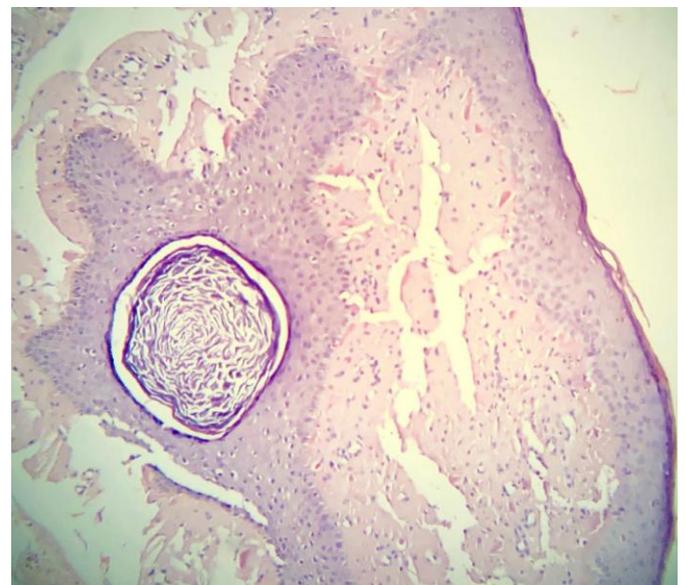


Figure 1: Eye lid biopsy in hematoxylin and eosin stain showing inclusion cyst lined by stratified squamous epithelium containing keratin.

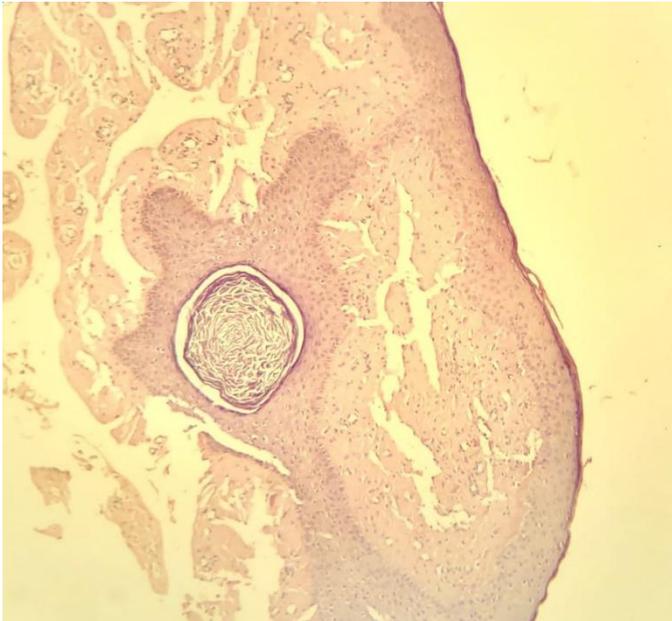


Figure 2: Eye lid biopsy in Congo red stain showing inclusion cyst lined by stratified squamous epithelium containing keratin and Congo red positive deposit.

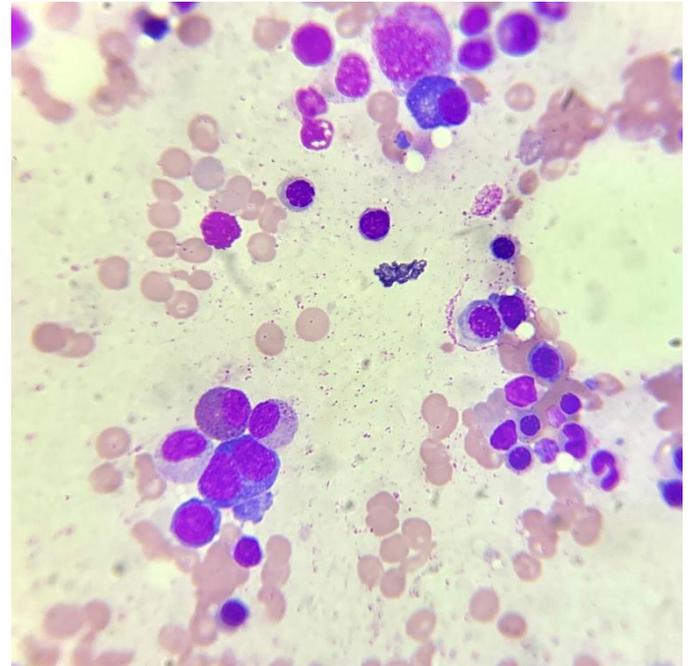


Figure 4: Bone aspiration cytology showing plasma cells.

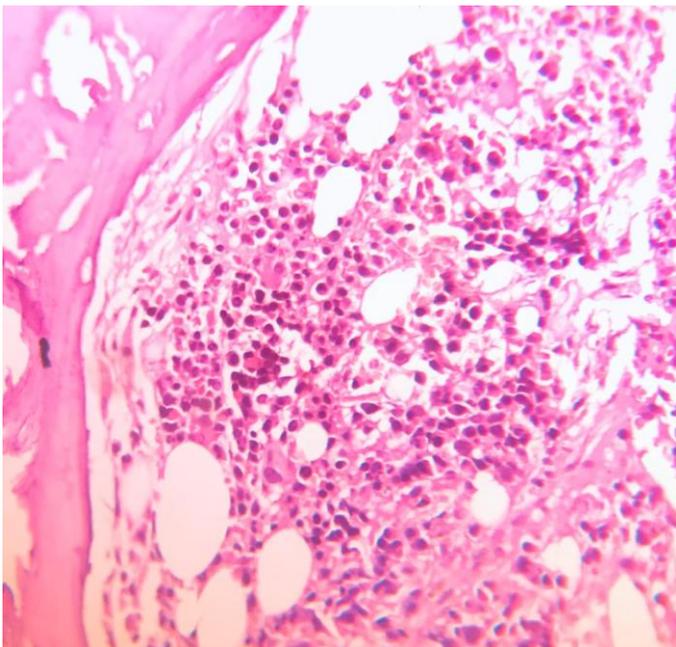


Figure 3: Bone marrow biopsy showing collection of plasma cells.



Figure 5: Multiple waxy nodulopapular swellings on both eye lids with purulent discharge

Discussion

Diagnostic criteria for Multiple Myeloma by International Myeloma Working Group⁴

1. Hypercalcemia: Serum calcium 1mg/dL more than the upper limit of normal or more than 11mg/dL
2. Renal impairment: Serum creatinine more than 2mg/dL or creatine clearance less than 40 ml per minute
3. Anemia: Hemoglobin more than 2g/dL below the lower limit of normal or less than 10g/dL
4. Bone lesions: One or more osteolytic lesion on X-ray, CT, or PET-CT

Any one or more of the following biomarkers of malignancy:

- Clonal bone marrow plasma cell percentage $\geq 60\%$
- Involved: Uninvolved serum free light chain ratio ≥ 100
- >1 focal lesions on MRI studies

Amyloidosis is a condition in which there is extracellular deposition of misfolded insoluble protein fibrils in the various organs and tissues. Amyloid diseases are grouped based on biochemical composition of the deposited fibrils, site of deposition- systemic or localized, familial or acquired and their clinical presentations.

The following are most commonly described systemic amyloid diseases: a) AL type, Primary Systemic Amyloidosis arising from clonal B cells or Plasma cells due to deposition of Immunoglobulin light chains and are associated with MM or lymphomas. b) AF type, Familial Amyloidosis caused by mutation in the transport protein of thyroid hormone and retinol-binding protein- transthyretin. c) AA type, Secondary Systemic Amyloidosis occurs in the setting of chronic inflammatory conditions due to deposition of Serum amyloid A, an acute phase reactant. d) $A\beta_2M$ type seen in patients on long term hemodialysis due to deposition of misfolded β_2 Microglobulin.

AL Amyloidosis

It is the most common type of systemic amyloidosis which is secondary to deposition of Ig light chains and is associated with MM or B cell lymphomas. It is generally seen after the age of 40 years and usually rapidly progressive and fatal if left untreated. The deposition can occur in any tissue or organ other than central nervous system and the deposits are composed of full light chains or their fragments along with glycosaminoglycans, amyloid p components and metal in ionic forms. The clinical presentation is based on the organ involved with kidneys being the most commonly involved. Cardiac

amyloidosis would manifest with cardiac failure secondary to restrictive cardiomyopathy.

Cutaneous amyloidosis can be localized cutaneous amyloidosis or systemic amyloidosis with cutaneous involvement. Cutaneous amyloidosis is seen in 40% cases with AL type amyloidosis and manifestation depends on site of deposition⁵. Most common forms are petechiae, purpura and ecchymosis and more rarer forms are shiny, waxy, macular, nodulopapular lesions⁶. Our patient presented with nodulopapular lesions around the eye even prior to onset of systemic symptoms. Our patient also had features of amyloid arthropathy of hip joint.

Conclusion

AL amyloidosis carries poor prognosis. Many a times cutaneous manifestation in systemic amyloidosis may precede systemic manifestations, hence, it is necessary to be familiar with spectrum of cutaneous manifestations of AL amyloidosis and to investigate at the earliest for diagnosis, treatment and prognostication.

Bibliography

1. Cowan AJ, Allen C, Barac A, Basaleem H, Bensenor I, Curado MP, et al. Global Burden of Multiple Myeloma: A Systematic Analysis for the Global Burden of Disease Study 2016. *JAMA Oncol.* 2018 Sep 1;4(9):1221–7.
2. Bladé J, Kyle RA. Multiple Myeloma in Young Patients: Clinical Presentation and Treatment Approach. *Leuk Lymphoma.* 1998 Jan 1;30(5–6):493–501.
3. Kyle RA, Gertz MA, Witzig TE, Lust JA, Lacy MQ, Dispenzieri A, et al. Review of 1027 Patients With Newly Diagnosed Multiple Myeloma. *Mayo Clin Proc.* 2003 Jan 1;78(1):21–33.
4. Jameson JL, editor. *Harrison's principles of internal medicine.* Twentieth edition. New York: McGraw-Hill Education; 2018. 2 p.

5. Saoji V, Chaudhari S, Gohokar D. Primary systemic amyloidosis: Three different presentations. Indian J Dermatol Venereol Leprol. 2009 Jul 1;75(4):394.
6. Wong C-K. Mucocutaneous manifestations in systemic amyloidosis. Clin Dermatol. 1990 Apr 1;8(2):7-12.