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Plasma cell infiltration of skin and pleural fluid: A case report on an unusual presentation of myeloma

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Abstract
Multiple myeloma is a plasma cell neoplasm associated with features of hypercalcemia, renal dysfunction and acquired immune abnormalities. We are reporting a rare case of an 80-year-old multiple myeloma patient with progressive disease with standard chemotherapy and developed cutaneous nodular lesion and pleural effusion. Biopsy of the skin nodule and pleural fluid cytology was suggestive of myelomatous infiltration. Simultaneous pleural and skin involvement is rarely reported in the literature.
Such cases are scarcely reported, poorly understood and thus we intend to add to the scientific committee.

Keywords: Myeloma, plasma cells, skin infiltration, case report

Introduction
Multiple myeloma is a malignancy caused by abnormal proliferation of plasma cells which produce multiple lytic lesions in the various bones in the body. The malignancy accounts for approximately 10% of hematologic malignancies [1]. The plasma cells most often invade the bone marrow but can be found in the spleen, liver, kidney, lungs, lymph nodes and other soft tissues in advanced stages of the disease. The myelomatous infiltration in the skin as well as in the pleural fluid carries a poor prognosis. Here we present a case with both skin and pleural fluid infiltration. Only a few such cases have been published.

Case Report
An 80 year old male, presented to the hospital with hematuria and upper respiratory tract infection. Investigations displayed increased creatinine levels. On further work up, his ESR was increased and rouleux formation was present in the peripheral smear, free lambda chain was elevated *(Table 1)*. Bone marrow aspiration was suggestive of multiple myeloma. Patient's bone marrow studies showed 26% abnormal plasma cells along with 4% plasma blasts and a diagnosis of multiple myeloma was made *(Figure 1 and 2)*. Flow cytometry also confirmed the diagnosis *(Figure 3). (His FISH (Fluorescence in- situ Hybridization) findings are shown in Figure 4).*

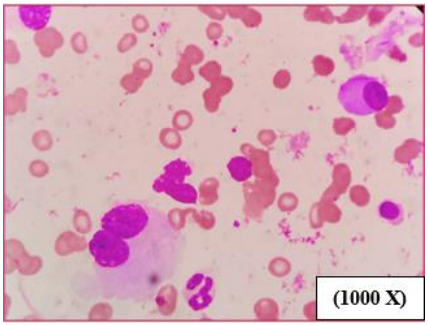


Fig 1: Bone Marrow Aspirate (Leishman stain) Abnormal plasma cells: 26% Plasma blasts: 04 %

Table 1: Lab Values of The Patient

	At The Time of Diagnosis	Before Death
HGB	6.9g/dL	7.6 g/dL
HCT	19.2%	22.9 %
Platelet Count	118.0 x 10^3/µL	111.0 x 10^3/µL
IgA	<44 mg/dL	-
IgG	615 mg/dL	-
IgM	<8 mg/dL	-
Free Kappa Chain	49 mg/L	-
Free Lambda Chain	9890 mg/L	-
Kappa/Lambda Ratio	0.0049	-
Serum Albumin	3.80 g/dL	2.50 g/dL
Globulin	3.70 g/dL	4.10 g/dL

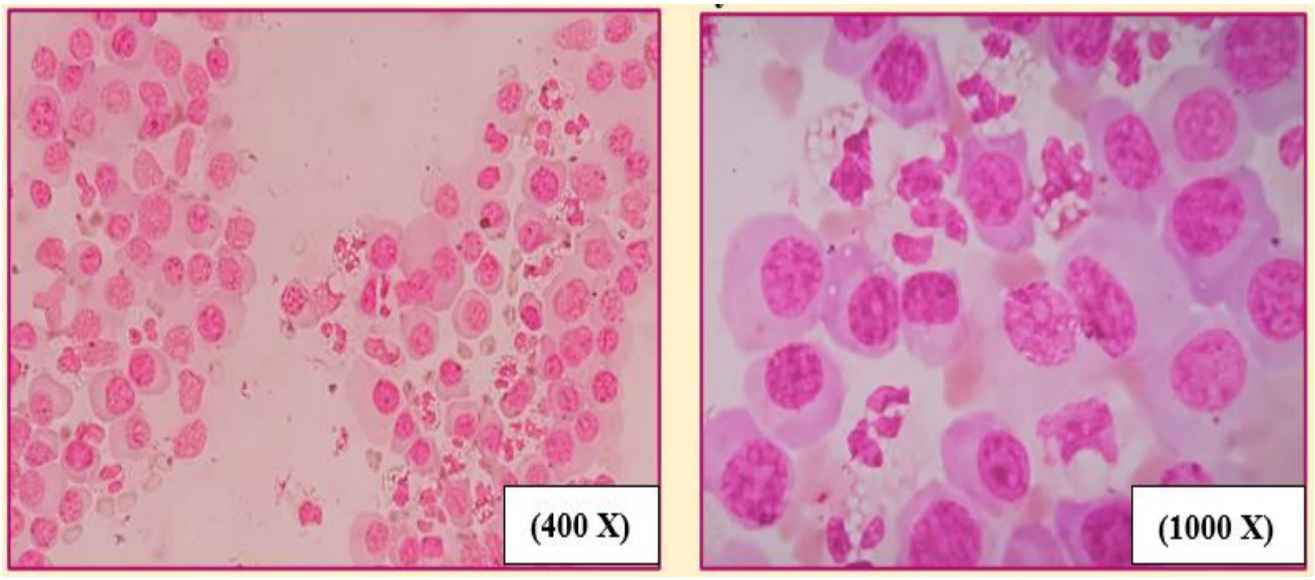
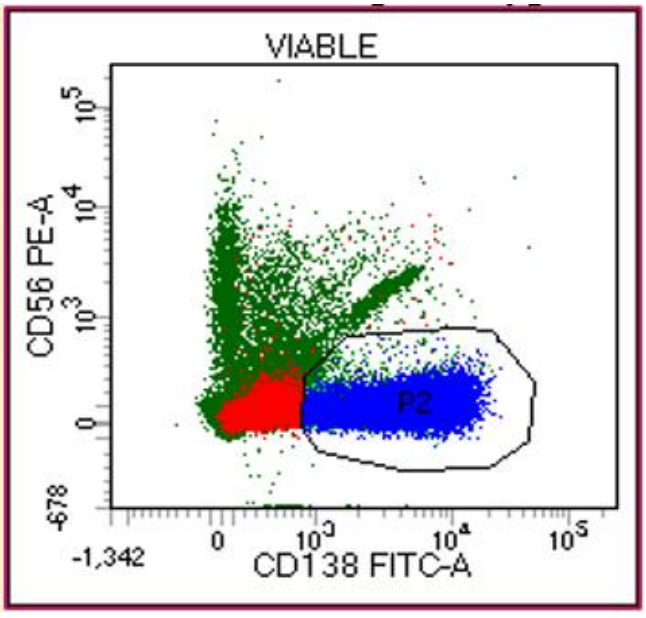
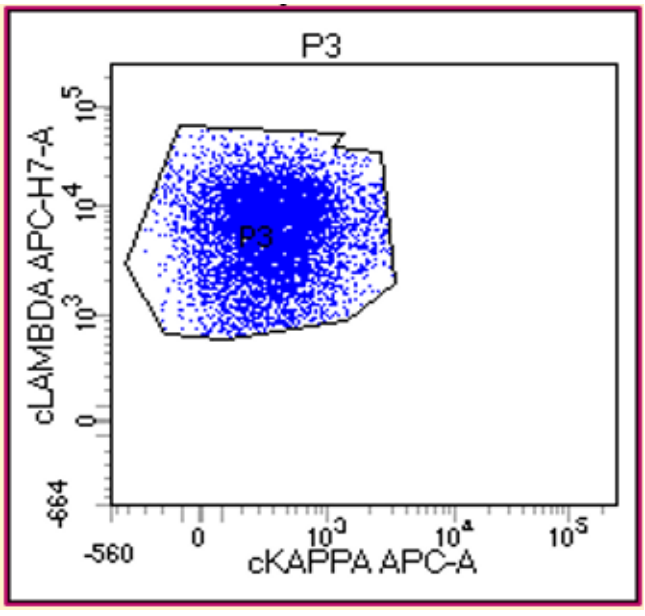


Fig 2: Bone Marrow Biopsy (Haematoxylin and Eosin stain) Plasma Cell Myeloma

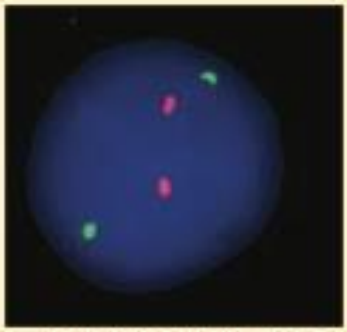


Graph 1: Blue population shows abnormal plasma cells (CD138 +)

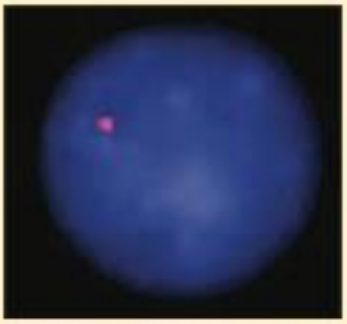


Graph 2: Abnormal plasma cells are c-lambda restricted

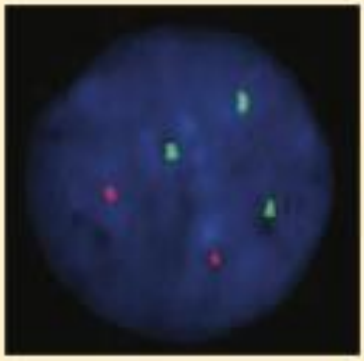
Fig 3: Flow Cytometry: Immunophenotypic features confirmed myeloma



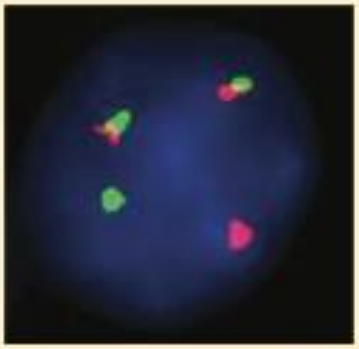
INTERPRETATION:
Deletion of 17p13 was not observed in any cells.
Specimen is negative for *p53* deletion.



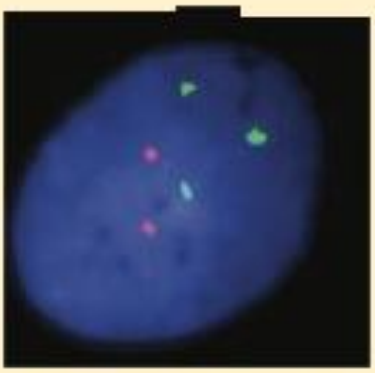
INTERPRETATION:
Del 13q14.3 signal was detected in 16% cells.
Specimen is positive for del13q14.3.



INTERPRETATION:
IgH/FGFR3 fusion signal was not detected in any cells.
Specimen is Negative for t (4;14).



INTERPRETATION:
IgH/CCND1 fusion signal was detected in 46% cells.
Specimen is Positive for t (11;14).



INTERPRETATION:
IgH/MAF fusion signal was not detected in any cells.
Specimen is Negative for t (14; 16).

Fig 4: Fish

Patient was started on first line of chemotherapy: Bortezomib+ Thalidomide+ Dexamethasone (VTD) but the disease progressed after 1st cycle of VTD. So, he was started on the second line of chemotherapy: Carfilzomib+ Dexamethasone+ Promalidomide. After 1st cycle of Carfilzomib based chemotherapy, patient developed painful cutaneous nodules on the arm *(Figure 5)* and pleural effusion.

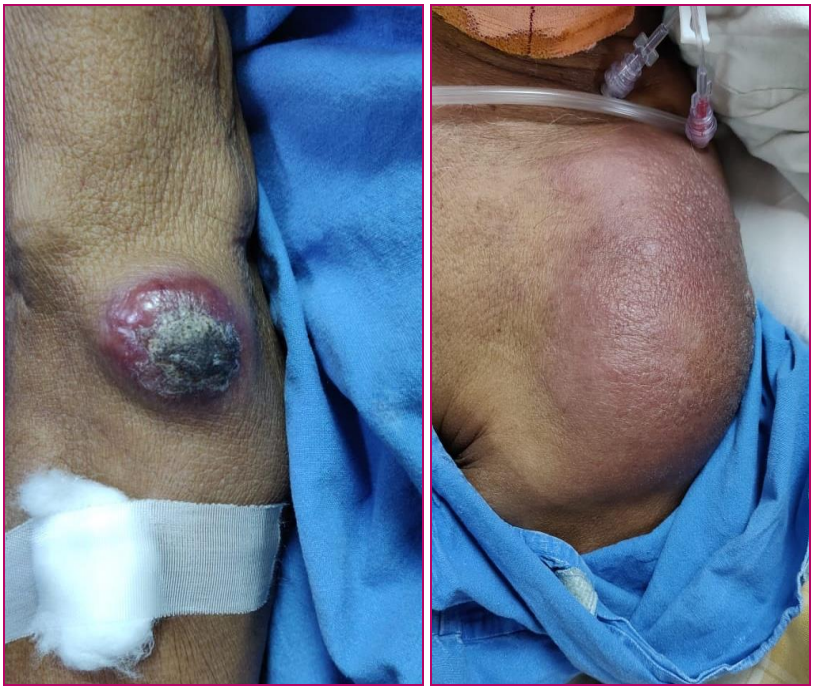


Fig 5: Cutaneous lesions: (a) Cubital fossa (b) Shoulder

The biopsy of the cutaneous lesions was suggestive of cutaneous infiltration by plasma cells *(Figure 6).*

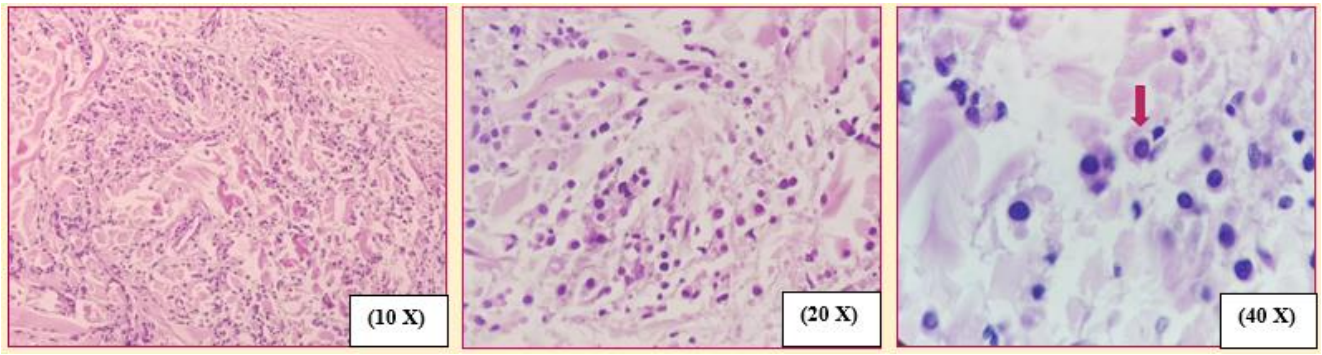


Fig 6: Punch Biopsy (Haematoxylin and Eosin stain) Cutaneous metastasis by myeloma

The patient eventually developed *Klebsiella* pneumonia. The pleural fluid was tapped and sent for evaluation. Cytologic examination confirmed infiltration of plasma cells into the pleural fluid *(Figure 7).*

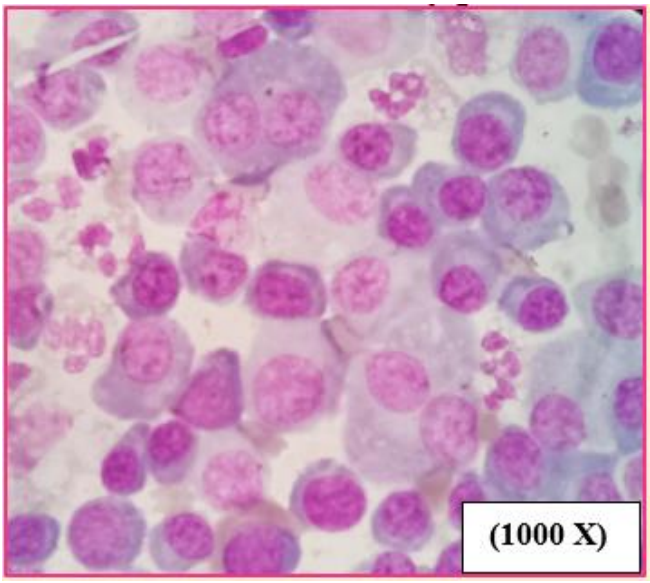
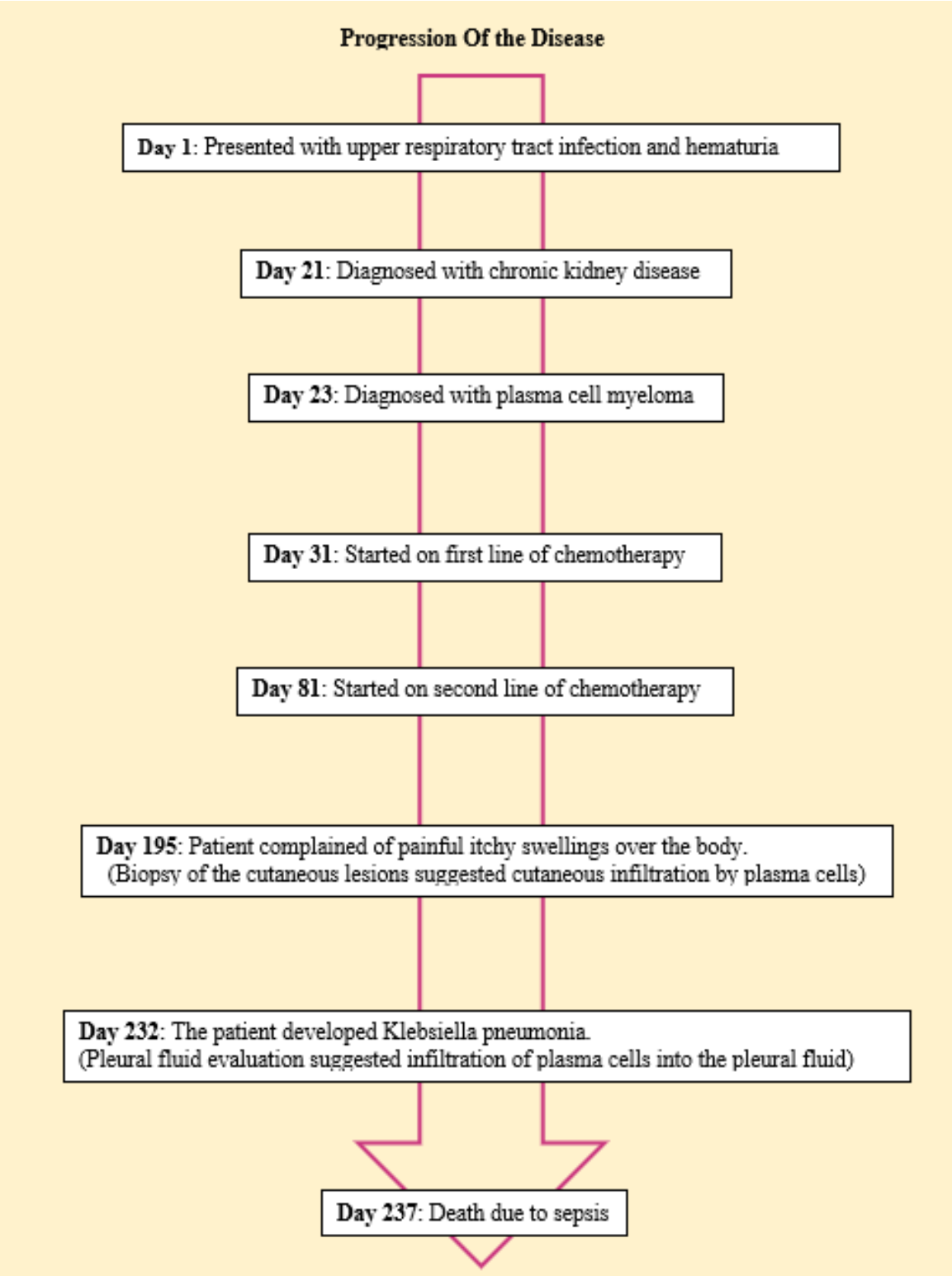


Fig 7: Pleural Fluid Cytology (Leishman stain) Pleural fluid infiltration by plasma cells

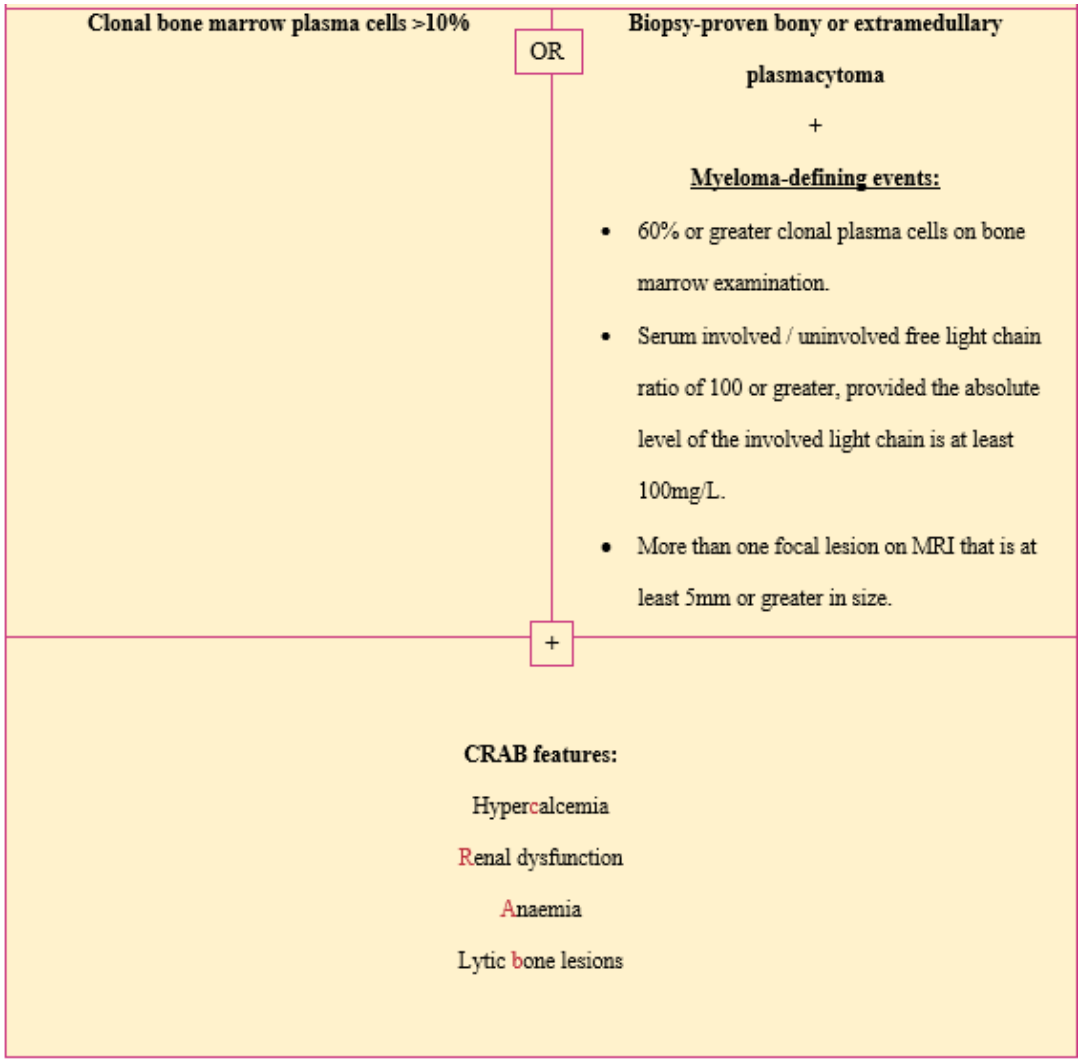
The patient developed urinary tract infection and sepsis. His condition gradually deteriorated resulting in death *(Disease progression in the patient is shown in Figure 8).*



Discussion

Multiple myeloma is a malignancy characterized by the proliferation of abnormal plasma cells in the bone marrow *(Table 2: IMWG criteria for defining multiple myeloma).*

Table 2: The Revised International Myeloma Working Group (Imwg) Criteria For Defining Multiple Myeloma [2]



Cutaneous involvement usually accounts for around 1 % of multiple myeloma patients and is associated with decreased overall survival [3]. Lesions such as amyloidosis, pyoderma gangrenosum, leukocytoclastic vasculitis, necrobiotic xanthogranuloma, pruriginous ichthyosiform dermatitis, alopecia can be observed in plasma cell myeloma and constitute the non-specific lesions associated with myeloma. The specific cutaneous involvement is the result of infiltration of plasma cells either by direct extension from underlying bone or by hematogenous spread [4-6].

If there is myeloma infiltration, the lesions are generally pink, red, papules, nodules, and/or plaques with variable size [5]. The lesions tend to be itchy and tender.

According to a multi-institutional retrospective study, the median time from the diagnosis of myeloma to skin involvement was 2 years. Patients have a median overall survival (OS) of 8.5 months from the time of skin involvement [7]. Myeloma is rarely suspected from skin disorders but even in the patients with minimal systemic manifestations, the presenting feature of myeloma may be cutaneous lesions and hence clinical suspicion becomes necessary to diagnose the malignancy early [8].

Pleural effusions due to myelomatous involvement is rare in myeloma patients, occurring in about 6% of the cases [9]. Common causes of pleural effusions in myeloma include congestive heart failure due to hyperviscosity or amyloidosis, renal failure, pulmonary embolism due to a hypercoagulable state or plasma embolization, a secondary neoplasm, infections due to immunosuppression (pneumonia, tuberculosis, AIDS, other viral illnesses). Affected patients are usually resistant to treatment and often relapse in spite of receiving appropriate chemotherapy [9]. The patients may show no respiratory symptoms or may have symptoms like dull chest pain, dyspnea, dry cough which are generally seen in pleural effusion [10]. It has been observed that the disease has worse prognosis if the patients have myelomatous pleural effusion [11].

It is rare to have cutaneous metastasis and pleural involvement leading to effusion in a myeloma patient. This indicates high tumor burden and almost always occurs in advanced stages.

According to a review on extramedullary disease in multiple myeloma, the incidence of such a disease in newly diagnosed myeloma patients is 3-5% and upto 20% in relapsed cases [12].

Clinical history and physical examination, regular testing (CBC, peripheral smear monitoring, calcium and creatinine levels, serum protein electrophoresis, regular urinalysis), bone marrow studies (aspiration and biopsy with cytogenetic monitoring, in situ fluorescent hybridization (FISH) and immunophenotyping), imaging (LDWCT, PET-) are recommended for the diagnosis of multiple myeloma by International Myeloma Working Group (IMWG).

The treatment is generally based on IMWG 2014 guidelines. Regardless of the treatment, the prognosis in patients having cutaneous infiltration or pleural fluid effusion or both

together remains poor [9]. Supportive measures addressing bone disease and associated complications, anemia, organ failure etc. are also being undertaken these days. Palliative care is also an important component of the treatment.
Our patient had skin infiltration and had progressive disease despite two lines of chemotherapy.

Conclusion

Simultaneous pleural and cutaneous involvement in myeloma is rare and has poor prognosis despite standard chemotherapy and not many cases have been reported. Such metastases are not specific to a stage and can occur at any stage of the malignancy. They decrease the chances of survival of the patient.
We conclude by saying that any skin lesion in myeloma cases, should raise the suspicion of infiltration and may indicate that myeloma is progressive. It may aid in deciding further management of the patient.
Can we have a diagnostic clue to early detect these cases? Should they have a different line of treatment? These questions still remain unanswered and require larger sized studies.

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