Recurrent Infections in a Patient with Multiple Myeloma

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Abstract

An 80-year-old woman with recurrent urinary tract infection presented to the orthopaedic OPD at KS Hegde Memorial Health Center, Bailur, with gradual onset of generalized weakness, fatigue, anorexia, musculoskeletal pain, and particularly severe backache. The patient was diagnosed to have anemia but renal function tests were normal. X-ray spine showed multiple compression fractures. Serum electrophoresis confirmed the diagnosis of multiple myeloma. In an elderly patient with myalgia, anemia, and recurrent infections, the differential diagnosis of multiple myeloma should be kept in mind as it is often missed by clinicians.

Keywords
- multiple myeloma
- anemia
- β2-microglobulin

Introduction

Malignant proliferation of plasma cells producing a monoclonal paraprotein characterizes multiple myeloma. Hypocalcaemia, hyperviscosity, renal failure, and bone pains/fractures are some of the typical presentations. The malignant proliferation of plasma cells in bone marrow can be detected by monoclonal protein in the blood or urine, and dysfunction of associated organs. Depending on the absence or presence of an organ lesion or dysfunction of the affected organ tissue, it is classified as asymptomatic or symptomatic. The patient has better prognosis especially in the early stages, where the presentation may vary, which makes the diagnosis difficult.[1-4] Multiple myeloma constitutes 1% of neoplastic diseases and 13% of hematologic cancers.[2,4,5] The adjusted annual age incidence is 5.6 cases per 100,000 people in the Western countries.[1] Solitary plasmacytomas and multiple myeloma can be thought of as a spectrum of disease, which ranges from localized clonal plasma cell infiltration to multiple extramedullary lesions, and osseous forms typically progress to multiple myeloma. Multiple myeloma is the most common primary osseous malignancy in adults, typically between the ages of 50 and 70 years, and it is more likely to affect men.[6,7]

The age of diagnosis of multiple myeloma is on an average 70 years—patients under the age of 35 years constitute 35%, 26% are in the range of 65 to 74 years, and patients above 75 years of age constitute 37%.[1,2] Polyclonal hypogammaglobulinemia is the main reason for the increased risk of infection in patients with multiple myeloma.[1,5] Reduction of CD4+ T cells, functional impairment of the natural killer cells, abnormalities in the complement system, and occasional granulopenia are other reasons for mortality in patients with multiple myeloma.[1,5,8] When compared with a patient who is hospitalized for any other reasons the risk of infection is 7 to 15 times more in a patient with the above risk factors.[1,5,8] The presence of at least 10% plasma cells in the bone marrow sample and the presence of monoclonal protein in serum or urine confirm the diagnosis of multiple myeloma. The presence of 30% plasma cells or evidence of plasmacytoma in the bone marrow points the diagnosis toward nonsecretory myeloma.[4]

Case Presentation

An 80-year-old woman presented to the orthopaedic OPD at KS Hegde Memorial Health Centre, Bailur, with complaints of lower back ache. On examination there was kyphosis and spinal movements were painful. X-ray spine showed multiple compression fractures. Blood investigations done in our laboratory showed Hb 9.1 g/dL, TC 8200, DC: P-78, L-18, E-7, ESR 98, serum creatinine 0.9 mg/dL, serum calcium 7.3 mg/dL. Patient was treated with Inj. Arachitol deep im once in 15 days, tablet Shelcal-CT 500 mg bd. After 1 month the patient again came back with similar complaints restricting her activities

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of daily living. Patient was admitted and detailed investigations were done by sending the blood samples to an outside sophisticated laboratory. The details of investigation are given as below (►**Tables 1–3**; ►**Figs. 1–3**)

Patient was then advised to consult medical oncologist. But the patient party was reluctant to seek higher treatment because of patient's age, terminal stage of disease, and the financial constraints and the patient was discharged against medical advice.

Past History

Patient had similar complaints of low back ache for which she had consulted at the orthopaedic OPD in our health center, two years back. On examination, there was kyphosis and tenderness over the LS spine; X-ray showed multiple osteoporotic compression fractures. Blood investigations—serum calcium 10.1 mg/dL and ALP 285 IU/L. Patient was treated with Inj. Zolantronic acid, tablet Shelcal-CT and analgesics. Patient also had complains of mass per vagina and white discharge per vagina. Urine analysis showed pus cells 15–20/hpf, RBC 1–2/hpf, and epithelial cells 10–15/hpf. She was referred to a gynecologist and was treated conservatively.

Discussion

One of the main reasons for the development of serious infections in immune-competent patients diagnosed with multiple myeloma is marked hypergammaglobulinemia which is caused by clonal proliferation in bone marrow. The leading cause of mortality in these patients of multiple myeloma is the severe episodes of infections ranging from 0.8% to 2.2% of the total multiple myeloma diagnosis every year. Bacterial infections associated with lung and urinary tracts are the most common infections seen in these patients. However, fungal and viral infections are also reported.[1,8] With the exception of patients with clonal proliferation in the adjacent bone the physical examination in these patients is usually normal. Destruction of bone, bone fractures, and pain are some of the manifestations of clonal proliferation. Anemia, hypercalcemia, renal failure, susceptibility to infection, coagulation problems, neurologic symptoms, and vascular problems due to hyperviscosity are some of the important features seen in these patients.

Looking at the present case, we had a patient with multiple musculoskeletal pain and urinary tract infection with white discharge per vagina. She was treated with broad-spectrum antibiotic like tablet metronidazole. But the patient continued to have symptoms of urinary tract infection (UTI) and WDPV. The presence of at least one of seven possible manifestations which occurs due to organ or tissue damage due to proliferating tumor is one of the important prerequisite for the diagnosis of symptomatic multiple myeloma.

1. Anemia with a decrease in hemoglobin of at least 2 g/dL compared with the normal value, or a hemoglobin below 10 g/dL.
2. Hypercalcemia greater than 10 mg/L (0.25 mmol/L) above normal or an absolute number greater than 110 mg/dL (2.75 mmol/L) of serum calcium.
3. Osteolytic lesions, osteoporosis, or compression fractures with no attributable cause.
4. Renal failure, with creatinine of more than 2 mg/dL or 173 mmol/L.
5. Symptomatic hyperviscosity.
6. Amyloidosis.
7. Recurrent bacterial infections (>2 severe episodes that required hospitalization over a period of 12 months).

It is very important to look into these abnormalities because without the signs of organ damage, the asymptomatic forms of multiple myeloma will require only conservative treatment or no treatment and only regular monitoring. The international system of stratification is used to state prognosis and decide proper management. According to the level of serum protein and β2 level the stratification system divides multiple myeloma in three stages[1,2,9,10:]

Stage I: serum β2-microglobulin <3.5 mg/L, serum albumin ≥ 3.5 g/dL.

Stage II: serum β2-microglobulin, <3.5 mg/L, plus serum albumin <3.5 g/dL; or β2-microglobulin of 3.5 to <5.5 mg/L, irrespective of serum level of serum albumin.

Stage III: serum β2-microglobulin ≥ 5.5 mg/L.

In the present case the laboratory test report revealed normocytic normochromic anemia and hypoalbuminemia. Our patient also showed an increase in β2-microglobulin concentrations (0.6) which are indicative of high tumor burden but the renal parameters were normal, which is generally elevated in patients of multiple myeloma which is indicative of renal failure and is one of the main predictors of disease progression.[1,8] With conventional chemotherapy, the median survival does not exceed four years currently.[5,10] Our patient was at stage III multiple myeloma as the levels of β2-microglobulin greater than 5.5 mg/L. Induction therapy, followed by high dose therapy and autologous hematopoietic stem cell transplant is the first line of therapy in these patients.[5] However, because of patient's age, terminal stage of disease and the financial constraints the patient party were reluctant to seek

Table 1 Serum protein electrophoresis

Fractions	%	Reference %	Concentration	Reference concentration
Albumin	42.1	55.8–66.1	3.3	3.6–5.4
Alpha 1	6.9	2.9–4.9	0.5	0.2–0.4
Alpha 2	12.7	7.1–11.8	1.0	0.5–1.0
Beta 1	6.5	4.7–7.2	0.5	0.3–0.6
Beta 2	7.9	3.2–6.5	0.6	0.2–0.5
Gamma	23.9	11.1–18.8	1.9	0.7–1.5

Table 2 Detailed hematologic parameters

Parameter	Result	Units	Limit
WBC	9.26	$10^3/\mu L$	4.00–11.00
Neutrophils	6.09	$10^3/\mu L$	2.00–7.50
Lymphocytes	2.37	$10^3/\mu L$	1.30–4.00
Monocytes	0.52	$10^3/\mu L$	0.15–1.40
Eosinophils	0.18	$10^3/\mu L$	0.00–0.60
Basophils	0.10	$10^3/\mu L$	0.00–0.15
Neutrophils %	65.8	%	40.0–75.0
Lymphocytes %	25.6	%	21.0–40.0
Monocytes	5.6	%	3.0–14.0
Eosinophils %	1.9	%	0.0–6.0
Basophils %	1.1	%	0.0–2.0
RBC	3.87	$10^5/\mu L$	4.00–5.50
Hb	10.9	g/dL	12.0–17.4
HCT	32.5	%	36.0–52.0
MCV	84.2	fL	76.0–96.0
MCH	28.2	pg	27.0–32.0
MCHC	33.5	g/dL	30.0–35.0
RDWsd	27.7	fL	46.0–59.0
RDWcv	12.6	%	0.0–16.0
PLT	301	$10^3/\mu L$	150–450
PCT	0.24	%	–
MPV	8.0	fL	15.0
PDWsd	19.1	fL	–
PDWcv	37.6	%	–
PLCR	30.65	%	–
PLCC	92	$10^3/\mu L$	–

Table 3 Other relevant blood investigations

Test	Result	Unit	Range
ESR	102	mm/hr	0–40
Alkaline phosphatase	88	IU/L	38–94
Bence–Jones proteins	Positive	–	–

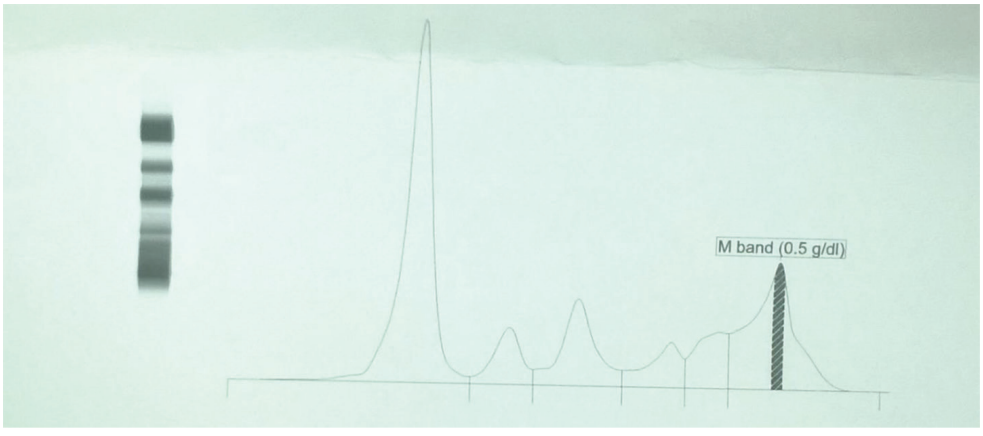

Fig. 1 Serum electrophoresis.

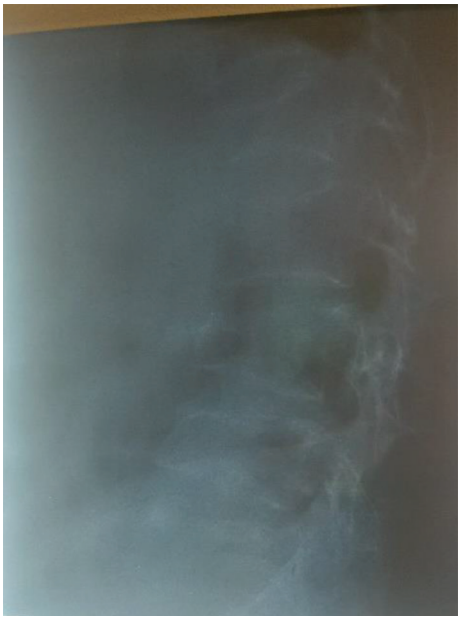

Fig. 2 X-ray spine showing multiple compression fracture.

Fig. 3 Patient of multiple myeloma admitted at the health center.

treatment at higher center. Age is not only an important factor for the survival of the patient, but also for chemotherapy tolerance.[11] It has been observed that the survival rate is 50 months in a patient below 65 years of stage II disease, whereas it is only 37 months in a patient above 65 years.[5] The treatment of choice in this group of patients is the new drugs, such as bortezomib, thalidomide, or lenalidomide, in combination with traditional chemotherapy.[1,5,8,12] Significant improvement in the complete remission rate and the overall survival has been observed with the use of these drugs.[12] Mepfalan or high doses of dexamethasone combined with one of the new drugs as thalidomide or bortezomib has been used as classical treatment schemes in the induction therapy of these patients.[8,13]

Conflict of Interest

None.

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