CASE REPORT

Cutaneous and pleural involvement in a patient with multiple myeloma

Olfa Saidane,¹ Maroua Slouma,² Slim Haouet,³ Leila Abdelmoula³¹Charles Nicolle Hospital, Tunis, Tunisia²Department of Rheumatology, University of Tunis El Manar, Tunis, Tunisia³Tunis El Manar University, Tunis, Tunisia**Correspondence to**

Dr Maroua Slouma, maroua.slouma@gmail.com

Accepted 19 September 2015

SUMMARY

Multiple myeloma (MM) is a malignant proliferation of a single clone of plasma cells and an excess of monoclonal immunoglobulin production. It is rarely associated with cutaneous and pleural involvement. We report a new case of a 62-year-old woman with a history of a symptomatic MM. Three months after chemotherapy initiation, she presented with subcutaneous nodules. Ultrasound-guided needle biopsy confirmed the diagnosis of cutaneous plasmacytomas. She underwent local radiation therapy leading to complete regression of subcutaneous nodules. One month later, she developed dyspnoea. Thoracic CT scan showed pleural thickening associated with pleural effusion. Pleural biopsy confirmed the diagnosis of pleural plasmacytoma. Chemotherapy including vincristine, doxorubicin and dexamethasone was administered. Cutaneous involvement and pleural effusion accompanying MM are uncommon. They are associated with poor prognosis.

BACKGROUND

Multiple myeloma (MM) is a malignant proliferation of a single clone of plasma cells. Pleural effusion and skin manifestations in patients with MM are uncommon. Cutaneous and pleural involvements are usually associated with poor prognosis. We present a unique case of a patient with a clinical history of myeloma who developed subcutaneous nodules and pleural involvement without extension from an underlying bony focus of disease.

CASE PRESENTATION

A 62-year-old woman, with no significant medical history, presented with a 6-month history of inflammatory back pain associated with intercostal neuralgia. There was no report of recent trauma or falls. Physical examination revealed tenderness over the area of the spinal process of T8. Neurological examination was unremarkable.

INVESTIGATIONS

Laboratory investigations showed an elevated erythrocyte sedimentation rate (62 mm/h). The complete blood cell count revealed anaemia (haemoglobin level of 9 g/dL). Serum level of calcium was within the normal range. Renal and liver function tests were unremarkable. Thoracic spine X-ray showed vertebral body collapse of T8. MRI of the spine revealed collapse of the vertebral body of T8 associated with compression of the spinal cord. X-ray of the skull, humeri, ribs, pelvis and femora did not show lytic bone lesions. Serum protein electrophoresis revealed a marked increase

in β -globulin classified by immunoelectrophoresis as IgA κ monoclonal gammopathy. Quantitative immunoglobulin tests revealed high serum IgA levels (675.8 mg/dL) with reduced IgG and IgM. Urine electrophoresis showed no Bence-Jones proteins. A bone marrow aspirate showed infiltration of malignant plasma cells of 15%. The diagnosis of symptomatic IgA κ MM was therefore confirmed. According to Durie-Salmon staging, the disease was classified as stage IIIA.

TREATMENT

The patient was eligible for autologous stem cell transplantation. An induction regimen was introduced including thalidomide and dexamethasone in addition to zoledronic acid. The patient also underwent radiation therapy to the T8 vertebrae (daily doses of 30 Gy delivered over 10 sessions), complicated by radiation oesophagitis.

OUTCOME AND FOLLOW-UP

After the third cycle of the induction regimen, haematological findings revealed disappearance of β -globulin spike, and bone marrow aspirate showed a decrease in the plasma cell infiltration, at 4%. Given the risk of gastrointestinal perforation related to radiation oesophagitis, autologous transplantation was deferred and the patient was considered in remission.

Three months later, she re-presented with slightly purplish subcutaneous nodules on the back and inner thigh. Spinal MRI visualised subcutaneous masses located in the posterior thoracic wall, with hypointensity in T1 and T2 ([figure 1](#)). Histopathology of ultrasound-guided needle biopsy showed proliferation of malignant plasma cells in the skin ([figure 2](#)). There was no significant vascular change. A diagnosis of MM with cutaneous metastasis was made. Local radiation therapy was decided on, leading to complete regression of the subcutaneous nodules.

One month later, the patient developed dyspnoea. Chest X-ray showed a large right-sided pleural effusion. Thoracic CT scan and MRI showed pleural thickening associated with pleural effusion ([figure 3](#)). Tuberculin skin test and Koch's bacillus research in sputum were negative. Culture of expectorated sputum and pleural fluid was unremarkable. Cytology of the pleural fluid showed plasma cells ([figure 4](#)) and pleural biopsy revealed pleural plasmacytoma ([figure 5](#)). Chemotherapy including VAD (vincristine, doxorubicin and dexamethasone) was administered. The patient was judged to be a poor candidate for autologous

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To cite: Saidane O, Slouma M, Haouet S, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-211197

Figure 1 Spine MRI T2-weighted sequences showing a vertebral collapse associated with spinal cord compression at T8 and subcutaneous masses located in posterior thoracic wall with hypointensity in sequence T2.

transplantation owing to cutaneous and pleural involvement. She died 12 months after the first clinical presentation.

DISCUSSION

MM is characterised by a clonal proliferation of malignant plasma cells in the bone marrow and an excess of secreted monoclonal immunoglobulins.¹ It is usually confined to the bone marrow, whereas extramedullary dissemination may occur, especially in advanced disease. The coexistence of cutaneous and pleural involvement in the same patient is rarely reported.^{2,3} This may occur at the time of diagnosis or in the course of the disease.

Skin disorders during the course of MM are divided into specific and non-specific manifestations.⁴ Specific skin lesions are

Figure 2 Histopathological features of cutaneous biopsy showing proliferation of malignant plasma cells in the dermis.

Figure 3 Thoracic MRI T2-weighted sequences showing pleural thickening associated with right pleural effusion.

related to extramedullary cutaneous plasmacytomas or secondary cutaneous involvement by extension from adjacent bone involvement, whereas non-specific manifestations are due to infections and drug side effects.⁵ Metastatic skin lesions without underlying bone tumours are uncommon. Less than 100 cases have been reported.^{6–8} In a case series of 284 patients with MM who underwent 494 biopsies, cutaneous plasmacytoma was found in 18 cases.⁹ Cutaneous metastases are characterised by a high variability in clinical presentation and skin lesion distribution including two configurations: an infiltrative type and nodular type.⁶ Subcutaneous nodules are typically violaceous and they may appear on any area of the skin, especially on the trunk, and rarely on the face or extremities.¹⁰ They are usually multiple and measure between 1 and 5 cm. This condition can be confused with several others, such as lymphoma, carcinoma and iatrogenic Kaposi sarcoma.⁶ These diagnoses were ruled out in our case and skin biopsy specimen showed proliferation of malignant plasma cells.

Pleural effusion associated with MM is infrequent.¹¹ Infectious causes of pleural effusion in this

Figure 4 Cytology of the pleural fluid showing plasma cells.

Figure 5 Pleural biopsy revealing proliferation of plasma cells in the dermis ((A) $\times 50$; (B) $\times 100$).

immunocompromised patient were initially discussed. However, culture tests of sputum and pleural fluid were negative. The diagnosis was based on the existence of plasma cells in the cytology examination of the pleural fluid and in the pleural biopsy specimen. Kintzer *et al*¹² reported on a study of 958 patients with MM, in whom pleural effusion occurred in 58 cases (6.1%). Moreover, in a case series of 133 patients with malignant pleural effusion, only one case of MM was found.¹³

Several mechanisms may explain the pleural effusion in myeloma.¹⁴ It can be caused by involvement of the pleura from adjacent skeletal or parenchymal tumours.¹⁵ It can also be due to a direct implantation of tumour nodules on the pleura.

Cutaneous plasmacytoma and pleural effusion are commonly seen in advanced MM. They can be associated with all classes of myeloma proteins. The IgG subtype is most commonly seen, followed by IgA subtype.^{4 14}

The treatment of pleural involvement has not yet been codified. To the best of our knowledge, there are no large series of pleural involvement in MM. Chemotherapy is often used.^{11 15} As in our case, Keklik *et al*¹⁶ opted for chemotherapy including VAD. Response rates do not exceed 70% in patients with advanced refractory disease.¹⁷

However, the use of radiation therapy to address cutaneous plasmacytomas has been reported in a few cases, with good response.^{3 6 18–21} In our case, radiotherapy led to complete regression of the subcutaneous nodules.

Despite the advanced stage of the disease, renal function was normal in our case. Decrease in creatine clearance is seen in approximately 50% patients with MM, but only 10% require dialysis.²² Renal involvement is mainly associated with high urinary excretion of 'light chains' (Bence-Jones proteins). Free light chains play a crucial role in causing renal damage. In our case, urine electrophoresis showed no Bence-Jones proteins. The sensitivity of urine electrophoresis tests is influenced by the type of urine collection and the degree of urine concentration.²³ Furthermore, Bence-Jones proteins and polyclonal immunoglobulin light chains are metabolised in the kidney, resulting in reduction of its excretion.²³

We reported a case of cutaneous and pleural involvements in MM. Both sites of involvement are associated with extremely poor prognosis regardless of the therapy used. They are considered as signs of high tumour burden. Death occurs within 12 months of developing cutaneous metastases.^{19 24 25}

Learning points

- Skin and pleural involvement in patients with multiple myeloma (MM) is rare and associated with extremely poor prognosis.
- MM may be associated with subcutaneous nodules. Their aspect is variable, but is typically violaceous. Metastatic skin lesions without underlying bone tumours are uncommon.
- Radiation therapy shows true efficiency in treating cutaneous plasmacytoma. Treatment of pleural effusion related to MM has not been codified.

Contributors MS wrote the first draft. OS performed the literature search. SH and LA revised the manuscript. All the authors approved the final draft.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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