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Rare case of plasmablastic myeloma diagnosed on lung biopsy

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SUMMARY

Plasmablastic myeloma is a rare variant of multiple myeloma characterised by neoplastic proliferation of single clone of plasma cells producing monoclonal immunoglobulins. A 60-year-old man presented to hospital with a 6-week history of chest pain, back pain, leg weakness and numbness. Imaging revealed a 75 mm left lobular lung mass with chest wall invasion, metastatic bony and soft-tissue deposits and spinal cord compression at T5 level. Lung biopsy, for suspected metastatic lung cancer, surprisingly showed features of plasmablastic myeloma. Protein electrophoresis demonstrated 2 g/L of IgG lambda paraproteinaemia and an increase in lambda light chains with reduced kappa/lambda ratio of 0.01. Bone marrow biopsy did not show evidence of infiltration by disease. The patient received radiotherapy to the spine; responded to third-line chemotherapy and received autologous stem cell transplant. This case adds to the rare causes of lung mass and is the first reported case of plasmablastic myeloma diagnosed on lung biopsy.

BACKGROUND

Multiple myeloma is a malignant proliferation of plasma cells mostly affecting the bone marrow and commonly presents with anaemia, hypercalcaemia, renal dysfunction, bone and skeletal involvement. It is the second most common haematological malignancy with median age of presentation of approximately 70 years.¹ There is a male predominance, and it is rare under 40 years of age. The annual age-adjusted incidence in the world is 2.1 per 100 000 and it is more common in males and in black Africans but less common in Asians.²

Plasma cell neoplasms account for 1% of all malignant tumours and about 13% of haematological malignancies can be attributed to multiple myeloma.³ The proliferation of neoplastic clone of plasma cells can manifest as a single lesion (solitary plasmacytoma) or as numerous lesions (multiple myeloma). Solitary extramedullary plasmacytoma (SEP) describes solid plasma cell tumours of soft-tissue origin as opposed to solitary plasmacytoma of bone.

The most common sites of extramedullary solitary plasmacytoma include upper airway tract, digestive tract, lymphatic systems and head and neck regions.^{4,5} An extramedullary plasmacytoma can arise in a myeloma patient during the disease irrespective of duration of illness, and it typically represents advanced disease. Extramedullary plasmacytoma is an unusual mode of presentation for newly diagnosed myeloma patients, but in these

unlucky cases the disease is often extensive, and the prognosis is poor.⁶

The causes of incidental pulmonary nodules can be categorised as benign or malignant. Common causes of a malignant nodule include primary lung cancer, lung metastases and carcinoid tumours. A benign pulmonary nodule can be caused by infectious granulomas and benign tumours such as a pulmonary hamartoma. Less common causes include vascular and inflammatory lesions and haematological malignancies.

In this report, we describe a rare case of plasmablastic myeloma presenting as a lung mass and diagnosed on lung biopsy. The patient went on to have chemotherapy and autologous stem cell transplantation with a good outcome.

CASE PRESENTATION

A 60-year-old man presented on 23 January 2019 with a history of chest pain, back pain, abdominal distention, leg weakness and numbness. Chest pain had started 6 weeks earlier, was sharp and mostly on the left side and worse with breathing. Pain was present all the time and was often made worse when laying down.

He reported increasing back pain while walking and had been taking pain killers for about 6 weeks prior to admission and was complaining of constipation. In addition, he had weakness and numbness of lower limbs suggestive of spinal cord compression.

There was no history of smoking and he only drank alcohol occasionally. He had no medical history of note and was not on any regular medications.

General physical examination was normal. There was no clubbing or palpable lymphadenopathy. Cardiovascular and respiratory examination was essentially normal. His abdomen was distended but without palpable hepatomegaly. Examination of lower limbs demonstrated minimal leg weakness.

INVESTIGATIONS

On admission the patient's blood count was normal: haemoglobin 138 g/L, white cell count $5.14 \times 10^9/L$ with a normal differential and platelets $256 \times 10^9/L$. Chemistry was normal with no evidence of renal failure or hypercalcaemia.

A contrast MRI scan of his spine showed widespread features of skeletal metastatic disease. At least three large soft-tissue deposits in the thoracic paraspinal space were noted, the largest on the left at level T2/T3. An intervertebral deposit at level T4/T5 was seen to be causing significant compression of the adjacent thoracic cord.



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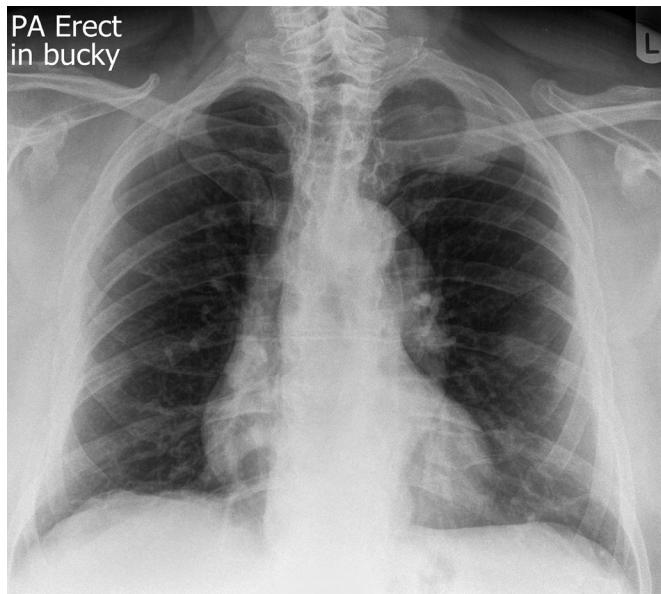


Figure 1 Chest X-ray showing left apical opacity. PA, posteroanterior.

A routine chest X-ray at the time showed a left upper lobe mass raising the suspicion of possible pulmonary tumour (figure 1). A contrast CT scan was done which showed a large lobular mass with chest wall invasion particularly involving the left third rib, measuring up to 75 mm in maximum diameter with adjacent chest wall muscular invasion (figure 2). A mild to moderate left-sided pleural effusion was noted. CT evidence of lumbar vertebral and pelvic bony metastatic appearances was also seen.

DIFFERENTIAL DIAGNOSIS

Suspecting lung cancer, lung biopsy was organised, which showed features of plasmablastic myeloma. The biopsy showed infiltration by sheets of atypical plasmacytoid cells with some multinucleated forms. Skeletal muscle was also seen. There was no lung parenchyma. Immunohistochemical staining demonstrated that this population was positive for CD138 and MUM1 and weakly positive for CD56. TTF1, p63, S100, AE1/AE3, CD3, CD20 and CD79a were negative. Ki67 was remarkably high (90%). Further immunostains performed at King's College Hospital reference laboratory revealed that CD38 was strongly positive, there was lambda light chain restriction seen on the immunostaining as well as ISH. Cyclin d1, CD45, pancytokeratin and kappa were



Figure 2 CT scan showing left upper lobe mass and left basal pleural effusion.

negative. Epstein-Barr virus encoded small nuclear RNAs was negative.

In light of the results of lung biopsy, myeloma screen and bone marrow aspirate and trephine were carried out. Immunoglobulin studies showed a slightly low IgA level of 0.62 g/L with a normal IgM level. Protein electrophoresis demonstrated the presence of 2 g/L of paraprotein consisting of IgG lambda paraprotein and lambda light chains. Light chain studies showed a normal free kappa concentration of 6.12 mg/L and an elevated free lambda concentration of 1178.1. His kappa/lambda ratio was reduced at 0.01. Bone marrow aspirate, trephine and immunophenotyping showed no evidence of infiltration by myeloma. Routine viral serology was negative for hepatitis B, hepatitis C and HIV 1/2.

TREATMENT

The patient received radiotherapy to his spine and was started on chemotherapy with bortezomib (Velcade), cyclophosphamide, doxorubicin and prednisolone (VCAP). Repeat CT scans showed a reduction in size of previous spinal lesions.

His treatment was complicated by steroid-induced diabetes for which he was started on insulin and was regularly monitored by the diabetes team at the district hospital in Eastbourne. He also had an episode of ureteric calculi which was managed conservatively.

He had a total of seven cycles of VCAP chemotherapy, but response was deemed partial, and a repeat CT showed several pathological fractures and evidence of disease progression. This included a left orbital root lesion causing proptosis and diplopia for which he had orbital radiotherapy. He also required further radiotherapy to his thoracic spine. Due to evidence of disease progression, the decision was made to start him on a second line chemotherapy regimen. The myeloma team at King's College Hospital further assessed him for possible autologous stem cell treatment.

He was admitted at the local hospital in Eastbourne on 10 September 2019 for the first cycle of daratumumab, velcade and dexamethasone chemotherapy. However, due to poor progress and disease progression, he was switched to third line treatment. He received dexamethasone, thalidomide, cisplatin, doxorubicin, cyclophosphamide and etoposide (DT-PACE) chemotherapy on 12 November 2019. He had the second cycle of DT-PACE chemotherapy on 10 December 2019 and repeat CT scans showed good response.

As a result of the good response to DT-PACE chemotherapy, he went onto an autologous stem cell transplantation on 29 January 2020 at King's College Hospital. He successfully engrafted his neutrophils on day 12. Post-transplantation, he developed severe mucositis and febrile neutropenia. He also developed superficial vein thrombosis involving the brachial vein around the peripherally inserted central catheter line which was removed.

OUTCOME AND FOLLOW-UP

A follow-up CT scan was done in early May 2020 following his stem cell transplant. This showed ongoing good response to therapy at his previously identified sites of disease, healing at the anterior ends of the left fourth rib was noted. A further reduction in the previously noted paraspinal soft-tissue was seen with now only minimal residual soft-tissue in the aortocaval region just above the bifurcation of the aorta.

He is currently doing well and is regularly followed up in the haematology clinic.

DISCUSSION

Plasmablasts are the most immature form of plasma cells and they make up 5%–15% of the cases of multiple myeloma.⁷ It has been established that plasma cells with plasmablastic morphology is an independent predictor of poor survival.^{7,8} Moreover, plasmablastic morphology is a powerful independent predictor of poor survival rate after autologous stem-cell transplantation for relapsed or primary refractory myeloma.⁹ Hence, early diagnosis of plasmablastic myeloma, the most aggressive subtype of multiple myeloma, is necessary for optimal patient management.

Primary extramedullary plasmacytoma can be differentiated from secondary disease by its lack of bone marrow involvement and absence of serum or urine monoclonal protein. In contrast, secondary extramedullary plasmacytoma can exist only in the presence of a primary plasmacytic neoplasm, such as multiple myeloma. Examination of the bone marrow is an important part of the diagnostic process as it helps to differentiate primary extramedullary plasmacytomas from cases of multiple myeloma with extramedullary spread. In our case, bone marrow aspirate, trephine and immunophenotyping showed no evidence of infiltration by myeloma. Hence, this is a case of primary extramedullary plasmablastic myeloma.

Invasion of the spine as a first diagnosis of myeloma in a case of extramedullary plasmacytomas is rare.¹⁰ This contrasts with multiple myeloma where spread to spinal cord is not uncommon. In the very few cases described in literature, the thoracic spine was the most common site of involvement and treatment options instigated depended on the size of the lesion and its effect on the spine.

Extramedullary plasmacytoma presenting as a lung mass has been described in the literature.¹¹ The diagnosis was made on CT guided percutaneous aspiration of the mass and serum immunofixation demonstrated IgG lambda monoclonal gammopathy. The patient in that case had no history of multiple myeloma and bone marrow and skeletal survey was negative for myeloma (figure 3).

Extramedullary plasmacytoma involving the paraspinal soft-tissue is not uncommon, but an SEP in the orbit is a rare presentation with only a handful of cases recorded in the scientific literature.^{5,12} In our case, the patient had proptosis and blurred vision. This needed aggressive management with radiotherapy to avoid loss of vision.

The patient was managed as a case of advanced myeloma with induction chemotherapy followed by stem cell transplantation.



Figure 3 Six weeks surveillance CT scan, post two cycles of VCAP chemotherapy, showing marked interval improvement in size of left upper lobe mass. VCAP, velcade, cyclophosphamide, doxorubicin and prednisolone.

He also received radiotherapy to his spine in view of involvement of spine.

To the best of our knowledge, this is the first case of plasmablastic myeloma where the diagnosis was made on lung biopsy. In conclusion, this unusual case adds to the rare causes of lung mass and it adds to the cohort of rare cases of plasmablastic myeloma presenting with spinal cord compression and involving the orbit.

Learning points

- ▶ Plasmablastic myeloma represents an aggressive subtype of myeloma and early diagnosis is crucial in the management of patients.
- ▶ Presentation of plasmablastic myeloma with a lung mass and its diagnosis on lung biopsy is an unprecedented finding. Also, spinal cord compression and orbital mass are rare presentations in plasmablastic myeloma.
- ▶ This case adds to the rare causes of lung masses which have a wide-ranging differential.
- ▶ Extramedullary myeloma can present in a myriad of ways. It may be a case of primary plasmablastic myeloma or may reflect a progression of multiple myeloma.
- ▶ Standard chemotherapy and autologous stem cell transplantation play an important role in the treatment of patients. Despite this, the plasmablastic subtype is associated with poorer outcomes even in patients who initially respond to treatment.

Contributors SQ and NS conceptualised the idea of writing up this case report. BA-S drafted the manuscript under the supervision of SQ and NS. RG is the main haematologist for the patient and ensured that the management of the patient was accurately captured in the report. BA-S obtained a signed patient consent on behalf of SQ, RG and NS. All authors read, edited and approved the final document prior to submission.

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