CASE REPORT

Metastatic melanoma: a rare cause of central airway obstruction

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SUMMARY

A middle-aged woman with recurrent malignant melanoma presented initially with massive left pleural effusion. There was a complete obliteration of the left main bronchus on flexible bronchoscopy caused by a mass. Serial cryo-debulking of the tumour was done under rigid bronchoscopy; however, the outcome was not favourable due to the aggressive tumour growth. Vemurafenib was planned after thoracic radiation. She was not keen for the biologics treatment due to financial constraints. We report a case of central airway obstruction due to recurrent aggressive melanoma. More evaluations are needed on the role of interventional pulmonologist for bronchoscopic debulking of this rapidly growing tumour as well as the role of biological agents in treating such cases.

BACKGROUND

Management of central airway obstructions (CAOs) may be difficult and it is dependent on the underlying aetiological cause. The morbidity is significant and appropriate treatment is crucial to avoid fatalities.

Melanoma is a rare tumour affecting cells containing melanocytes.¹ Predominantly, it affects the skin; however, other organs may also rarely be the primary sites. Less than 5% of malignant skin tumours are due to malignant melanoma but the latter causes almost 60% mortality of all skin cancers.² It is highly aggressive with frequent distant metastases, for example to brain and bone. Metastasis to lung can occur, and the lungs can also be the primary site as in previous reports.³

We report this interesting case of CAO cause by rapidly growing malignant melanoma nodules which were not responding to debulking procedure using serial cryoprobe under flexible bronchoscopy.

CASE PRESENTATION

A middle-aged woman complained of worsening shortness of breath over few days with a prolonged history of constitutional symptoms. There was no history of cough, fever, night sweat or contact with tuberculosis. Of note, she was diagnosed with malignant melanoma 2 years ago. The primary site was at the left inguinal region which had metastasised to thorax and left hip in which she had received radiotherapy previously. However, subsequently she was lost to follow-up prior to this current presentation. Clinically she was weak and

tachypneic with respiratory rate of 30 breaths per minute. Chest examination was consistent with massive left pleural effusion. Chest drain was inserted and drained nearly 2 L of exudative effusion over few days.

The patient was also complaining of pain over left iliac fossa radiating to lower limb. It was described as dull aches which can be excruciatingly painful at times. On examination, there was a 2.5 cm x 2.0 cm subcutaneous nodule at the left mid-thigh which was fixed to underlying muscle. The overlying skin was normal with no abnormal pigments or ulcers seen.

INVESTIGATIONS

Blood parameters including cultures were all negative for infection. Pleural fluid analysis was consistent with exudative effusion; however, atypical cell was not seen.

Subsequent chest radiograph showed total left lung collapse.

CT scan of thorax showed left main bronchus stenosis with endobronchial lesion from the mediastinal nodes ([figure 1](#)).

A spirometry was performed revealed a restrictive ventilatory defect. Forced expiratory volume in 1 s FEV₁ was 1.59 L (64% predicted), forced vital capacity (FVC) was 1.87 L (67%) and FEV₁/FVC ratio was 96%.

She underwent flexible bronchoscopy under conscious sedation which revealed total occlusion of the left main bronchus with necrotic whitish material which infiltrated into the main carina ([figure 2A](#)). The histopathological examination was consistent with metastatic melanoma. The malignant cells expressed S100 (nuclear staining of moderate intensity) and HMB45 (cytoplasmic staining of strong intensity). The malignant cells were cytokeratin negative.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis for central airways obstructions with exudative pleural effusions:

- ▶ Primary endoluminal carcinoma (Bronchogenic, adenoid cystic, mucoepidermoid, carcinoid)
- ▶ Metastatic carcinoma to airway (bronchogenic, renal cell, breast, thyroid, colon, sarcoma, melanoma)
- ▶ Laryngeal carcinoma
- ▶ Lymphoma

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Figure 1 Coronal CT of thorax showed endobronchial invasion (A) with left main bronchus stenosis (B).

- ▶ Pneumonia with mucous plug and parapneumonic effusion
- ▶ Pulmonary tuberculoma and pleural involvement
- ▶ Sarcoidosis
- ▶ Foreign bodies aspirations

TREATMENT

Two attempts for serial debulking of the tumour using flexible cryoprobe (via rigid bronchoscopy) two weekly apart were unsuccessful as it failed to achieve recanalisation of the obstructed left main bronchus. The tumour was rapidly growing and new nodules have infiltrated the distal trachea as evidenced by serial bronchoscopy (figure 2B).

She was given options regarding potential systemic therapy, for example, chemotherapy (temozolomide or dacarbazine), vemurafenib or ipilimumab. The regimen for temozolomide is 200 mg/m² orally for 5 days every 4 weeks. Alternatively, intravenous dacarbazine dose is between 150 to 200 mg/m²/day for 5 days or at a single dose of 800 to 1000 mg/m², with doses repeated every 3 to 4 weeks. The other options are vemurafenib with a dose of 960 mg orally two times per day or ipilimumab which is given 3 mg/kg intravenously every 3 weeks for a total of 4 doses.

She only received radiation therapy to the thigh as unfortunately she was not keen for the systemic or targeted therapy.

OUTCOME AND FOLLOW-UP

While in ward she required nasal prong oxygen of 3 L/min. The thigh pain slowly improved with the radiation therapy and regular analgesics. Following completion of the irradiation (60 Gy in 30 fractions), she opted to rest at home while accepting palliative care visits. Unfortunately, she succumbed at home few weeks later.

Figure 2 Total occlusion of the left main bronchus with necrotic whitish material which infiltrated into the main carina (A). New nodules seen infiltrating the distal trachea (B).

DISCUSSION

Melanoma is one of the fastest growing malignancies with the skin being the most common primary site. Approximately 5%–10% of patients with metastatic melanoma have no primary site.^{4 5} Our patient primary site had left inguinal region as the primary site.

Lung is one of the most common sites of metastasis of melanoma of extrapulmonary origin with an incidence of 70%–82%.⁶ A previous analysis of 130 patients with metastatic melanoma to the thorax in a single centre revealed different presentation of metastatic melanoma, for example, multiple pulmonary nodules, solitary nodule, miliary pattern, mediastinal and/or hilar adenopathy, pleural effusion, lytic bony lesions, extrapleural mass and combined lesions.⁷ In one epidemiologic study, only 4.5% of endobronchial metastases were due to metastatic melanoma.⁸

In our literature research, there were two similar cases of endobronchial metastatic melanoma causing left main bronchus⁹ and bilateral main bronchus occlusion respectively.^{10 11} Some other reported cases of endobronchial metastasis of melanoma includes lower lobe occlusion and pigmented endobronchial submucosa patches.^{12 13}

CAO denotes a variety of disease processes that impede airflow within the central airways, trachea and mainstem bronchi which may cause noticeable signs and symptoms. In turn, it also causes significant mortality and morbidity. The causes may either be benign, for example tracheomalacia, or malignant, including primary lung or metastatic cancers.

Symptoms related to CAO due to melanoma in our case may be as acutely as seen in foreign body aspiration as compared with other slowly growing malignant obstructions. Her spirometry result was consistent with CAO. In addition, the feature of flow-volume loop which may show blunting graph may suggest that airway narrowing to approximately 8–10 mm in diameter.

Prognosis of stage 4 melanoma metastatic to the lung is 7%–9%¹⁴ which is worse than primary lung malignancy. The discovery of BRAF mutation was found in approximately 50% of patients with melanoma. Since further development of targeted therapies (against BRAF and MEK), for instance vemurafenib, dabrafenib, trametinib, an overall improvement of survival is seen.¹⁵

Surgical resection with either lobectomy or pneumonectomy is the first-line treatment if solitary mass. It may represent the best chance of long-term survival, especially in localised pulmonary lesion.¹⁶ Melanoma has traditionally been viewed as a prototypical radio-resistant cancer. Hence, the roles of adjuvant or definitive radiation therapy remain controversial. However, based on recent studies, there may be a significant role for radiation therapy in melanoma treatment under certain clinical circumstances.¹⁷ For example, it is often used to relieve symptoms caused by the metastasis, especially to bones and brain.

Endoscopic treatment of endobronchial melanoma can be offered in selected patients who are not suitable for systemic treatment and can be offered as palliation to achieve recanalisation of obstructed segments. Dalar *et al* reported a patient with bilateral main bronchi stenosis who underwent endobronchial treatment with diode laser and rigid bronchoscopy.¹¹ However, further literature research is needed to evaluate the role of combination therapy of cryo-debulking of the central airway tumour, with neo-adjuvant chemotherapy or radiotherapy.

In summary, this case highlights a case of CAO due to aggressive melanoma. Endoscopic treatment of obstructed segments is a potential treatment to explore.

Compared with surgery, endoscopic treatment is less invasive without the added perioperative morbidity and mortality; however, this service is not widely available in most hospitals.

Learning points

- Despite its rarity, melanoma is an aggressive type of malignancy which carry high cancer-related morbidity and mortality.
- Melanoma may recur as long as 10 years after initial treatment, therefore surveillance and follow-up are mandatory.
- Central airway obstructions due to melanoma are also rare and the debulking procedure using flexible cryoprobe bronchoscopy may be difficult.

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