CASE REPORT

CD34-negative solitary fibrous tumour resistant to imatinib

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SUMMARY

A 75-year-old man presented to our hospital with multifocal thickening of the left pleura and left pleural effusion. Histology of the pleura showed uniform and bipolar spindle cells with moderate mitosis in a collagenised stroma. It further showed abundant blood vessels in a haemangiopericytoma-like pattern. These findings were strongly suggestive of malignant solitary fibrous tumour (SFT). The tumour showed negative staining for CD34. The loss of CD34 expression could imply histologically high-grade tumour, as reported previously. Imatinib, a multityrosine kinase inhibitor with targets, including platelet-derived growth factor receptor (PDGFR)- α and PDGFR- β , has antitumour activity in some patients with SFT. Unfortunately, imatinib treatment failed to control disease progression in the present case that expressed PDGFR- β , but not PDGFR- α . This report described a case of CD34-negative SFT resistant to imatinib.

BACKGROUND

Solitary fibrous tumour (SFT) is a rare soft tissue sarcoma, often occurring in the visceral pleura.¹ Its morphological pattern varies and there are no distinctive immunohistochemical or electron microscopic features.² Staining for CD34, which is a useful test for distinguishing from endometrial stromal sarcomas, is positive in many cases of SFTs.^{3–4} However, loss of CD34 expression has been documented in some cases of SFT and is associated with unfavourable outcome.^{5–6} Imatinib mesylate is a multityrosine kinase inhibitor that targets platelet-derived growth factor receptor (PDGFR), BCR-ABL and c-kit.^{7–9} The antitumour activity of imatinib has been seen in aggressive fibromatosis and dermatofibrosarcoma, which express PDGFR- α and PDGFR- β .¹⁰ It is yet obscure that imatinib, targeting PDGFR- α and PDGFR- β , has antitumour activity in patients with SFT lacking CD34. This report describes an imatinib-resistant case of SFT that was negative for CD34 and expressed PDGFR- β , but not PDGFR- α .

CASE PRESENTATION

A 75-year-old man presented to our hospital with multifocal thickening of the left pleura and with left pleural effusion (figure 1). He underwent surgical biopsies of the pleura. The specimens were composed of uniform and bipolar spindle cells with moderate mitosis in a collagenised stroma. Further, abundant blood vessels were noted in a haemangiopericytoma-like pattern (figure 2A). These findings were strongly suggestive of

malignant SFT. The tumour showed negative staining for CD34 as well as for cytokeratins, S-100, smooth muscle actin, epithelial membrane antigen, c-kit and PDGFR- α . Staining was positive for PDGFR- β (figure 2B) and vimentin. A diagnosis of SFT negative for CD34 was made.

DIFFERENTIAL DIAGNOSIS

The morphology of spindle cell pleural tumour in our case indicated SFT. Our differential diagnosis included mesothelioma and other sarcoma, like endometrial stromal sarcoma and synovial sarcoma. Vimentin is expressed in various epithelial cancers, including SFT and mesothelioma, whereas cytokeratin has been shown to be a reliable marker for malignant mesothelioma and is usually negative in SFT of the pleura.³ Negative findings for cytokeratin, smooth muscle actin, S-100 and c-kit are consistent with SFT manifestation.¹¹ CD34 is a myeloid progenitor cell antigen that is also present in endothelial cells and subsets of fibroblasts. CD34 expression is found in most cases of SFTs, but absent in malignant mesotheliomas and endometrial stromal sarcomas.^{3–4} Although CD34 is thought to be a useful marker in the diagnosis of SFT,² one should bear in mind that its expression can be lost in high-grade tumours or with repeated recurrences.^{5–6} The conversion of a CD34-positive SFT to a CD34-negative lesion is associated with malignant transformation.¹²

TREATMENT

Owing to the extent of the disease, the tumour was deemed unresectable. No standard treatment protocols have been devised for patients with unresectable SFT. On the assumption that the inhibition of PDGFR might be beneficial in controlling malignant SFT, the patient underwent treatment with

Figure 1 CT scan showed multifocal thickening of the left pleura and left pleural effusion.

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Figure 2 (A) H&E staining showed that abundant blood vessels were noted in a haemangiopericytoma-like pattern. (B) The tumour tissue expressed platelet-derived growth factor receptor β .

imatinib after providing written informed consent. Imatinib was administered orally at a dose of 600 mg/day.

OUTCOME AND FOLLOW-UP

Thoracic radiography on day 8 showed an increased volume of the bilateral pleural effusions. Left ventricular ejection fraction, as evaluated ultrasonographically, was within the normal range. CT scan showed a slight deterioration of pleural thickness. Since we were unable to determine whether these findings represented disease progression or imatinib-induced fluid retention, imatinib therapy was terminated. The disease continued to progress with the increasing volume of pleural effusions and the patient died.

DISCUSSION

SFT of the pleura is a mesenchymal tumour, and the majority of patients with SFT are symptomatic and present with large tumours.¹ CD34 is a myeloid progenitor cell antigen that is also present in endothelial cells and various subsets of fibroblasts. CD34 expression is found in most cases of SFTs with few exceptions.^{3–4} Therefore, CD34 is regarded as a useful positive marker for SFT within the differential diagnosis. However, CD34 expression can be lost in histologically high-grade tumours or tumours from patients with repeated recurrences.^{5–6} Furthermore, the conversion of a CD34-positive SFT to a CD34-negative lesion is associated with malignant transformation.⁵ Negative findings for cytokeratin, smooth muscle actin, S-100 and c-kit are consistent with the diagnosis of SFT.¹¹ The pleural tumour in the present case has histological manifestations of SFT on H&E staining and had immunohistochemical features of a typical SFT, except for the loss of CD34 expression.

De Pas *et al*¹³ described the successful use of imatinib in a patient with a chemotherapy-resistant and radiotherapy-resistant advanced malignant SFT that stained positively for PDGFR- α and PDGFR- β . Indeed, PDGFR- α and PDGFR- β in SFT reportedly play a role in malignant potency.¹⁴ In the present case, the tumour tissue expressed PDGFR- β , but not PDGFR- α , and imatinib failed to control the growth of the tumour. One of the explanations for the different results achieved in the case reported by De Pas *et al* and our case are related to the magnitude of inhibitory potency against tumour growth. The absence of expression of PDGFR- α might be associated with an

insufficient inhibitory efficacy of imatinib in our case. Another possibility is that the loss of CD34 expression may be associated with unfavourable outcomes.^{5–6} In conclusion, this report described a case of CD34-negative malignant SFT that was resistant to imatinib.

Learning points

- ▶ CD34 staining is positive in many cases of solitary fibrous tumours (SFTs), whereas the loss of CD34 expression has been documented in the cases with unfavourable outcome. Distinctive immunohistochemical or electron microscopic features in SFT have not been established.
- ▶ High expressions of platelet-derived growth factor receptor (PDGFR)- α and PDGFR- β in sarcomas, including SFT, reportedly play a role in malignant potency.
- ▶ Imatinib displayed insufficient antitumour activity in a case of a spindle-cell pleural tumour-expressing PDGFR- β , but not PDGFR- α , which progressed rapidly.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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