CASE REPORT

Pulmonary inflammatory myofibroblastic tumour after Hodgkin's lymphoma

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SUMMARY

Positron emission tomography (PET)/CT plays a major role in staging, assessing response to treatment and during follow-up of paediatric Hodgkin's lymphoma (HL). Owing to high sensitivity to detect viable tumoural tissue, negative PET/CT is highly predictive of survival. However, ¹⁸F-FDG is not specific for malignant disease and may concentrate in numerous benign/inflammatory lesions that may cause 'false-positive' results and follow-up PET/CT studies should be interpreted with caution. We report a case of pulmonary inflammatory myofibroblastic tumour, which developed during follow-up in a young patient with complete remission of a stage IIB HL and was fully treated with surgical resection.

BACKGROUND

Hodgkin's lymphoma (HL) accounts for 5% of paediatric malignancies. ¹⁸F-FDG positron emission tomography (PET)/CT plays a major role in staging, assessing response to treatment and during follow-up of the disease. Owing to high sensitivity to detect viable tumoural tissue, negative PET/CT is highly predictive of disease-free survival.¹ However, ¹⁸F-FDG is not a specific tracer and may be taken up by numerous inflammatory/benign lesions. Inflammatory myofibroblastic tumour (IMT), previously known as inflammatory reactive lesion simulating a neoplasia is now considered as a neoplastic lesion. There is only one case reported in the literature of an adolescent with HL who developed IMT after chemotherapy and radiotherapy.² We report a case of an adolescent with HL who developed IMT 3 years after complete response to chemotherapy and radiotherapy.

CASE PRESENTATION

A 14-year-old girl presented with a progressive general weakness, loss of appetite, night sweats and pruritus. Physical examination revealed cervical, supraclavicular and axillary adenopathies. Laboratories were all negative. CT showed a mediastinal mass and multiple supra-diaphragmatic adenopathies. Initial ¹⁸F-FDG PET/CT showed very intense uptake in the mediastinal mass and enlarged lymph nodes. There was no extranodal or sub-diaphragmatic abnormality. Excisional biopsy revealed nodular sclerosing HL while bone marrow biopsy was negative. This stage IIB HL was treated with chemotherapy (GPOH-HD-2002-TG2 protocol) followed by fractionated radiotherapy of the mediastinal bulk, left axilla and right supraclavicular region (19.8 Gy in total). End treatment

¹⁸F-FDG PET/CT showed no residual active lesion (figure 1A). At 3 years of follow-up, a CT scan demonstrated a juxtascissural pulmonary nodule of 6 mm short axis in the left inferior lobe.

INVESTIGATIONS

As recurrent disease was suspected, an ¹⁸F-FDG PET/CT was performed and showed moderate ¹⁸F-FDG uptake in the nodule with a maximum standard uptake value (SUV_{max}) of 2.3 g/mL. There was no other abnormal ¹⁸F-FDG uptake focus (figure 1B). At that time, this nodule was not considered as recurrent HL but rather as a possible benign/inflammatory lesion, and it was decided to continue observation. One year later, the solitary nodule increased in size (11 mm short axis) and metabolic activity (SUV_{max}=8.6 g/mL, figure 1C), while there were no symptoms of inflammatory/infectious lung disease and laboratories were normal.

DIFFERENTIAL DIAGNOSIS

Regarding the apparition of a new asymptomatic lesion in a previously treated patient with HL, several differential diagnoses should be considered. First of all an HL recurrence should be suspected. Moreover, primary or metastatic neoplasm should be ruled out before considering infectious or inflammatory benign lesion.

TREATMENT

Although the lesion continued to grow slowly, a wedge resection of the left inferior lobe was performed. Microscopic examination showed a well-demarcated non-encapsulated lesion (figure 2A) composed of a mixture of myofibroblasts and inflammatory cells including histiocytes and numerous plasma cells (figure 2B), consistent with a diagnosis of IMT. There was no evidence of HL.

OUTCOME AND FOLLOW-UP

Thoracic X-ray and MRI performed 1 and 2 years later did not demonstrate any recurrence.

DISCUSSION

IMT is a non-encapsulated, but well-circumscribed lesion composed of a variable mixture of collagen, inflammatory cells (plasma cells, lymphocytes, histiocytes and eosinophils) and usually cytologically bland spindle cells showing myofibroblastic differentiation³; up to 10% of cases show calcification and/or foci of necrosis.⁴

IMT may occur at any age (range 9 days–88 years) and can develop throughout the body, the

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To cite: Ilic V, Dunet V, Beck-Popovic M, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-202491

Figure 1 ^{18}F -FDG PET/CT during follow-up. (A) November 2005: no lesion after completion of chemotherapy; (B) January 2009: solitary 6 mm short-axis nodule of the left inferior lobe with moderate ^{18}F -FDG uptake ($\text{SUV}_{\text{max}}=2.3$ g/mL); (C) December 2010: solitary nodule of the left inferior lobe with increased size (11 mm short axis) and increased ^{18}F -FDG uptake ($\text{SUV}_{\text{max}}=8.6$ g/mL). PET, positron emission tomography; SUV_{max} , maximum standardised uptake value.

lung being the most common site.⁵ Its incidence is 0.04–1.2% and it is the most common primary pulmonary tumour before 16 years of age.^{6–7} Hence, in children without an underlying malignancy, a solitary peripheral pulmonary nodule or mass is more likely to represent an IMT than a lung cancer. Patients remain asymptomatic in 50% of cases, the disease being incidentally detected on chest X-ray.⁸ Symptomatic patients may present with cough, dyspnoea, chest pain or haemoptysis, symptoms being related to the location/size of the lesion. Both sexes are equally affected. It most frequently presents as a single, well-circumscribed, round/ovoid intrapulmonary nodule measuring 1–10 cm in diameter, but multifocal disease⁹ and polypoid endobronchial lesions have also been described.^{10–11}

The pathogenesis of IMT remains unclear. Although IMT was described as a non-neoplastic process characterised by the uncontrolled growth of inflammatory cells⁴ in response to tissue damage, it is now considered as a mesenchymal neoplasm of intermediate biological potential, owing to its tendency for local recurrence and the possibility of early or delayed metastasis.³ It may occur after completion of therapy for cancer.^{8–10} In a clinicopathological review of 20 patients with pulmonary IMT, Pettinato *et al*¹⁰ described two patients with a history of lung cancer: one 17-year-old patient with stage IV HL was treated with chemotherapy followed by radiotherapy and developed pulmonary IMT 12 years later; the second patient

developed IMT 19 years after being treated with radiotherapy for Wilms' tumour with pulmonary metastases. Kovach *et al*⁵ also reported the possibility of a concomitant neoplasm within the resected IMT in 5 of 44 cases. Moreover, recent studies have identified chromosomal 2p23 abnormalities, near-anaplastic lymphoma kinase oncogene, occurring in about 50% of IMTs, lending support to the concept of a neoplasm origin.¹²

The imaging findings are non-diagnostic and a primary or metastatic neoplasm must be considered in the differential diagnosis. Agrons *et al*¹¹ described a single mass in 90%, multiple lesions in 5% and hilar infiltration in 16%.

Several cases of ^{18}F -FDG-positive IMT in different localisations such as the liver, spleen or more frequently chest^{2–9–13} have been reported. Matsuoka *et al*¹³ reported a case of a patient with lung nodule suspicious for primary lung cancer, which was positive on PET/CT ($\text{SUV}_{\text{max}}=5.8$ g/mL). Owing to rapid growing within 2 weeks, resection was performed and histopathology revealed IMT. Howman-Giles *et al*² reported the case of a 16-year-old boy with stage IVA HL invading the lung who developed IMT in the lung included in the field of radiotherapy 16 months after completion of therapy. The IMT presented high ^{18}F -FDG uptake ($\text{SUV}_{\text{max}}=6.8$ g/mL) on the PET/CT.

IMTs may also be associated with another primary tumour. Zheng *et al*¹⁴ reported a case with coexistent pulmonary IMT

Figure 2 (A) Well-demarcated but not encapsulated tumour on whole-mount H&E cross-section. (B) Tumour composed of a mixture of inflammatory cells (lymphocytes, plasma cells and foamy macrophages) and bland spindle cells.

and carcinoma; on ^{18}F -FDG PET/CT the lesion with high ^{18}F -FDG uptake was considered malignant and the lesion with low ^{18}F -FDG activity was considered benign; histology subsequently demonstrated that the ^{18}F -FDG-positive lesion was an IMT and that the ^{18}F -FDG-negative lesion was an adenocarcinoma. This inconsistency may be caused by the mechanism of ^{18}F -FDG accumulation in IMT. Indeed, ^{18}F -FDG uptake by IMT is considered to be related to the inflammatory cells in the tumour rather than in the fibrotic stroma. As ^{18}F -FDG accumulation in IMT depends on the varying amount of inflammatory and fibrotic cells,¹⁵ the imaging pattern may vary from very low to high uptake. Consequently, IMT should be suspected in patients with radiochemosensitive malignant disorders such as HL and ^{18}F -FDG-positive lesion during follow-up, but definitive histology remains mandatory.

Treatment of IMT is mainly surgical. Complete surgical resection of the lesion is the diagnostic and therapeutic method of choice^{6–8} and ensures an excellent long-term prognosis.⁸ As in our case, wedge resection is recommended for peripheral lung tumours, but lobectomy may be necessary if the lesion is more centrally located. However, a complete resection may be

challenging, which explains the possibility of recurrence (2–25%), especially for extrapulmonary and laryngotracheal lesions.^{6–16–18} In case of contraindication to surgical resection, steroid or chemotherapy rather than radiation therapy is recommended.⁸ ^{18}F -FDG PET/CT may be useful to assess response to treatment.^{19–20}

Acknowledgements The authors would like to acknowledge Dr Igor Letovanec and Dr Michel Gonzalez for their help in the management of the patient and in providing the histology images.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Learning points

- Inflammatory myofibroblastic tumour is a mesenchymal neoplasm of intermediate biological potential that may occur at any age and can develop throughout the body.
- Patients are asymptomatic in 50% of cases.
- The imaging findings are non-diagnostic and a recurrence, primary or metastatic neoplasm must be considered in the differential diagnosis.
- Complete surgical resection of the lesion is the diagnostic and therapeutic method of choice.

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