A 72-year-old woman with a persistent cough and abnormal chest X-ray

Introduction

T-cell lymphomas are a form of lymphoproliferative disease broadly categorized as being either primary cutaneous or peripheral. There is considerable overlap in their clinical presentation, but confirming the precise disease subtype is critical since it has implications for prognosis and treatment strategy. Its rarity means guidelines for treatment are limited, with more aggressive approaches usually reserved for high risk or refractory cases.

This article reports the case of a woman previously treated for presumed primary cutaneous T-cell lymphoma who developed isolated pulmonary recurrence at a 3-year interval – a rare finding in this condition and indicative of this actually being a form of peripheral T-cell lymphoma all along.

Discussion

T-cell lymphomas are a heterogeneous group of lymphoproliferative conditions. In broad terms, they are classified as primary cutaneous T-cell lymphomas or peripheral T-cell lymphomas. However, peripheral T-cell lymphoma can involve the skin and even present as isolated skin lesions, so there is considerable overlap. It is increasingly recognized that subtypes of cutaneous T-cell lymphoma and peripheral T-cell lymphoma are very different with respect to their clinical behaviour and response to treatment (Willemze et al, 2005). This has led to a separation of those that display more benign behaviour, such as lymphomatoid papulosis and cutaneous anaplastic large cell lym-

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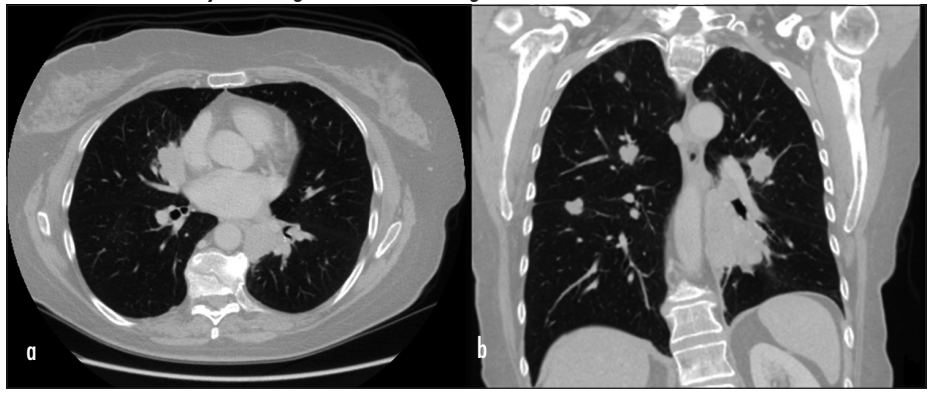
Figure 1. a. Axial and (b) coronal computed tomography images demonstrating bilateral parenchymal and endobronchial nodularity with larger left lower and right middle lobe soft tissue masses.



Case Report

A 72-year-old woman was seen in clinic with a 3-month history of persistent dry cough and chest X-ray arranged by her GP that had demonstrated bilateral pulmonary nodules. The patient's medical history was notable only for a skin cancer – labelled as a primary cutaneous T-cell lymphoma – diagnosed 3 years previously and successfully treated with excision biopsy and radiotherapy. Other than a persistent cough she described no concerning features including haemoptysis, weight loss, anorexia, dyspnoea or chest pain. She was a lifelong non-smoker with no occupational risk factors for lung disease. On examination the patient was afebrile with normal resting oxygen saturations. Cardiovascular and abdominal examinations were unremarkable; pulmonary examination revealed fine inspiratory crackles at the left base only.

Routine bloods including full blood count, clotting screen, renal function, liver function and serum calcium were within normal limits. Computed tomography scan of the thorax (*Figure 1*) demonstrated a 5 cm soft tissue mass narrowing the left main bronchus with further smaller nodules visualized within the large airways and lung parenchyma bilaterally. Subsequent whole body positron emission tomography scan confirmed that pathological fludeoxyglucose uptake was confined to the thorax only.

Flexible bronchoscopy identified multiple pink gelatinous lesions throughout the bronchial tree (*Figure 2a*) with the largest masses narrowing the left main and right middle lobe bronchi. Biopsies (*Figures 2b* and *c*) revealed infiltration of the bronchial mucosa with neoplastic cells strongly expressing CD30 and CD2, scattered staining for CD4 and negative for other markers including CD56, synaptophisin, cytokeratin, CD20 and ALK-1. MIB-1 proliferative index was greater than 80%. These immunohistochemistry results prompted comparison with the skin biopsy histology from 3 years previously, demonstrating morphological similarities and allowing confirmation of the diagnosis of recurrent peripheral T-cell lymphoma with isolated pulmonary disease.

The patient underwent treatment with combination chemotherapy (six cycles of CHOP – cyclophosphamide, doxorubicin, vincristine and prednisolone) to complete remission and 1 year later remained systemically disease-free on interval positron emission tomography-computed tomography. She intermittently develops transient migratory skin lesions (consistent with a pattern of lymphomatoid papulosis) that have been biopsied and confirmed as CD30-positive peripheral T-cell lymphoma, and remains under long-term haematology outpatient follow up.

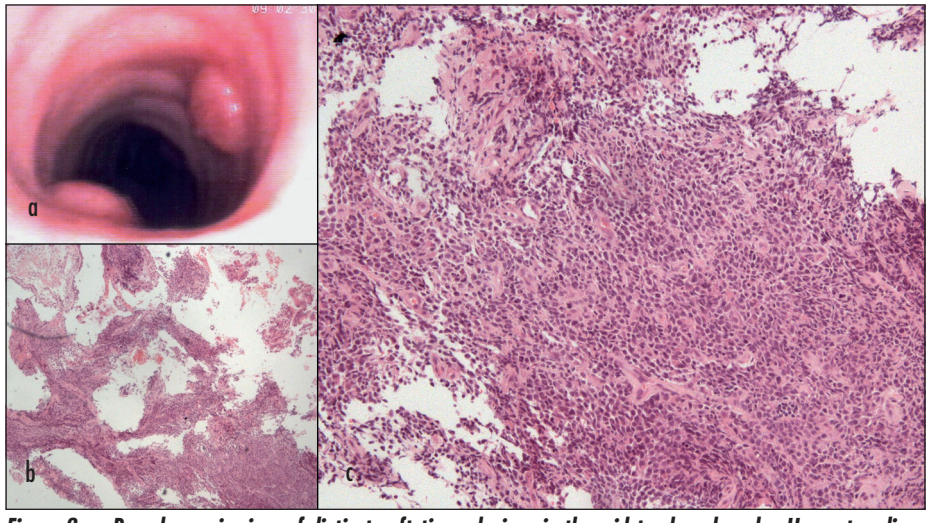


Figure 2. a. Bronchoscopic view of distinct soft-tissue lesions in the mid-trachea. b and c. Haematoxylin and eosin stain of endobronchial biopsies showing infiltration of atypical lymphoid cells at (b) x10 and (c) x20 power.

phoma, from clinically aggressive forms including HTLV-1 positive adult T-cell lymphoma where the median survival is less than 6 months.

Peripheral T-cell lymphoma is a rare condition which accounts for 10% of cases of non-Hodgkin lymphoma. This fact, in combination with the heterogeneity of the disease, has presented a significant challenge in developing guidelines. Collaborative work through the International peripheral T-cell lymphoma Project has compensated by combining data from multiple sources to inform the evidence base for both prognostic and therapeutic purposes (Foss et al, 2011), although individualized treatment strategies for patients remain some way off (Moskowitz et al, 2012). Pulmonary and particularly endobronchial disease in the context of peripheral T-cell lymphoma is unusual and, as with other types of visceral involvement, associated with a worse prognosis. Treatment usually involves combination chemotherapy; more aggressive approaches such as autologous haemopoietic stem cell transplantation and radiation therapy are controversial and generally used in patients whose disease is either refractory or considered high risk on the basis of subtype and prognostic index (Sonnen et al, 2005). BJHM

Foss FM, Zinzani PL, Vose JM et al (2011) Peripheral T-cell lymphoma. *Blood* **117**(25): 6756–67 (doi: 10.1182/blood-2010-05-231548)
Moskowitz AJ, Lunning MA, Horwitz SM (2012) Should patients with aggressive peripheral T-cell lymphoma all be treated the same?: no… well yes, …but maybe not for long. *Cancer J* **18**(5): 445–9 (doi: 10.1097/PPO.0b013e31826aeeb2)
Sonnen R, Schmidt WP, Muller-Hermelink HK, Schmitz N (2005) The International Prognostic Index determines the outcome of patients with nodal mature T-cell lymphomas. *Br J Haematol* **129**(3): 366–72 (doi: 10.1111/j.1365-2141.2005.05478.x)
Willemze R, Jaffe ES, Burg G et al (2005) WHO-EORTC classification for cutaneous lymphomas. *Blood* **105**(10): 3768–85 (doi: 10.1182/blood-2004-09-3502)

LEARNING POINTS

- T-cell lymphomas are divided into primary cutaneous and peripheral forms, with further subtypes of disease within these broad categories.
- The clinical manifestations of each subtype may be similar and confuse the overall picture; however, an accurate diagnosis is crucial since it has implications for the patient and clinician in terms of prognosis and therapeutic decision making.
- Pulmonary involvement by peripheral T-cell lymphoma is rare, particularly in isolation, and like other visceral manifestations can be associated with a worse long-term outcome.
- More aggressive approaches to treating T-cell lymphoma should be actively considered in patients whose disease subtype or clinical picture suggests they are a high-risk case, although guidelines for treatment remain some way off as a result of the rarity of the condition.