Pulmonary lymphangitic carcinomatosis presenting as severe interstitial lung disease in a 15-year-old female

To the Editor:

Pulmonary lymphangitic carcinomatosis (PLC) is a metastatic lung disease characterised by the diffuse infiltration and obstruction of the pulmonary parenchymal lymphatic system by tumour cells [1]. It is an extremely rare diagnosis in paediatrics and we believe that this is the first reported case in a child, presenting as interstitial lung disease without a known primary tumour.

A 15-yr-old Caucasian female was transferred to our hospital (Birmingham Children’s Hospital, Birmingham, UK) for further assessment and management of respiratory failure, secondary to presumed interstitial lung disease. 8 weeks previously she had presented to her local hospital with a 5-week history of cough and shortness of breath associated with lethargy, poor appetite and early satiety. On examination she was hypoxic with bilateral wheeze and crackles. Bilateral perihilar shadows and increased bronchovascular markings were seen on the chest radiograph. Atypical pneumonia was diagnosed and she received oxygen, oral erythromycin and inhaled salbutamol. She recovered but after discharge required two courses of oral prednisolone and salbutamol for wheeze and shortness of breath.

She deteriorated while visiting relatives in the Birmingham area of the UK and required admission for cough, shortness of breath and haemoptysis. On examination she was tachypnoeic, tachycardic and hypoxic but not clubbed. There was generalised decreased air entry and bilateral inspiratory crackles on auscultation. Her blood tests were unremarkable apart from elevated C-reactive protein (54 mg L\(^{-1}\)). A chest radiograph and subsequent computed tomography (CT) scan of her chest showed extensive, bilateral interstitial changes (fig. 1). A diagnosis of presumed interstitial lung disease was made. The differential diagnoses are summarised in table 1.

The patient’s family were from the travelling community but lived in a brick house with central heating. Although she was a nonsmoker, her parents smoked heavily. She was not sexually active and denied any solvent or recreational drug use. Apart from brief contact with pigeons 8 months prior to presentation there was no history of exposure to organic dusts. She admitted poor compliance with thyroxine that had been prescribed after she was diagnosed with hypothyroidism aged 6 yrs.

A wide range of investigations were performed (table 1) including a flexible bronchoscopy and bronchoalveolar lavage. After these procedures the patient required intubation and ventilation with high-frequency oscillation ventilation (HFOV). A blood culture from the referring hospital (Birmingham City Hospital, Birmingham, UK) grew Haemophilus influenzae and intravenous piperacillin with tazobactam and ciprofloxacin were commenced.

Once bacterial, fungal and Pneumocystis carinii pneumonia infection were excluded (day 3), high dose i.v methyl-prednisolone was started. Despite this, the patient continued to deteriorate with worsening respiratory failure. A lung biopsy was discussed at length between members of the paediatric respiratory, intensive care and surgical teams, as well as the family. The consensus was that as the patient was on HFOV and the lesions were peripheral, a transbronchial biopsy would have been technically difficult and unlikely to produce a diagnostic biopsy. It was also thought that the patient’s unstable clinical condition meant that an open biopsy carried an unacceptable risk of significant complications or death. Therefore, the biopsy was delayed to allow for any clinical improvement which would decrease these risks. Antimicrobial therapy was extended empirically to cover for possible Mycobacterium tuberculosis, fungal and P. carinii infection. By day 14, despite almost maximal HFOV (mean airway pressure 28 cmH\(_2\)O, amplitude (AP) 120, inspiratory oxygen fraction 100%), her condition deteriorated further. She required a noradrenaline infusion and chest radiograph showed increased interstitial changes and bilateral pleural effusions. In view of her deteriorating condition and the absence of definitive diagnosis, lung biopsy was reconsidered. It was thought unlikely that the patient’s condition would improve and that the patient was at high risk of dying while on the ventilator. After counselling the family about the severe risks, it was decided that an open lung biopsy should be performed in an attempt to make a diagnosis. This was performed on the paediatric intensive care unit on day 16. She tolerated the procedure without complications.

![FIGURE 1. a) Chest radiograph showing bilateral coarse interstitial shadowing. b) High-resolution computed tomography scan of the chest. The image is degraded by movement due to patient dyspnoea. The thickened interlobular septae is suggestive of interstitial lung disease.](image-url)
The lung biopsy showed multiple tumour thrombi within the lymphatic vessels, around airways and arteries, and along the pleural surface (fig. 2). A sample of pleural fluid obtained during the procedure revealed large atypical cells, probably epithelial in origin. A diagnosis of PLC from a primary adenocarcinoma was made. The diagnosis and poor prognosis was discussed with the parents. Life support treatment was withdrawn on day 19 and she died shortly afterwards. The family refused a post mortem.

Intrathoracic metastases occur in 30–40% of patients with malignancy and 6–8% of these patients have PLC [1]. It most commonly affects patients aged 40–49 yrs and is rare in younger patients. There is one paediatric case report of PLC in a patient with renal adenocarcinoma [2] and a case series of six young adults (average age 26 yrs) with PLC from occult stomach carcinoma [3]. The present case is the first to report PLC in a child from an occult malignancy presenting with symptoms and signs of interstitial lung disease.

The spread of tumour cells to the pulmonary lymphatic system or the adjacent interstitia causes thickening of the bronchovascular bundles and septa. The interstitia is further thickened by a desmoplastic reaction caused by the proliferation of tumour cells and lymphatic dilation [4, 5]. The primary tumours most commonly associated with PLC are: breast (33%), stomach (29%), lungs (17%), pancreas (4%) and prostate (3%) [1, 4]. The preferred diagnostic procedure for PLC is lung biopsy (transbronchial or open). The pulmonary microvascular cytology may be of value when a lung biopsy is refused or thought to be too hazardous [6].

In this case it was decided that a transbronchial biopsy was unlikely to be diagnostic and an open lung biopsy was therefore favoured. Early in her admission, as it was hoped the patient’s condition would improve, an open lung biopsy was thought to carry an unacceptable risk of significant complications or death. This is supported by a recent review which reports the mortality rate of open lung biopsy in mechanically ventilated patients as 54% [7]. With hindsight it can be argued that despite the patient’s condition the biopsy should have been performed on day 3 as she had deteriorated further by the time it was performed on day 16. In practice, lung biopsy should be performed as early as it is practical and safe to do so.

PLC can present with dyspnoea and cough and, as with our patient, this may precede the diagnosis of the primary tumour. In the case series mentioned previously, the most prominent symptom other than progressive dyspnoea was weight loss [3]. Even if histologically confirmed, the chest radiograph is normal in 30–50% of cases. A variety of chest radiographs and CT changes are reported and can mimic those of sarcoidosis [4]. The prognosis for patients with PLC is extremely poor with less than half surviving past 3 months [1]. Despite this there are case reports of platinum-based chemotherapy leading to transient remission [8].

In summary, PLC is a rare but important cause of respiratory compromise that may present with the signs and symptoms of interstitial lung disease in a child.

| TABLE 1 | Differential diagnoses, investigations and results |
|---------|-----------------------------------------------|
| Differential diagnosis | Investigation | Result |
| Bacterial LRTI | BAL microscopy and culture | Negative |
| Viral LRTI | BAL viral PCR and culture | Negative |
| Fungal LRTI | BAL cytology and culture | Negative |
| PCP | BAL cytology and PCR | Negative |
| Pulmonary TB | BAL acid-fast bacilli stain and culture; Mantoux test | Negative |
| Hypersensitivity pneumonitis | IgG and IgE precipitating antibodies to inhaled organic dusts | Negative |
| Connective tissue disorder | Autoimmune screen | Negative |
| Sarcoïdosis | Serum ACE | Normal |
| Alveolar haemorrhage syndrome | ANCA, anti-GBM and BAL-haemosiderin laden macrophages | Negative |
| Histiocytosis | Bone marrow aspirate | Normal |
| Immunodeficiency | Lgs and HIV tests | Normal |
| Congenital or acquired cardiac abnormality | Echocardiogram | Normal |

LRTI: lower respiratory tract infection; PCP: Pneumocystis carinii pneumonia; TB: tuberculosis; BAL: bronchoalveolar lavage; Ig: immunoglobulin; ACE: angiotensin-converting enzyme; ANCA: anti-neutrophil cytoplasmic antigen; anti-GBM: anti-glomerular basement membrane antigen. *: Goodpasture’s disease or granulomatosis with polyangiitis (Wegener’s).

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Pulmonary nocardiosis in immunocompetent patients: can COPD be the only risk factor?

To the Editor:

Pulmonary nocardiosis is a rare disorder that mainly affects immunocompromised patients. Several risk factors have been identified, such as corticosteroid therapy, chronic obstructive pulmonary disease (COPD), cystic fibrosis and bronchiectasis. Diagnosis of nocardiosis is difficult as bacteriological culture can be problematic. However, if observations are atypical, clinicians should consider Nocardia in immunocompetent patients, particularly when the patient is also suffering from COPD. Herein, we ask whether COPD alone is a risk factor for pulmonary nocardiosis.

We report the case of a 71-yr-old female smoker suffering from COPD who had not received inhaled or oral (bolus or long-term) corticosteroid therapy. She had suffered from bronchiectasis after pulmonary tuberculosis 60 yrs previously. She presented to the hospital with an exacerbated chronic cough that had lasted several months and chronic fever, with no weight loss. Prior to admission, amoxicillin followed by spiramycin therapy was not effective. Laboratory evaluation showed hyperleukocytosis (14,130 cells per mm$^3$, with 10,753 polynuclear neutrophils per mm$^3$) and C-reactive protein 75 mg/L (normal range <5 mg/L)).

An intravenous antimicrobial therapy of trimethoprim–sulfamethoxazole (cotrimoxazole) and amikacin was administered for 15 days followed by oral only trimethoprim–sulfamethoxazole (cotrimoxazole) and amikacin (MIC: 0.01 mg/mL) and trimethoprim–sulfamethoxazole (cotrimoxazole) and amikacin (MIC: 0.01 mg/mL) and trimethoprim–sulfamethoxazole (cotrimoxazole) and amikacin (MIC: 0.01 mg/mL).

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