CASE REPORT

Positron emission tomography aids diagnosis of relapsing polychondritis

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SUMMARY

A 39-year-old man presented to the hospital in April 2011 with a 2-month history of tonsillitis, night sweats, fatigue, weight loss, shortness of breath on exertion and a dry cough. He was a non-smoker, previously fit and well with no regular medication. Examination of the respiratory, cardiovascular and gastrointestinal systems was normal; he appeared generally well. C reactive protein and erythrocyte sedimentation rate were raised. A CT of the thorax showed mediastinal thickening and mediastinal lymphadenopathy. Whole body ¹⁸F-fluorodeoxyglucose positron emission tomography showed diffuse tracheobronchial activity. Tracheal and lymph node biopsies showed non-specific features. Lung function tests showed an obstructive picture. A diagnosis of relapsing polychondritis was made. Immunosuppressive treatment was started, initially with oral methotrexate and prednisolone, later progressing to intravenous methylprednisolone and intravenous cyclophosphamide. Repeat bronchoscopy showed improvement in inflammation; however, the patient's symptoms were not improved. The patient's symptoms and lung function currently remain stable on maintenance oral prednisolone.

BACKGROUND

Relapsing polychondritis (RP) is a rare, systemic autoimmune disorder characterised by recurrent episodes of destructive inflammation affecting cartilaginous tissues. Widespread chondritis of peripheral joint, auricular, nasal, laryngeal and tracheobronchial cartilages is often observed. Inflammation of other proteoglycan-rich tissues including the eyes, heart valves, aorta, inner ears and kidneys may also occur. The incidence of RP is around 3.5/million.¹ One-third of patients with RP also have another concurrent autoimmune disease. Serious complications of RP include joint deformity, epiglottitis, pulmonary infection, blindness, chest wall weakness, respiratory failure, aortic/mitral regurgitation, aortic dissection and glomerulonephritis-associated renal failure. Recent studies have also shown that patients with RP have an average survival rate of 94% at 8 years postdiagnosis (this is significantly lower in patients with renal involvement).¹

Pulmonary involvement of RP manifests with airway obstruction and significant reduction in exercise capacity. Airway symptoms include hoarse voice, aphonia, wheeze, stridor, non-productive coughing and dyspnoea. Cartilage inflammation can lead to laryngeal collapse during inspiration and/or tracheal collapse during expiration.² Secondary infection can also occur. Bronchial

inflammation can cause bronchial stenosis, thickening, obstructive bronchiectasis and dynamic tracheobronchial collapse. Pulmonary function tests may identify early findings of airway involvement in asymptomatic patients. Disease activity in RP is assessed using clinical signs, inflammatory markers (C reactive protein (CRP) and erythrocyte sedimentation rate (ESR)), high-resolution CT of the thorax and bronchoscopy. Currently, there is no single diagnostic investigation for RP. In this case, we used ¹⁸F-fluorodeoxyglucose positron emission tomography (FDG-PET) to aid diagnosis of RP.

CASE PRESENTATION

A 39-year-old man presented to the hospital in April 2011 with a 2-month history of tonsillitis, night sweats, fatigue, weight loss, shortness of breath on exertion and a dry cough which had not settled despite four courses of antibiotics. He was a non-smoker, drank alcohol moderately, worked in an office and was previously fit and well with no regular medication. He had no significant medical history or family history. Examination of the respiratory, cardiovascular and gastrointestinal systems was normal; he appeared generally well. Exercise tolerance on the flat was around 200 yards, and he reported shortness of breath on moderate activity (eg, climbing stairs).

INVESTIGATIONS

The main investigation results are detailed in [table 1](#). Serial lung function measurements are detailed in [table 2](#).

DIFFERENTIAL DIAGNOSIS

This case concerns a middle-aged man presenting with night sweats, weight loss, fatigue, dry cough and shortness of breath on exertion. A CT of the thorax showed tracheal thickening and mediastinal lymphadenopathy. With this combination of history and imaging, we have to consider several potential diagnoses, including lymphoma, tuberculosis (TB), sarcoidosis, vasculitis and RP. Biopsies of the lymph nodes, trachea and tonsils showed non-specific features, therefore making the diagnoses of lymphoma, TB, sarcoidosis and vasculitis less likely. FDG-PET showed a diffuse tracheobronchial activity ([figure 1](#)), thereby supporting a diagnosis of RP.

TREATMENT

In May 2011, the patient was started on 75 mg prednisolone once daily, with 30 mg lansoprazole for gut protection and two tablets of Adcal D3 daily for bone protection. In June 2011, the dose

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Table 1 Summary of investigations

Investigation	Results
Full blood count	Haemoglobin 11.2 g/dL Platelets $558 \times 10^9/L$ Neutrophils $9.68 \times 10^9/L$
C reactive protein	121
Erythrocyte sedimentation rate	114
Urea and electrolytes	Normal range
Liver function tests	Normal range
Serum ACE	Normal range
Auto-antibodies	
▶ Antinuclear antibody	Negative
▶ Rheumatoid factor	Negative
▶ Anti-dsDNA antibody	Negative
▶ Anticardiolipin antibody	Negative
▶ Extractable nuclear antigens	Negative
▶ Antineutrophil cytoplasmic antibody	Low positive (1 in 15 perinuclear pattern)
Complement C3 and C4	Normal range
Serum free light chains	Normal range
Urine dipstick	Trace blood and protein
Urine albumin : creatinine ratio	Normal
HIV screen	Negative
Viral hepatitis screen	Negative
Echocardiogram	Normal. Left ventricular systolic function=61%
CT of thorax (May 2011)	Tracheal thickening and mediastinal lymphadenopathy
Whole body FDG-PET	Significant metabolic activity present in the left oropharyngeal tonsil and left cervical lymph nodes. Also diffuse tracheobronchial activity present (figure 1)
Biopsies of lymph node, trachea and tonsils	Non-specific features, with no evidence of vasculitis, TB, sarcoidosis or lymphoma
FDG-PET, ^{18}F -fluorodeoxyglucose positron emission tomography; TB, tuberculosis.	

of prednisolone was reduced to 50 mg daily; the patient was also started on methotrexate 10 mg once weekly and folic acid 5 mg once weekly.

By July 2011, the patient's night sweats had improved; however, his respiratory symptoms of shortness of breath on exertion had shown no improvement. His inflammatory markers had now normalised (CRP<3, ESR=16). Lung function tests showed severe airflow obstruction with normal gas transfer ([table 2](#)). He was given three infusions of 500 mg methylprednisolone. Following these infusions, his dose of prednisolone was reduced over the next 2 months to 20 mg daily, and the dose of methotrexate increased to 20 mg once weekly.

Table 2 Serial lung function measurements

Date	FVC	FEV ₁	FEV ₁ /FVC	TLco	Kco
July 2011	4.74	1.03	21.7	10.4	1.74
September 2011	4.75	1.06	22.3	9.6	1.60
March 2012	4.35	1.02	23.4	9.9	1.64
August 2012	4.74	1.18	24.9	10.5	1.69
October 2012	4.63	1.16	25.1	10.3	1.69
January 2013	4.69	1.20	25.6	10.8	1.71

FEV, forced expiratory volume in 1 s; FVC, Forced vital capacity.

Figure 1 ^{18}F -fluorodeoxyglucose positron emission tomography showing diffuse tracheobronchial activity (in red).

In early September 2011, a repeat CT of the thorax was performed, which showed that tracheal thickening was significantly reduced compared with previous CT in May 2011, but the trachea still remained abnormal with evidence of narrowing. There was also significant air trapping within the lungs, and the calibre of the distal airways in the bronchi was found to be reduced. Bronchoscopy showed widespread inflammation of the trachea and bronchi with expiratory collapse, but with no focal stenosis which would have been amenable to dilation/stenting ([figure 2](#)).

Methotrexate was stopped and the patient was started on intravenous cyclophosphamide at 15 mg/kg in November 2011. Adjunctive 100 mg intravenous methylprednisolone was given with the first three doses of cyclophosphamide, and a small dose of oral prednisolone reducing to 7.5 mg/day was continued. The patient received 10 doses of cyclophosphamide in total, over a period of 8 months.

By August 2012, the patient reported considerable symptomatic improvement with improved exercise tolerance. Repeat bronchoscopy was performed in August 2012 and showed clear resolution of the endobronchial inflammation previously seen in 2011. The endobronchial biopsies showed mild chronic neutrophilic inflammation. There were a few CD20 B cells in the mucosa. Lung function tests in August 2012 showed small improvement in airflow obstruction ([table 2](#)).

In September 2012, the patient was advised to start a second-line immunosuppressant such as azathioprine or mycophenolate mofetil for maintenance therapy but decided not to do so. He remained on a low dose of prednisolone alone. Bronchodilator reversibility assessment in October 2012 showed no change. Lung function tests in October 2012 remained unchanged from August 2012 ([table 2](#)). His flow volume loop showed a marked

Figure 2 Bronchoscopy image showing widespread inflammation of trachea and bronchi, but with no focal stenosis present.

airway collapse on expiration. This was likely due to the tracheal damage he had from the RP.

OUTCOME AND FOLLOW-UP

The patient was last seen in clinic in January 2013. Lung function tests showed further small improvement in airflow obstruction (table 2). Incremental shuttle walk test showed no desaturation during exercise, which was mainly limited by breathlessness. He has managed 8 min and 45 s on a shuttle walk test and did not desaturate significantly. It was decided that he would remain on 7.5 mg prednisolone daily, and would be followed up in clinic with lung function tests in 6 months. If the patient developed any sign of deterioration in either symptoms or lung function tests, then a second-line immunosuppressant (either azathioprine or mycophenolate mofetil) would be considered.

DISCUSSION

In this case, we showed that FDG-PET can be used to aid the diagnosis of RP. The use of FDG-PET to aid diagnosis of RP has also previously been described by Geeter and Vandecasteele,³ Sato *et al*⁴ and Czepczynski *et al*.⁵ The mainstay of current medical therapy is immunosuppression (eg, corticosteroids, methotrexate, cyclophosphamide, azathioprine and mycophenolate mofetil).^{1–6} In this case, the use of prednisolone and cyclophosphamide was successful in treating the inflammation, but symptoms remained unchanged. No clinical trial data are currently present to support the use of biologicals in the treatment of RP, mainly due to low incidence of this condition. Review of published case reports show that biological therapies have been successful in roughly 50% of cases; however, experience with biologicals in RP is still very limited.⁷ Silicone airway stents can also be considered to treat airway stenosis where tracheobronchomalacia is the dominant feature; however, stent migration is a potential complication of this treatment. Permanent expandable stents are generally not used in airway stenosis associated with RP due to the poor prognosis. Ventilation regimes such as BiPAP and CPAP may also be considered to improve oxygen saturations overnight.⁶ Tracheostomy or tracheal resection may

be required if severe subglottic stenosis occurs. Heart valve replacement and valvuloplasty can also be considered in cases of valve disease secondary to RP.

Learning points

- ▶ ¹⁸F-fluorodeoxyglucose positron emission tomography can be used to aid the diagnosis of relapsing polychondritis.
- ▶ Immunosuppression can successfully treat the inflammation in relapsing polychondritis; however, symptoms may not be improved.
- ▶ Further work into the use of biological therapies in the management of relapsing polychondritis is required.

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Competing interests None.

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