^{18}F-fluorodeoxyglucose positron emission tomography for the assessment of endobronchial involvement in granulomatosis with polyangiitis

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ABSTRACT

Bronchial stenosis is an uncommon but potentially life-threatening complication of granulomatosis with polyangiitis (GPA). The development of lower respiratory tract stenoses in patients with GPA is thought to be the result of persistent inflammation of the cartilaginous tissue. New assessment methods for this severe GPA complication are highly needed. Herein, we show the value of 18F-fluorodeoxyglycose positron emission tomography/computed tomography (18F-FDG-PET/CT) in the diagnosis, prediction of progression to bronchial stenosis and response to treatment of endobronchial involvement in a patient with GPA.

Introduction

Granulomatosis with polyangiitis (GPA) is the most common of the antineutrophil cytoplasmic autoantibody (ANCA)-associated vasculitides. Bronchial stenosis is an infrequent but devastating complication of GPA thought to be the result of persistent inflammation of the cartilaginous tissue (1, 2). The presentation of stridor, hoarseness or dyspnoea in patients with GPA requires prompt clinical and radiological evaluation. Although bronchoscopy, computed tomography (CT) and magnetic resonance imaging (MRI) have shown its potential to detect tracheobronchial disease in patients with GPA, these imaging tools are not useful in differentiating disease activity from damage (1). New and non-invasive assessment methods to detect this severe GPA complication are highly needed. We report herewith the value of 18F-fluorodeoxyglycose positron emission tomography/computed tomography (18F-FDG-PET/CT) in the diagnosis, prediction of progression to bronchial stenosis and response to treatment of endobronchial involvement in a patient with GPA.

Clinical presentation

A 76-year-old man presented to our hospital with a 2-day history of cough, episodic haemoptysis, low-grade fever and malaise. Two months earlier, he was diagnosed with a unilateral persistent otitis media with effusion. Blood tests at admission revealed increased acute-phase reactants parameters (CRP 73 mg/L; normal range <10 mg/L, and ESR 90 mm/h; normal range 1-20 mm/h), a slightly low haemoglobin of 7.7 mmol/L (normal range 8.5-11.0 mmol/L) and a normal creatinine and estimated glomerular filtration rate. Urinalysis was normal and blood cultures were negative. A chest X-ray showed multiple bilateral pulmonary nodules of variable size with random distribution. Bronchoscopy revealed diffuse inflammation and ulcerative lesions of the trachea and main bronchi (Supplementary Fig. S1A). A biopsy of the left bronchus showed chronic inflammation with vasculitic changes (Supplementary Fig. S1B, 1C) and testing for PR3-ANCA was positive (58 IU/ml; negative < 2 IU/ml). 18F-FDG-PET/CT displayed intense radiotracer uptake in all the pulmonary nodules but also in the nasal mucosa, subglottic region and bronchial tree (Fig. 1A, 1B). A diagnosis of GPA was made, and our patient received three pulses of intravenous methylprednisolone 1000 mg, followed by prednisone 60 mg in a tapering dose and rituximab 1000 mg on day 0 and 14 with an excellent clinical recovery. Two months after the diagnosis, our patient reported moderate dyspnoea and harsh cough. A new 18F-FDG-PET/CT showed complete resolution of radiological changes in the lungs but persistent radiotracer uptake (Fig. 1C) and a diffuse narrowing of >2 mm (from 9 mm to 6.7 mm) in the left main bronchus (Fig. 1D). Besides increasing the dose of prednisone to 1 mg/kg, one month later our patient experienced dyspnoea at rest and a CT-scan showed a new pulmonary nodule, a left main bronchus stenosis of 75% caliber and atelectasis of the left upper lobe (Supplementary Fig. S2A, 2B). Cyclophosphamide 15 mg/kg was added to the treatment administered intravenously at weeks 0,2 and 3, and then every 4 weeks for four months. Furthermore, the bronchial stenosis was treated with laser therapy with significative improvement of the dyspnoea. Three months after the last cyclophosphamide treatment the patient was clinically and serologically

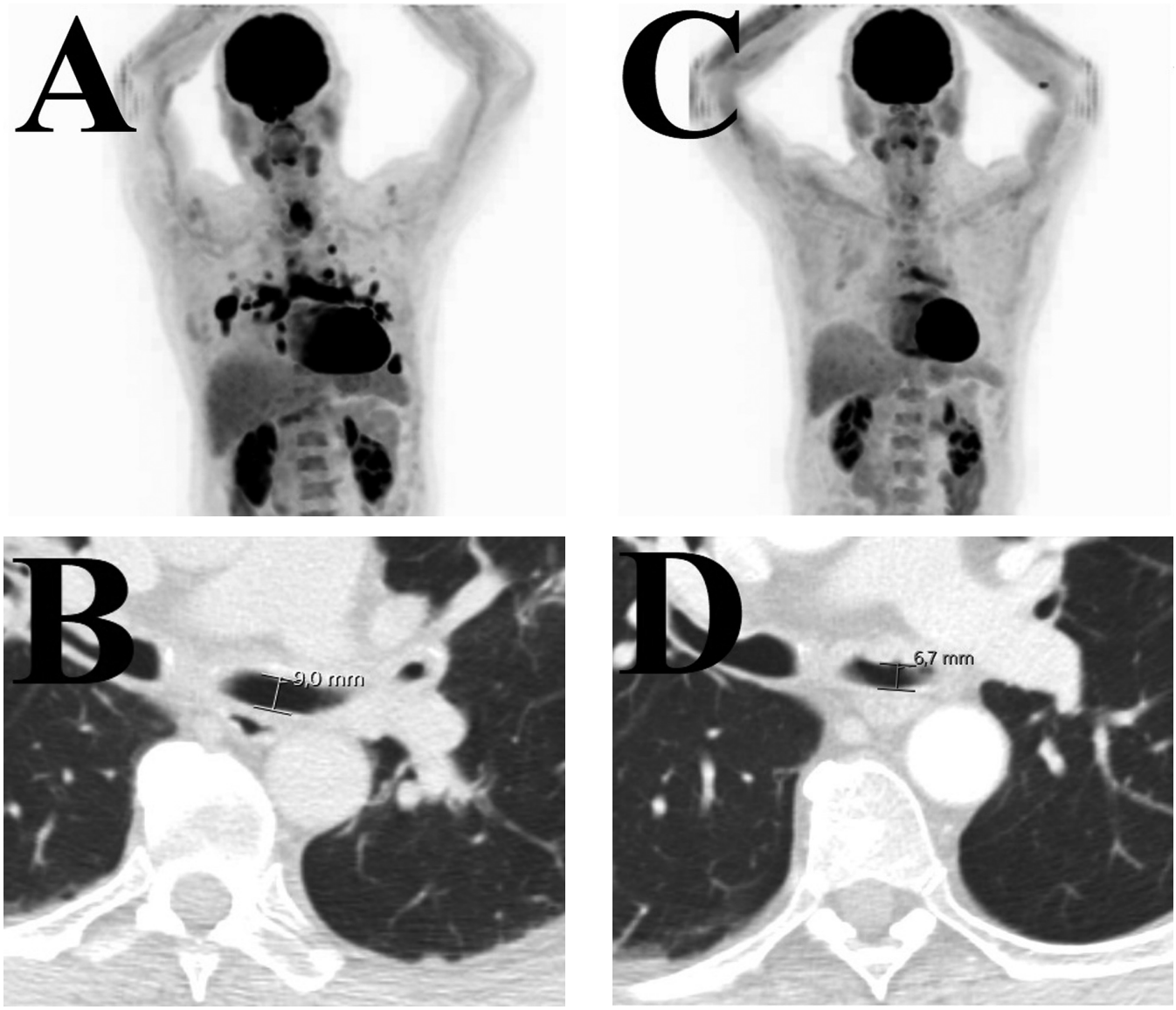

Fig 1. (**A**) 18F-FDG-PET/CT at diagnosis showed high FDG uptake in multiple pulmonary nodules, main and segmental bronchi and subglottic region. (**B**) Axial image of the chest CT-scan shows a 9 mm diameter of the left main bronchus at the time of diagnosis. (**C**) 18F-FDG-PET/CT two months after the diagnosis shows persistent high FDG uptake in the main left bronchus. (**D**) Axial image of the chest CT-scan after two months shows a narrowing (diameter 6.7 mm) of the main left bronchus. 18F-FDG-PET/CT: 18-fluorodeoxyglucose positron emission tomography/computed tomography.

in remission and a new 18F-FDG-PET/CT showed no signs of GPA activity, obstruction or stenosis of the endobronchial tree.

Discussion

GPA is a rare systemic vasculitis, affecting mainly the upper airways, lungs and kidneys. Endobronchial involvement is reported in <6% of these patients, is more likely to present together with other additional pulmonary manifestations like pulmonary nodules and often leads to airway obstruction (1). Bronchial stenoses frequently evolve independently regardless of disease activity and are refractory to conventional systemic regimens (2). Bronchoscopy is a valuable tool not only for identifying bronchial or tracheal stenosis but also in the evaluation of other GPA-related manifestations such as ulcerating tracheobonchitis, inflammatory pseudotumours and haemorrhage (3). Furthermore, several imaging tools such as CT and MRI have been used to detect signs of tracheobronchial disease such as airway narrowing and wall thickening (4). However, these imaging modalities are not able to differentiate between active disease and fibrotic sequelae or cartilage destruction.

18F-FDG-PET/CT has been previously found to be helpful in the diagnosis and follow-up of patients with other rheumatological diseases (5). In patients with relapsing polychondritis, 18F-FDG-PET/CT accurately demonstrated the distribution of inflammation and destruction of the cartilaginous tissue (4). The role of this imaging technique in patients with GPA has been scarcely evaluated. 18F-FDG-PET/CT can detect multiple sites of disease and it has been suggested that lesions of the upper respiratory tract and lung are more clearly detected by 18F-FDG-PET/CT than by CT scan alone (6, 7). A role of this imag-

ing method in the detection of cartilage involvement of soft tissue in the nasal cavity and subglottic region of patients with GPA has been proposed (5-8). We also believe that this imaging technique is a very promising tool for the assessment of lower respiratory tract involvement and follow-up of stenotic complications in patients with GPA. Our case illustrates how the presence of FDG uptake in the respiratory tract in patients with GPA correlates with inflammation of cartilaginous tissue and how this inflammation, when insufficiently treated, leads to the development of bronchial stenosis. Therefore, the presence of this residual inflammation in the bronchial tree detected by 18F-FDG-PET/CT should prompt the clinician to change or intensify immunosuppression.

In conclusion, 18F-FDG-PET/CT is a valuable tool to evaluate inflammation in the tracheobronchial tract in GPA and to identify those patients at risk for developing tracheobronchial stenoses. Based on our experience with this patient we believe that 18F-FDG-PET/CT is a potential imaging biomarker for the early diagnosis, monitoring of disease extent and activity and assessment of therapeutic response of endobronchial involvement in patients with GPA.

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