



Case report

The obstructive siblings: Relapsing polychondritis without chondritis?



Haavard A. Sæverud*, F. Borchsenius, H. Mellem, P. Finstad, Ole H. Skjønberg

Dept. of Pulmonary Medicine, Oslo University Hospital, Ullevål, Kirkeveien 166, 0407 Oslo, Norway

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ABSTRACT

Progressive narrowing of the central airways due to diffuse inflammation is a potential life-threatening condition. A number of diseases have been described as possible causes. We present two siblings with severe central airway obstruction. Despite considerable efforts we have not been able to match the clinical appearance of our patients with the diagnostic criteria of any of the disease entities known to cause this condition.

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1. Case reports

Patient no 1 is a man who was 49 years old at the time of admission. He is a never-smoker who has worked several years as a carpenter. He had been occupationally exposed to stone dust, but not to asbestos. Patient no 2 is his two years younger sister who was admitted to our hospital, also at the age of 49. She is a never-smoking woman, working in an office, and had no known exposure to harmful dusts. They were both previously healthy, the brother born deaf, though, assumingly because his mother was infected with rubella during pregnancy. They have no known hereditary diseases, and there are no other siblings. None of them have had any trauma or had a tracheostoma, nor have they had previous recurrent infections.

Both presented with worsening dyspnoea, cough and non-characteristic chest pain over a period of 4–6 months, and both had been treated by their GPs with antibiotics, without any improvement.

At the time of admission, patient no 1 had spirometry values consistent with airway obstruction with FVC 4.5 l (98% of predicted), FEV1 2.7 l (73%). The sister's initial spirometry showed FVC

2.6 l (77%), FEV1 1.2 l (41%), FEV1/FVC 0.46, and a considerable compromised inspiratory curve. They both had TLC between 70 and 80% predicted, RV 80–90% and DLCO within the normal range on serial measurements. Both had an elevated CRP, 61 for patient no 1 and 47 for patient no 2. Blood leukocyte and eosinophils were normal, there was no hypercalcemia, and ACE levels were in the lower normal area.

Extensive diagnostic investigations were undertaken for both patients. CT-scans showed diffuse circumferential thickening of the trachea and main bronchi, including pars membranacea tracheae, scattered intramural calcification and considerable narrowing of the tracheal and bronchial lumina (Figs. 1 and 2). There were no external compression or emphysema.

Bronchoscopy revealed a generally swollen and inflamed mucosa with visually poorly defined tracheal and bronchial cartilage in both patients. There was a fixed airway narrowing affecting the trachea and main bronchi, with no apparent dynamic changes throughout the respiratory cycle. After a period of medical treatment, repeated bronchoscopy showed reduced inflammatory changes but was otherwise similar.

There was no growth of mycobacteria, other bacteria or vira in lavage fluid from the airways. Bronchial biopsies revealed chronic unspecific inflammation. There were no signs of granulomatous inflammation, vasculitis or amyloidosis in a Congo red staining. Unfortunately there was no cartilage in the bronchial biopsies. Additional biopsies from auricular cartilage, conchae and costal cartilage were normal. All biopsies obtained from the siblings were compared, and deemed identical. Electron microscopic evaluation of the biopsies has not been performed. We have not performed biopsies of subcutaneous fat or rectal mucosa.

Abbreviations: ANA, anti-nuclear antibody; ANCA, anti-neutrophil cytoplasmic antibody; ACE, angiotensin converting enzyme; CMV, cytomegalovirus; CRP, C-reactive protein; CT, computer tomography; DLCO, diffusing capacity of the lung for carbon monoxide; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; GP, general practitioner; RF, rheumatoid factor; RPC, relapsing polychondritis; WG, Wegener's granulomatosis; TLC, total lung capacity.

* Corresponding author. Tel.: +47 22119232.

E-mail addresses: uxhvs@ous-hf.no (H.A. Sæverud), uxfrbo@ous-hf.no (F. Borchsenius), hame@ous-hf.no (H. Mellem), uxplfi@ous-hf.no (P. Finstad), o.h.skjønberg@medisin.uio.no (O.H. Skjønberg).

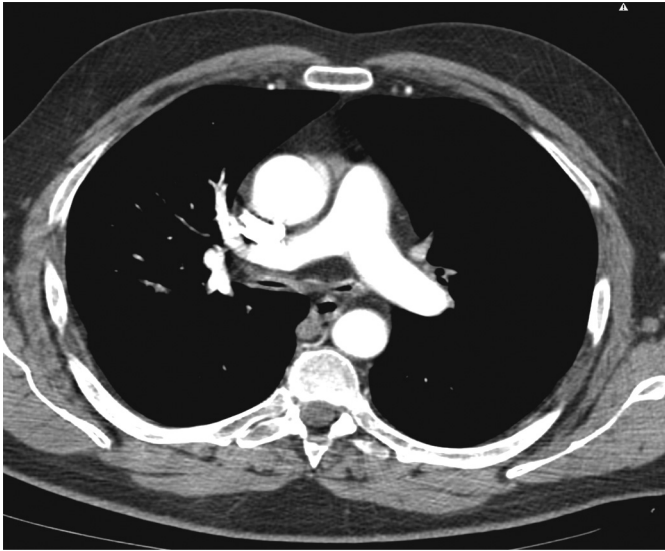


Fig. 1. CT-scan of patient no 1 just below carina with thickening of the airway walls and compression of the lumina of both main bronchi.

Positron-emission tomography of patient no 2 whilst receiving both cyclophosphamide and prednisolon, did not show any activity in trachea, bronchi or lung parenchyma.

CT of the sinuses were normal apart from minor edema in the right maxillar sinus of patient no 2.

Serologic testing was negative for CMV and *Mycoplasma pneumoniae*, *Bordetella pertussis*, ANA, ANCA and RF. Skin testing for aspergillus was negative, and the total IgE was normal. Renal function was normal, and there was no proteinuria or signs of nephritis. Serum-electrophoresis showed non-specific inflammation.

Both patients have received immunosuppressive therapy with prednisolone, and cyclophosphamide was added. Patient no 1 received azithromycin as immunomodulation, and patient no 2 has received azathioprine, without any effect on symptoms. They also

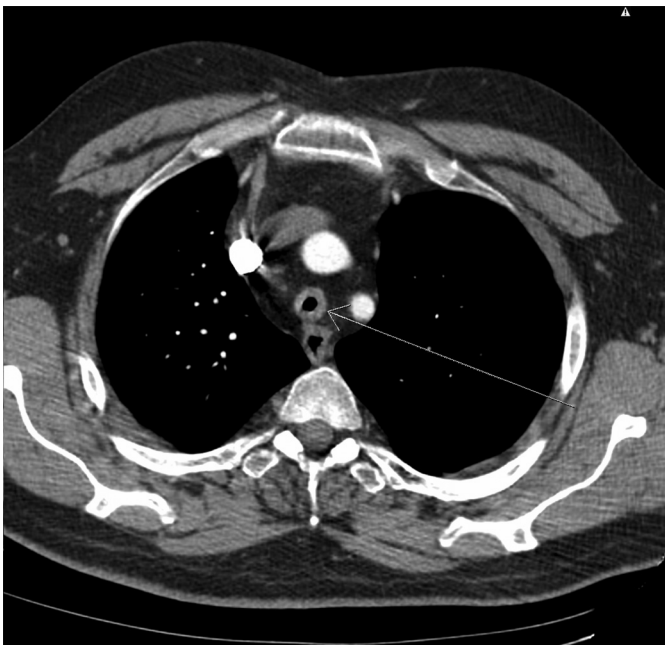


Fig. 2. CT- scan from patient no 1 showing circumferential tracheal thickening (arrow) and narrowing of the lumen.

received inhalations with budesonide/formoterol, salbutamol and ipratropium bromide ad libitum, with uncertain effect.

Initially the condition deteriorated for both patients with progressive worsening of symptoms, inspiratory stridor and declining spirometric values. The condition of patient no 1 has been stable during the last two years with FVC 2.8 l (63%) and FEV1 0.9 l (26%). Cyclophosphamide has been replaced by azathioprine, and he still receives prednisolone and azathioprine, 5 years after the initial presentation.

The rapid deterioration of patient no 2 was initially halted when treatment was instituted. After a time she progressed, though, and eventually received rituximab, without any significant effect. There is, however, still a minor effect of large doses of steroids. She still suffers from considerable obstruction of the central airways, resembling what is seen in patient no 1, her latest spirometry values being FVC 2.7 l (83%), FEV1 0.8 l (29%) (Fig. 3). In the course of the disease the obstruction of her left main bronchus was subtotal, requiring implantation of an endobronchial silicon stent. This was removed after only 3 weeks due to persisting symptoms. Both siblings have experienced several exacerbations requiring antibiotics and elevated steroid doses.

Due to the initial progressive nature of the condition and the severely compromised lung function lung transplantation was considered for both patients shortly after presentation. After consultations with the transplant center this was considered not to be an option, due to the involvement of the main bronchi and the trachea.

2. Discussion

We present two siblings with severe rapidly progressive obstruction of the central airways at the age of 49. Despite extensive investigation we have not been able to reveal a diagnosis consistent with the criteria of disease entities known to involve the large airways, with amyloidosis, Wegener's granulomatosis (WG) and relapsing polychondritis (RPC) being the most likely culprits.

A diagnosis of amyloidosis is dependent on the presence of amyloid fibrils in a Congo red staining. This could not be shown in our patients.

Neither did we find histologic or other signs of vasculitis as described by The American college of rheumatology and the Chapel Hill consensus conference.^{1,2} Using European Medicines Agency's algorithm for classification of vasculitides³ the siblings are unclassifiable.

According to McAdam RPC implies combinations of chondritis in multiple sites, such as auricles, nose or respiratory tract, a non-erosive seronegative inflammatory polyarthritis, ocular inflammation and audiovestibular damage.^{4,5} In addition a histological confirmation is considered necessary if the case is not clinically obvious.

Although not firmly established there has been some indications of an association between the HLA genotypes DR4 and DR6 and RPC.⁶ Both our patients were tested, but none of them had the genotypes in question.

None of the siblings thus fulfil the criteria for RPC or WG. Domestic and international consultation has not resulted in significant progress regarding the diagnosis.

The fact that two siblings present with identical complaints at the same age might suggest an inherited predisposition, but we have not been able to establish neither a plausible syndrome, nor have we found similar cases of any disease entity affecting siblings reported in the literature. We have considered an autoimmune pathogenesis to be likely, and that is the rationale for giving immunosuppressive medication. In our opinion the condition resembles RP more than WG or amyloidosis, but as they have only single organ involvement we have been unable to formally classify it as such.

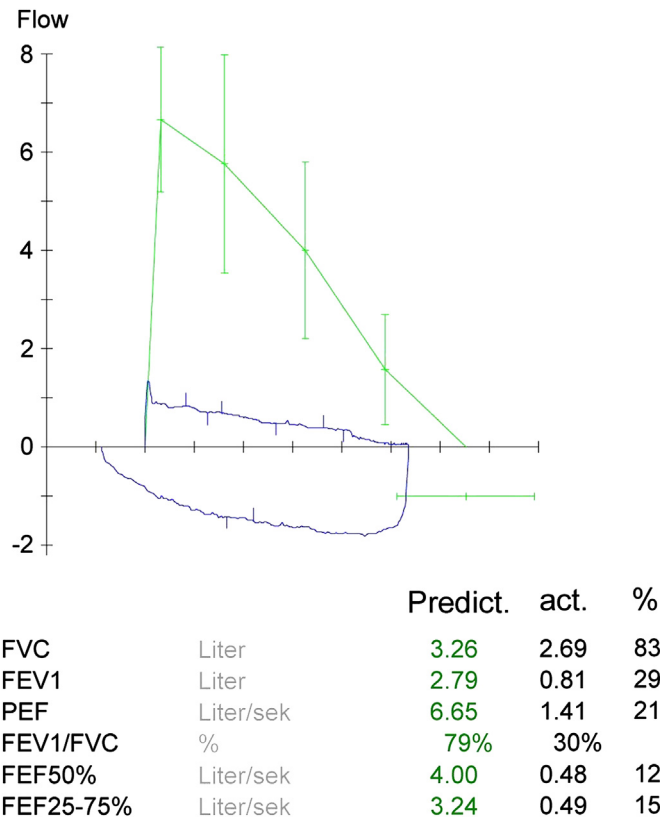


Fig. 3. Spirometry of patient no 2, 4 years after presentation, showing both inspiratory and expiratory obstruction.

We now turn to a broader audience eagerly awaiting responses that might help us unveil a diagnosis.

Conflict of interest

None of the authors have disclosed any conflict of interest.

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