CASE REPORT

Recurrent respiratory infections and unusual radiology: a woman with Kartagener's syndrome

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SUMMARY

A 39-year-old woman with known situs inversus and a medical history of asthma had been suffering from recurring bronchial pneumonias and sinusitis for as long as she could remember. After being treated several times with antibiotics due to the frequent respiratory infections and after a CT scan that showed bilateral bronchiectasis, she was referred to the department of respiratory diseases, where another confirming X-ray and a bronchoscopy were performed based on a suspicion of Kartagener's syndrome.

BACKGROUND

Kartagener's syndrome was first described in the early 1900s as a condition characterised by a combination of chronic sinusitis, bronchiectasis and situs inversus.¹ It is, possibly, related to the more commonly seen entity, primary ciliary dyskinesia (PCD), which is associated with a number of respiratory clinical manifestations due to ciliary dysfunction, such as chronic bronchitis, bronchiectasis, chronic rhinosinusitis and chronic otitis media; male infertility is another relatively common manifestation of PCD, due to defects in axonemal components in the sperm tail.^{2,3} The pathophysiology of PCD, a congenital autosomal recessive disorder, is the absence and/or dysmorphic features of the dynein arms in airway cilia due to a variety of specific mutations in cilia coding genes.⁴ A combination of a low incidence rate (1/15 000 among Caucasians)² and, sometimes, a confusing clinical presentation, makes this a rather tricky and difficult clinical problem when it comes to diagnosis. Many of the typical clinical manifestations and components involving Kartagener's syndrome can easily be confused with other potential underlying causes, which is why the condition is worth extra attention despite its relatively rare occurrence.

CASE PRESENTATION

A 39-year-old woman of Somali origin was referred to the Department of Respiratory Medicine and Allergy in February 2015. The patient had asthma and dyspnoea during physical activity, and a chronic cough with heavy mucus production, since childhood. More lately, the patient experienced worsening symptoms (especially of the cough) and had been treated with antibiotics several times in Somalia as well as in Sweden after she moved from her homeland. She also experienced chest pain. In January 2015, she was successfully treated with amoxicillin, due to a *Haemophilus influenzae*

infection verified by sputum culture; once again, antibiotics helped to treat the concomitant infection, but only temporarily improved her symptoms, which worsened again a few weeks after the treatment. The patient was also affected by frequent urinary tract infections as well as recurrent symptoms indicating sinusitis. She denied fever, weight loss or night sweats, and had no active or passive smoking history. Her sister had a history of unspecific respiratory symptoms, otherwise, her family clinical history was not relevant. None of her relatives were known to have a situs inversus, nor had they ever received a diagnosis of bronchiectasis or sinusitis. Only one sister had problems with chronic cough in Somalia, but her chest X-ray was reportedly normal. There was no consanguinity in her relatives, with her parents coming from two distant different towns.

INVESTIGATIONS

On initial physical examination, the patient was in good general condition and compensated at rest, with a pulse oximetry showing a saturation of 94–95%. Heart rate was regular without murmurs. On lung auscultation, there were both inspiratory and expiratory ronchi (sibilant as well as whistling, as in the presence of secretions, easier to hear immediately after cough). Furthermore, fine wet basal rales, especially on the right lung, were heard. The rales decreased slightly after the patient had been coughing for a while.

A CT of the thorax carried out in July 2014 showed bilateral basal bronchiectasis under the left and right lobes, more pronounced on the right.

In March 2015, a pulmonary X-ray confirmed bilateral basal bronchiectasis as well as revealed a coexisting inflammatory component, predominantly on the right. The chest X-ray and CT scan both showed a situs inversus (figures 1 and 2).

The overall picture raised the suspicion of Kartagener's syndrome, so a bronchoscopy with bronchial biopsy was performed. There were abundant white secretions already in the trachea.

On inspection of the left bronchial tree, three lobar bronchi were seen, as normally seen in the right lung; also, the right lung of the patient was divided into two lobes, as the left lung normally is.

Copious purulent secretions were removed from the lower lobe bronchi on the right, by aspiration via the bronchoscope. Less conspicuous secretions were seen in the middle lobe on the left. Apart from these, no other significant abnormalities were detected by the bronchoscopy. Samples for bacterial screening were taken from the right lower lobe.

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Figure 1 (A) Chest X-ray: situs inversus, peribronchial opacities in the anatomical right lower lobe; (B) CT of the thorax, coronal plane reconstruction, situs inversus with bilateral bronchiectases, more accentuated in the anatomical left lower lobe.

Biopsies were taken from the bronchial mucosa for electronic microscopy.

Cultures showed growth of *H. influenzae* and *Streptococcus pneumoniae*. All other test results for other commonly occurring bacterial, viral and fungal infections were negative.

DIFFERENTIAL DIAGNOSIS

Considering the chronic respiratory manifestations (the recurring respiratory infections, history of asthma, history of productive cough with conspicuous mucus secretions), some important differential diagnosis must be taken into consideration.

Tuberculosis, perhaps the most important differential diagnosis, considering the patient's symptoms and country of origin,⁵ was ruled out via several cultures from sputum and bronchoscopy samples that turned out negative for *Mycobacterium tuberculosis*.

The patient was purified protein derivative (PPD) positive (20 mm) but she had been BCG vaccinated.

Non-tuberculous mycobacteria (NTM) can cause pulmonary infections. Infection occurs by the inhalation of dust or aerosols, but it is not transmitted from humans to humans. About 80 different mycobacterial species have been identified, most of them opportunistic (between 25% and 50% of AIDS patients in Europe and the USA are infected with NTM).^{6,7} Patients with pulmonary disease caused by NTM present symptoms such as prolonged cough and sputum production.⁷ In this case, NTM was ruled out by negative culture results for atypical mycobacteria in bronchial secretions from the bronchoscopy.

Fungal infections such as *Aspergillus*, *Candida* and *Pneumocystis jiroveci* are all differential diagnoses that also have to be considered. As for aspergillosis, invasive pulmonary forms occur primarily in patients with severe immunodeficiency as well as in terminally ill patients and those with chronic obstructive pulmonary disease. Chronic necrotising aspergillosis is a locally invasive form, seen mainly in patients with mild immunodeficiency or chronic pulmonary disease. Aspergilloma and allergic bronchopulmonary aspergillosis are non-invasive forms that occur mostly in patients with asthma or cystic fibrosis. The clinical manifestations vary among these different form of aspergillosis, but overall, the symptoms are often non-specific, with prolonged cough, sputum production, dyspnoea and, sometimes, bronchopneumonia with fever.^{8,9} Infections by *Candida* and *P. jiroveci* represent a major threat to patients with immunodeficiency.¹⁰ In this case, samples from the bronchoscopy *Aspergillus*-DNA, *Candida*-DNA, *P. jiroveci*-DNA as well as antigens for *Aspergillus*, turned out to be negative. Histological examination of the bronchial biopsies showed no sign of fungal infections of any kind.

Clinical suspicion of opportunistic infections was in any case low, as the patient was not immunocompromised.

Electron microscopy analysis of the bronchial biopsies showed a dearth of dynein arms, with an average of 2.0 outer dynein arms (normal reference value >7.5) and 0.9 inner dynein arms (normal reference value >3) (figure 3), confirming the diagnosis of Kartagener's syndrome.^{11,12} Furthermore, almost complete absence of both outer and inner dynein arms

Figure 2 CT axial plane: bilateral bronchiectasis in the lower lobes more prominent on the right.

Figure 3 Electronic microscopy on bronchial biopsies. Ultrastructural image of the cilia (nasal cilia) showing the absence of the outer and inner dynein arms (×60 000).

together with the classical Kartagener's syndrome presentation would strongly suggest a mutation in the KTU gene (chromosome 14 open reading frame 104 gene).¹¹

TREATMENT

The treatment of Kartagener's syndrome is basically focused on controlling symptoms, and treating and preventing new respiratory infections.^{3 11 12} To ease breathing and to improve mobilisation of mucus, the patient underwent a specific programme of physiotherapy and received sodium chloride inhalations. A coughing and huffing exercise, an airway clearance technique for chronic lung disease patients, was used, and the patient was instructed to perform the exercises twice a day. The patient also had regular telephone contact with a physiotherapist and a follow-up visit to evaluate the result of the exercises. Huffing means that the patient, after a normal to maximal inhalation, exhales heavily with the epiglottis fully open. In this way, the risk of bronchospasm is decreased and the stress affecting the base of the pelvis is less compared to that during normal coughing. After detachment of the mucus by huffing, the patient can easily cough to further evacuate it. Furthermore, the patient also received information about the value of increasing her endurance and was instructed to take long daily walks.

The bacterial infection, discovered after sampling at the bronchoscopy, was successfully treated with amoxicillin 750 mg three times daily for 2 weeks, and the patient experienced a sustained improvement of her symptoms, mostly thanks to physiotherapy and to all the procedures to control mucus production and to clear mucus from the bronchial tree.

OUTCOME AND FOLLOW-UP

The patient had not been affected by new infections at 4-month follow-up, and her cough and sputum production had significantly improved. She is continuing with the respiratory physiotherapy and with the procedures to improve the management of secretions in the bronchial tree and to prevent new infections. Regular follow-up is planned via the specialists at our outpatient clinics and with the physiotherapists in our department.

DISCUSSION

The diagnosis Kartagener's syndrome is not difficult, per se, once suspected. What is difficult is to keep this diagnosis in mind, since the symptoms are non-specific and common to many other more frequent respiratory conditions. Furthermore, clinical manifestations can easily be mistaken for commonly occurring infections. However, the association with situs inversus is peculiar and should help to raise a diagnostic suspicion. The importance of early diagnosis and symptomatic treatment as well as prevention of

Learning points

- ▶ Common symptoms can hide rare diseases of the lungs, and the patient can be misdiagnosed for years before receiving appropriate treatment.
- ▶ Situs inversus is an uncommon radiological presentation, and should at once raise suspicion of genetic disorders with multiorgan involvement.
- ▶ Referring patients to highly specialised centres is often necessary to grant them access to the proper diagnostics and to specialised treatment. This patient experienced a diagnostic and therapeutic delay for years, due to the fact that important clinical signs were not recognised.

infections is emphasised by the progressive degeneration in respiratory function in patients with PCD if untreated; lung function can be maintained with adequate pharmacological treatment and regular physiotherapy.¹³

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Contributors CR collected the data and drafted the manuscript. CO-V conducted the electronic microscopy and drafted the manuscript. JP was responsible for the radiology and drafted the manuscript. GF was responsible for the clinical case, collected data and drafted the manuscript.

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Patient's perspective

In the last few years I had problems with coughing and breathing; I was always tired and this was influencing my life. I felt bad about others seeing me cough. I'm happy to know my diagnosis, to know that it's not a danger to others, such as tuberculosis or other infections could have been. I'm happy to know that I can do something to improve my health.

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