Delayed Diagnosis of Kartagener Syndrome in a Fertile Young Man – An Unusual Case

Fatima Alhamed Alduihi
Department of Internal Medicine, Aleppo University Hospital, Aleppo, Syria

Primary ciliary dyskinesia (PCD) is an autosomal recessive disease characterised by dysfunction of ciliary motility associated with impaired mucociliary clearance. Kartagener syndrome, by definition, is a triad of situs inversus, bronchiectasis and chronic sinusitis, and is a subdivision of PCD. It can cause abnormal sperm motility and infertility in men, and can also cause infertility in women because of impaired cilia motility in fallopian tubes. In this case report, a 31-year-old male, non-smoker, born to non-consanguineous parents, presented to the emergency department with severe breathlessness and chest pain. He had a bad cough with yellow sputum. High-resolution computerised tomography showed bronchiectasis, and ultrasonography showed dextrocardia without situs inversus. He was treated with imipenem and amikacin according to sputum culture for 2 weeks, and then he was discharged on inhaled tobramycin. The distinctive aspect of this case, is that not only was this the first time this patient had been diagnosed with Kartagener syndrome, but he is also fertile (he had fathered two children), which is considered rare, but not impossible, in such cases. Fertility, as this case shows, does not therefore exclude Kartagener syndrome, and clinicians must suspect it in every case of dextrocardia, chronic sinusitis and bronchiectasis, because misleading the diagnosis can develop poor prognosis.

Keywords
Kartagener syndrome, situs inversus, fertility, primary ciliary dyskinesia

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Corresponding Author: Fatima Alhamed Alduihi, Department of Internal Medicine, Aleppo University, Aleppo, Syria. E: dr.duihi88@hotmail.com; ORCID: https://orcid.org/0000-0003-1083-9005; Twitter: @FatimaDuihi

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Primary ciliary dyskinesia (PCD) is an autosomal recessive disease characterised by dysfunction of ciliary motility associated with impaired mucociliary clearance. Kartagener syndrome is characterised by the triad of: sinusitis, bronchiectasis and situs inversus. Situs inversus is a condition whereby the visceral organs are completely, or partially, arranged in a mirror-image reversal of their normal positions. The percentage of patients with PCD that exhibit situs inversus varies, but in general, it is around 50–70%. Infertility is common in men with Kartagener because of impairment of sperm motility.

Case presentation
A 31-year-old male, non-smoker, born to non-consanguineous parents, presented to the emergency department with severe breathlessness and chest pain. He had a bad cough with yellow sputum for 7 days prior. He was treated with cephalosporins without any benefit. He also reported episodes of headache and recurrent cough, which had been persistent for up to 1 year. The patient married 12 years ago and has two children. The first was born 8 years ago (after 4 years of marriage), and the second 5 years ago. He has had no further children.

Upon examination, the patient displayed reflexes of a conscious and oriented person. His blood pressure was 110/70 mmHg, heart rate was 108 beats/minute, and respiratory rate was 22 breaths/minute. Oximetry on admission was 84% and temperature was 38°C. The patient had a cough with purulent sputum but no haemoptysis. Clubbing was seen in both hands (Figure 1). The patient also presented with auscultation of chest reflexes, wheezing and bilateral coarse crackles, which were heard more clearly on the right side. Auscultation of heart sounds revealed an apex beat heard on the right side.

Dyspnoea was the dominant symptom. No lymphadenopathy in two sides. Investigations carried out included complete blood count, haemoglobin 11.87 g/dl, white blood cell 8.5 x 10^9/L; C-reactive protein 140.7 mg/L; and serum amylase and lipase, which were normal. Chloride sweat test was 12 mEq/L, which is within normal limits (Table 1). Pulmonary function tests revealed severe restriction (Table 2). Posterior anterior chest X-ray on admission showed dextrocardia (Figure 2). Simple sinusitis photo showed the patient had a deviated left nasal septum with sinusitis.

A computed tomography (CT) scan was then performed and revealed bronchiectasis (Figure 3), meaning the patient was at an increased risk of developing tuberculosis; therefore, we recommended that the patient attended the respiratory clinic for further follow-up. Unfortunately, even after treatment, the patient developed ground-glass opacity on CT, and the lesion was doubled (Figure 4).
Ultrasonography was performed and showed no situs inversus totally. A semen analysis showed 75 million spermatozoa with 80% motility; however, the patient mentioned that the count was only 9 million 3 months ago. Sputum for acid-fast bacilli (AFB) staining (three times) however, the patient mentioned that the count was only 9 million 3 months ago. Sputum for acid-fast bacilli (AFB) staining (three times) was negative for Mycobacterium tuberculosis. Sputum was positive for an isolate of Citrobacter spp., which was resistant to cefotaxime, lincomycin, rifampicin, gentamycin and nitrofurantoin. This could explain why the patient did not benefit from treatment with cephalosporin. The patient in this case has two children which was reported in our patient was dextrocardia. Patients with situs inversus totally have been reported to cause non-syndromic asthenozoospermia, and as a result, infertility is not uncommon in patients with PCD. About 50% of male patients with PCD are infertile due to lack of sperm motility. The patient described here had not previously been diagnosed with Kartagener, had never undergone high-resolution CT.

As Kartagener syndrome is a form of PCD, the motility of cilia will be affected by this disease, and as a result, infertility is not uncommon in patients with PCD. About 50% of male patients with PCD are infertile due to lack of sperm motility. Though it is worth noting that most infertile patients with Kartagener syndrome have a normal spermatozoid count, but with a structural defect and a lack of motility, which is a result of the genetic causes linked to PCD. Disorders of cilia motility may be congenital or acquired. Up to 6.3% of patients with PCD have heterotaxy, and most of those have cardiovascular abnormalities; one such abnormality which was reported in our patient was dextrocardia. Patients with situs abnormalities have more ciliary outer dynein arm defects and fewer inner dynein arm defects, in addition to central apparatus defects and more mutations in ciliary outer arm genes (DNAI1 and DNAH5). To date, pathogenic variants in DNAH1, SEPT12, SLC26A8, CATSPER1, CATSPER2 and ADCY10 have been reported to cause non-syndromic asthenozoospermia, and DNAI1, DNAH5, DNAAF2, CCDC39, DYNC1I1 and LRRC6 have been implicated in primary ciliary dyskinesia and syndromic asthenozoospermia. The case we have presented here supports the syndromic asthenozoospermia.

### Table 1: Laboratory examinations

| Parameter             | Unit of Measurement | Description | Predicted Value | Test % of Predicted Value |
|-----------------------|---------------------|-------------|-----------------|---------------------------|
| White blood cells     |                     |             |                 |                           |
| Granulocytes          | 8.5 x 10^9/L        |             |                 |                           |
| Lymphocytes           | 73.6%               |             |                 |                           |
| Haemoglobin           | 26.4%               |             |                 |                           |
| Hematocrit            | 11.87 g/dl          |             |                 |                           |
| Platelets             | 319 x 10^9/L        |             |                 |                           |
| Glucose (not fasting) | 155 mg/dL           |             |                 |                           |
| Urea                  | 12 mg/dL            |             |                 |                           |
| Alanine transaminase  | 9 units/L           |             |                 |                           |
| C-reactive protein    | 140.7 mg/L          |             |                 |                           |
| Chloride in sweat     | 12 mEq/L            |             |                 |                           |
| Creatinine            | 0.68 mg/dL          |             |                 |                           |
| Amylase               | 60 U/L              |             |                 |                           |
| Lipase                | 34 U/L              |             |                 |                           |

### Table 2: Pulmonary function test

| Parameter | Unit of Measurement | Description | Predicted Value | Test % of Predicted Value |
|-----------|---------------------|-------------|-----------------|---------------------------|
| Best FVC  | l/tps               | Best Forced vital capacity | 4.08 | 1.84 | 45.1 |
| FVC       | l/tps               | Forced vital capacity | 4.08 | 1.84 | 45.1 |
| FEV1      | l/tps               | FEV in 1 second | 3.55 | 1.29 | 36.3 |
| PEF       | l/second            | Peak expiratory flow | 8.73 | 2.36 | 27.0 |
| FEV6      | l/tps               | FEV in 6 second | 4.28 | 1.75 | 40.9 |
| PIF       | l/second            | Peak inspiratory flow | 1.36 |     |     |
| FEV1/FVC  | %                   | FEV1 as % of FVC | 82.5 | 69.9 | 84.7 |
| FEV6/FVC  | %                   | FEV6 as % of FVC | 95.1 |     |     |
| FEV1/FEV6 | %                   | FEV1 as % of FEV6 | 73.5 |     |     |
| FEF       | l/second            | Forced mid-expiratory flow | 4.65 | 0.93 | 20.0 |
| MEF 75%   | l/second            | MEF @ 25% FVC | 7.4D | 1.92 | 25.9 |
| MEF 50%   | l/second            | MEF @ 50% FVC | 4.83 | 1.23 | 25.5 |
| MEF 25%   | l/second            | MEF @ 75% FVC | 2.11 | 0.39 | 18.5 |
| FET 100%  | second              | Forced expiratory time | 6.4 |     |     |

**FCV** = forced vital capacity; **FEV** = forced expiratory volume; **FET** = forced expiratory time; **MEF** = mid-expiratory flow; **PEF** = peak expiratory flow; **PIF** = peak inspiratory flow.
Infertility in male patients with Kartagener syndrome is due to the lack of sperm motility, while in females it is due to defective ovum transport because of dyskinetic motion of oviductal cilia. Prognosis in these patients is poor in general, even with treatment. The patient in our case will require comprehensive follow-up, as he is at increased risk of tuberculosis. Tuberculosis is common complication in patients with lower lobe bronchiectasis. Sputum AFB staining in the present case was negative for Mycobacterium tuberculosis; however, there remains a high risk of developing tuberculosis. At this stage, surgery would not improve this patient because bronchiectasis is present in both lungs, and if surgery was chosen, both lungs would need to be transplanted, which is not possible in Syria, and recurrent infections should be controlled by antibiotics. There have been reports that support the use of sinus surgery in such patients, but this is an area where further investigation is required.

### Conclusion

Kartagener syndrome is a form of PCD that physicians should be aware of. It must be suspected in every patient presents with chronic sinusitis, bronchiectasis and dextrocardia, even if there is complete situs inversus or not. Infertility is common in such patients; however, the fertility of the patient in this case did not exclude the diagnosis of PCD. It is important to conduct a CT scan for every patient with dextrocardia. Finally, treatment of recurrent respiratory infections with antibiotics is the basis for controlling the disease, and surgery for sinusitis may be good last resort.

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**Figure 2: Posterior anterior chest X-ray shows dextrocardia**

**Figure 3: A computed tomography scan showing bronchiectasis**

**Figure 4: Computed tomography scan after treatment**

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