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Case Report

Kartagener's Syndrome and Diabetes Mellitus - The Ciliary Defect

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Abstract

Kartagener's Syndrome (KS) is a rare autosomal recessive disorder. It consists of situs inversus, recurrent sinusitis, and bronchiectasis due to defective cilia. We propose that the ciliary defect in KS can also cause pancreatic islet cell damage, leading to diabetes mellitus. **Case Report:** Our patient is a 42-year-old male admitted to our hospital with a lower respiratory tract infection and hyperglycemia. On evaluation, he was detected to have Kartagener's syndrome. The patient also gave a history of 10 kg weight loss over the last 3-4 months with polyuria and polydipsia. Laboratory results revealed hyperglycemia with HbA1c 9.2%. He denied any family history of diabetes mellitus. His BMI is 23.6 kg/m². The patient was treated with intravenous antibiotics and intravenous fluids. Blood sugars were managed with basal-bolus insulin while in the hospital. The patient recovered and was discharged with oral antidiabetic drugs and basal insulin. The patient regularly follows up in the outpatient clinic and is doing reasonably well. **Conclusion:** Diabetes mellitus may develop in Kartagener's syndrome patients as a result of underlying ciliary defects, according to our hypothesis. Ciliary defects might also be a possible cause of diabetes mellitus as a result of this.

Keywords: Kartagener's Syndrome; Diabetes Mellitus; Ciliary Defect; Primary Ciliary Dyskinesia

Introduction

Kartagener's Syndrome (KS) is an autosomal recessive genetic disorder. KS has a classical triad of situs inversus, chronic recurrent sinusitis, and bronchiectasis [1]. Mutations at the DNAI1 and DNAH5, which encode the outer dynein arm components of cilia [2], lead to impaired ciliary motility. Defect in the ciliary motility leads to defective clearance of respiratory secretions, which results in recurrent chest infections followed by bronchiectasis and chronic sinusitis. In addition, there is evidence of the presence of cilia in the islet and ductal cells of the pancreas [3]. The ciliary defect can cause abnormalities in the pancreatic duct, damage to the acinar cells in the pancreas, and reduced insulin secretion, all of which contribute to the development of diabetes mellitus [3].

Case Report

A 42-year-old male presented to the clinic with a history of fever, cough, and blood-tinged sputum production of three days in duration. He had a high-grade fever and chills, along with myalgia and anorexia. Cough was associated with sputum mixed with streaks of blood. He denied any chest pain or dyspnea. He did not have any preexisting illness and was not on any anticoagulants.

On further probing, he gave a history of an intermittent cough for many months with the need for antibiotics. The patient stated that he maintains a balanced diet and exercises regularly. He also mentioned that although his appetite was good, he was still losing weight. He has lost around 10 kgs in the last 3-4 months with a history of polyuria and polydipsia.

On examination, the patient was febrile with a temperature of 38.4°C. Heart rate was 110/min, blood pressure was 110/74 mm

of Hg, and respiratory rate was 22/min. His oxygen saturation was 94 % on room air. Chest examination revealed extensive bilateral coarse crepitations, especially at the bases. Random blood sugar was 380 mg/dl, and HbA1c was 9.2%. A complete blood count revealed a 14500/cu mm white cell count with 90% polymorphs. Hemoglobin and platelet counts were normal. His kidney function and liver function tests were normal. Urine ketones were negative, and there was no acidosis.

Chest X-ray (Figure 1) and CT chest (Figure 2 and Figure 3) revealed dextrocardia, situs inversus, and extensive bilateral bronchiectasis with patchy consolidation. X-ray paranasal sinus (Figure 4) revealed bilateral maxillary sinusitis. The patient also gave a history of dextrocardia in one of his brothers and sisters. He has been married for the past ten years and has no children. Semen analysis revealed oligospermia. Given his clinic-radiological findings and family history, a diagnosis of Kartagener's syndrome was considered. He was also found to have a lower respiratory tract infection with sepsis and hyperglycemia. The patient was treated with intravenous and nebulized antibiotics. Hyperglycemia was managed with basal-bolus insulin and IV fluids while in the hospital. Due to underlying bronchiectasis, the patient was discharged home on continued nebulized antibiotics for four weeks. On follow-up, he also received Pneumococcal, H. influenza, and Meningococcal vaccines and has been advised to take the yearly influenza vaccine. Blood sugars are currently managed with sitagliptin plus metformin and basal insulin. The patient is on regular follow-ups.

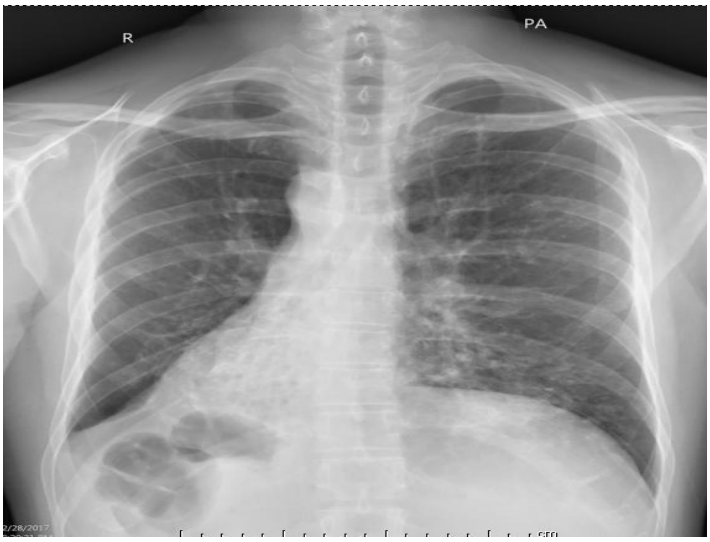
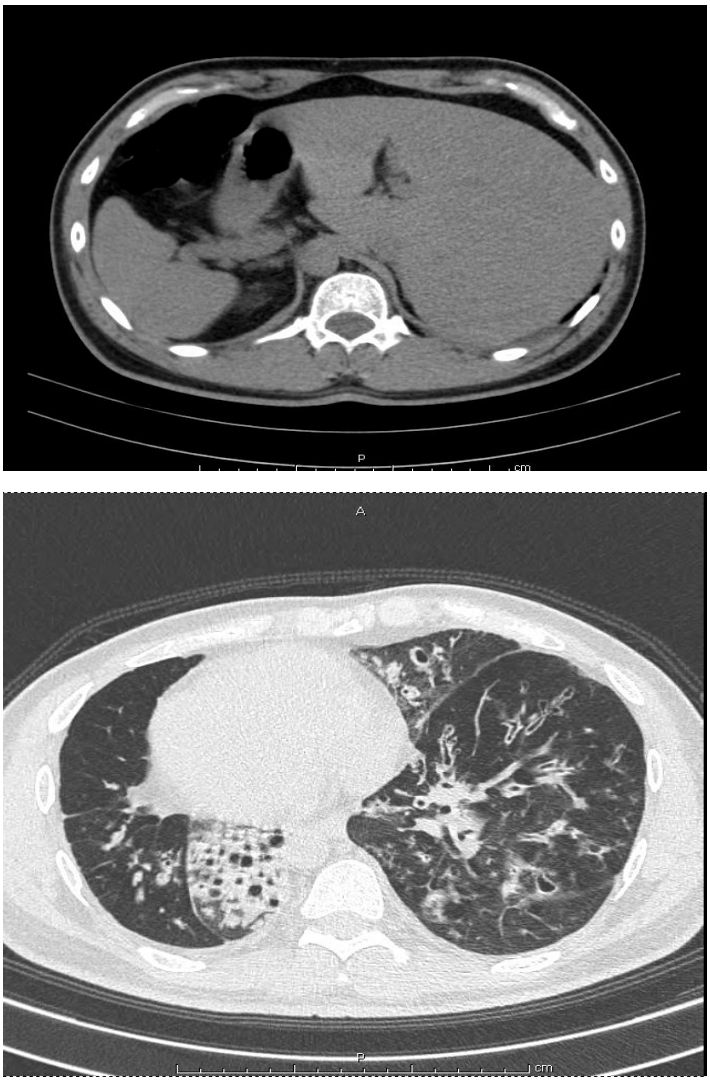


Figure 1: Chest x-ray showing dextrocardia; gastric bubble on right side and liver shadow on left side. Patchy infiltrates suggestive of pneumonitis.



Figures 2 and 3: Computed Tomography of Chest (Lung and Mediastinal window) showing bilateral bronchiectasis and situs-inversus. Liver on left side and spleen on right side of abdomen.

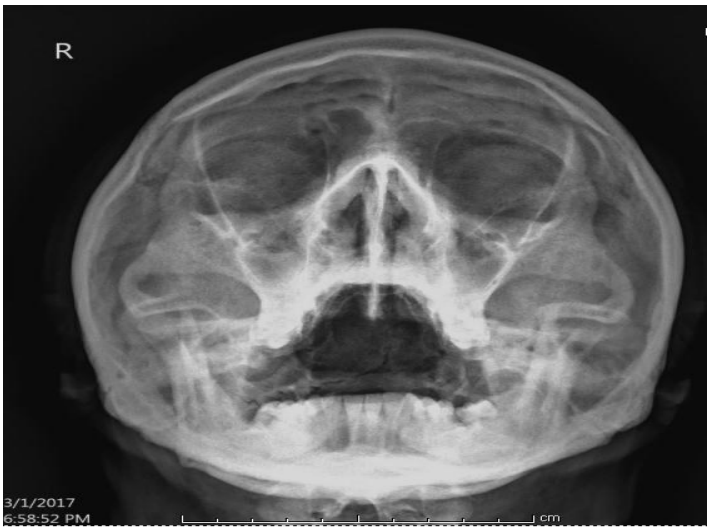


Figure 4: X-ray paranasal sinus showing bilateral maxillary sinusitis.

Discussion

Kartagener's Syndrome (KS) is an autosomal recessive genetic disorder subtype of Primary Ciliary Dyskinesia (PCD). It is usually described as a triad of situs inversus, chronic recurrent sinusitis, and bronchiectasis [1]. The prevalence of Kartagener's is 1 case per 10,000- 20,000 live births [4] and affects both males and females equally [5]. Within the human body, cilia are found in multiple organ systems, and within the human respiratory tract, ciliated cells contain 200 to 300 cilia on their surface [6]. There are two distinct types of cilia; Primary cilia specialize in mechanosensory sensory, and signaling function and motile cilia specialize in motility [7].

Mutations at the DNAI1 and DNAH5 encode the cilia's outer dynein arm components, impairing ciliary motility[1]. In the respiratory system, ciliary dysfunction leads to poor clearing of secretions, resulting in repeated infections and bronchiectasis. In addition, male patients with KS present with infertility due to defective sperm flagellar movement, while females with KS present with reduced infertility caused by defective ovum transport [8].

KS can be diagnosed through diagnostic criteria, along with an early childhood history of rhinitis and chronic bronchial infections; the patient should have one or more of the following (1) Situs inversus in the patient or sibling (2) Alive but immotile spermatozoa (3) Transbronchial mucociliary clearance that is reduced or absent (4) Electron microscopy showing Cilia with ultrastructural defect [9]. In addition to the diagnostic criteria, screening tests such as the exhaled nitric oxide and saccharin tests are used to assess the mucociliary function of nasal epithelial [10,11]. The diagnosis of situs inversus is made with X-rays and CT scans. Additionally, Kartagener's patients undergo sperm analysis. Treatment of KS is a supportive treatment to control infection and reduce complications.

The pancreas is a secretory gland that plays a vital role in regulating glucose homeostasis. Studies have shown that primary cilia have been found within the endocrine pancreas in α-, β-, and δ-cells and play a role in sensory and signaling [12]. DiIorio P et al. also reported that cilia in the pancreatic tissue are mainly located on the islet and ductal cells of the pancreas [3]. Although the pancreas contains mainly Primary Cilia, a study conducted by Cho et al. proposed that the role of primary cilium extends beyond a sensory role and might be classified as sensory-dominant motile cilia [13]. The study demonstrates that beta cell primary cilia contain dynein arms and central pairs. These active cilia enable beta cells to detect nutrients and hormone secretion [13]. The study also proposed a strong association between cilia movement and insulin secretion; therefore, it is an integral part of the beta cell function [13].

Acinar cell loss and abnormalities in the pancreatic ductal structure may result from ciliary movement defects [3]. This defect eventually leads to insulin secretion defects, causing diabetes mellitus [3].

Our patient had no family history of diabetes mellitus, was not overweight or obese, and led a healthy lifestyle. With that said, hyperglycemia in our patient was likely due to gradual pancreatic insufficiency because of the underlying ciliary defect. With continuous follow-ups, our patient has had reasonable blood sugar control with oral antidiabetic drugs and basal insulin. Even though defects in insulin secretion and deficiency due to an underlying ciliary defect may not be absolute, yet, we recommend that patients with primary ciliary dyskinesia be screened regularly for the development of diabetes mellitus. Patients should also be advised regarding healthy lifestyles to help prevent or delay the metabolic consequences of the underlying ciliary defect.

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