



Case Study

KARTAGENER'S SYNDROME - VERSATILE PRESENTATIONS

Belaldavar B P^{1*}, Ankale N R¹, Tubachi J¹ and Khadabadi S N¹

*Corresponding Author: **B. P. Belaldavar**, ✉ puttawwa@rediffmail.com

Primary ciliary dyskinesia (PCD) is a rare genetic disorder with an autosomal recessive mode of inheritance. About 50% of PCD patients develop situs inversus and Kartagener's syndrome, which has been classically described as a triad of dextrocardia, sinusitis and bronchiectasis, and male infertility; its incidence is estimated to be around 1:15000. Patient presents with recurrent attacks of upper and lower respiratory tract infections since childhood, sinusitis, mucopurulent nasal discharge, anosmia, otitis media, bronchiectasis and recurrent episodes of wheezing. In addition, as sperm motility and fallopian tube transport of ova are dependent on normal cilia motility, PCD patients may also suffer from infertility. Physical examination may show dextrocardia secondary to situs inversus. Because of the unusual constellation of clinical features crossing various organ systems, the diagnosis is often delayed even though the first signs may present in infancy. The differential diagnosis includes neonatal respiratory distress, asthma and allergic rhinitis or sinusitis, cystic fibrosis, or primary immunodeficiencies. Hence confusing the treating doctor and putting the patient in distress. We present series of such cases.

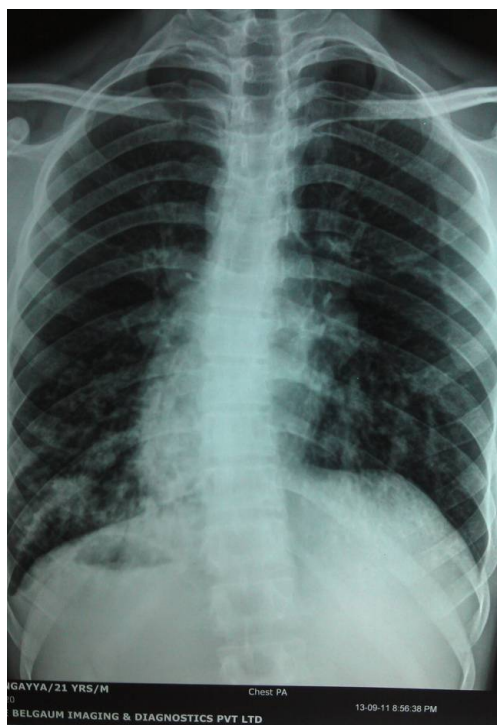
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CASE 1

A 14 year old boy presented with nose block since childhood and recent onset recurrent episodes of epistaxis on straining and cough with mucoid expectoration associated with pain abdomen. He had torticollis which was present since birth. His overall built was stunted. On clinical examination he was found to have heart sounds prominent over right side of chest. Metabolic causes for stunted growth were ruled out. USG abdomen showed situs inversus totalis. CT confirmed the

same and showed dextrocardia, and also revealed bronchiectatic changes in the lungs (Figure 1). However he had no complaints of sinusitis nor any other otorhi-nological problem. He was managed conservatively. After 1 year he presented with antrochoanal polyp of left nasal cavity. It was managed conservatively as patient was not fit for anaesthesia. Further regular physiotherapy and antibiotics were given and he was discharged on short course of intranasal steroids.

¹ KLE university's Jawaharlal Nehru Medical College with Dr. Prabhakar Kore Hospital & Medical research Centre, Belgaum, Karnataka, India. Pin code: 590010

Figure 1: x Ray Chest Showing Dextrocardia

CASE 2

A 21 yr old male presented with recurrent productive cough since childhood for which he has been taking treatment since then with no relief. He had breathlessness on exertion, nose block with copious nasal discharge since 3 years, pulmonary tuberculosis was ruled out. He gave no history of excessive sneezing or itching and watering eyes and had no ear complaints. His medical record showed that he received several courses of antibiotics, antihistamines, bronchodilators, inhaled and even oral corticosteroids but the response was only incomplete and transient.

His family history pointed out towards first degree consanguinous marriage in parents, death of father and maternal grandfather due to alleged recurrent respiratory problems.

On examination, anterior rhinoscopy showed septal deviation to right, inferior turbinate hypertrophy on left side. While posterior rhinoscopy revealed copious discharge in choanae. Nasal endoscopic examination showed presence of thick mucopurulent discharge forming a film like layer over both nasal cavities, whitish in colour, and tenacious on suctioning, both the middle turbinates were covered with polypoid mucosa (Figure 3). Bilateral maxillary and ethmoid sinuses were tender. However the ears were normal and throat showed granular appearance. Systemic examination revealed bilateral leathery crepts over chest and normal heart sounds were heard best on right side of the chest.

Blood counts, renal and liver function tests were normal. Chest X ray revealed dextrocardia which was supported by ECG. CT scan PNS showed bilateral maxillary and ethmoid sinus mucosal thickening, non pneumatization of frontal sinus with hypopneumatization of sphenoid sinuses and both nasolacrimal ducts were blocked. HRCT showed cystic bronchiectasis in both lungs with situs inversus (Figure 2).

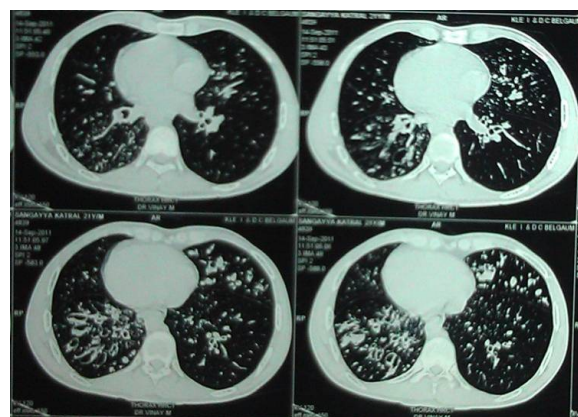
Figure 2: HRCT Thorax Showing Cystic Bronchiectasis

Figure 3: Endoscopic View of Thick Purulent Secretions (Arrow) Over Right Middle Meatus Being Suctioned



Other routine and relevant investigations were performed except semen analysis for sperm motility because the patient was unmarried and declined to do so.

CASE 3

A 15 year old girl who is the younger sister of the case 2, had the similar history of productive cough, breathlessness, nasal block, with additional complaints of bilateral ear discharge since 3 years, profuse, intermittent, mucopurulent and non foulsmelling. Similarly she has been taking treatment since childhood with partial relief, she has attained menarche and has no gynaecological complaints

Examination revealed similar systemic findings. Additionally she had copious discharge in external auditory canal and bilateral medium sized central perforation of tympanic membrane. Nasal endoscopy revealed thick whitish copious discharge lining the nasal cavities and the middle turbinate mucosa was polypoidal anteriorly.

The investigations like blood counts, renal and liver profile was normal. CT para nasal sinus showed similar non pneumatized frontal sinus and hypopneumatized sphenoid with bilateral maxillary sinusitis. Similarly HRCT and ECG also showed same findings as her sibling mentioned above.

Considering the clinical picture of the patients, presence of chronic sinusitis, situs inversus, bilateral cystic bronchiectasis in combination confirmed the diagnosis of Kartagener's syndrome in these patient.

The condition was explained to the patients and treated with antibiotics, mucolytics and steam inhalation. Aural toileting was done regularly. The breathlessness was controlled with salbutamol inhaler and budesonide nasal spray. Patients were immunized against influenza and advised to do so annually. Regular chest physiotherapy and postural drainage was also started.

CASE 4

Another 17 year old presented with recurrent cough with expectoration, bilateral ear discharge and decreased hearing since childhood and non development of speech. In the immediate post natal period he had history of birth asphyxia and breathing difficulty for which he was hospitalised in neonatal ICU for a month. Subsequently he recovered but as a child he had frequent LRTI. His global milestones were delayed. There is history of first degree consanguineous marriage in family, however no other siblings are having similar complaints.

He was found to be moderately mentally retarded with an IQ of 46, with delayed speech development.

ENT examination revealed bilateral medium sized central perforation of tympanic membrane

and thick viscid foul smelling nasal discharge with deviated nasal septum to right. He has bilateral crepts on auscultation of the chest with heart beats heard more loudly on right side of chest.

X-ray PNS showed hypopneumatised sinuses, ECG showed dextrocardia, confirmed on ECHO (Figure 4). Chest X ray showed bilateral diffuse bronchiectasis.

Figure 4: X Ray Para Nasal Sinuse Showing Hypopneumatised Sinuses and Haziness of Maxillary and Ethmoid Sinuses



DISCUSSION

PCD is an autosomal recessive disorder that results in dysfunctional ciliary motility and impaired mucociliary clearance, with reported incidence ranging from 1 in 15,000 to 60,000 live births. Patients with PCD typically present with chronic recurrent infections of the upper and lower airways, sinusitis, and otitis media, due to dysfunction of the synchronous beating and propulsion of ciliated epithelium (Savitha *et al.*, 2006).

About half the cases of PCD are grouped as Kartagener's syndrome which is autosomal recessive disorder, a subgroup of immotile cilia syndrome which has situs inversus (heterotaxy). With an incidence of one in 4000 to 35000 population, it accounts for one tenth of the cases of bronchiectasis and about one sixth of the cases of situs inversus.

Kartagener's syndrome is named after Kartagener who reported series of cases with sinusitis, situs inversus including dextrocardia and bronchiectasis in 1933. It was in 1975 male infertility was added to it (Jonathan Rutland Robbert DE Longh, 1999).

Pathology

It is caused by a defect in the dynein arm structure of cilia, due to which ciliary movement, and consequently its function, are impaired. Ciliary movements are responsible for the rotation and orientation of internal organs in the 10 to 15 days of gestation. In PCD the underlying ciliary dysfunction causes incomplete rotation or malrotation of one or many internal organs, most commonly the heart (Afzelius, 1976).

In the paranasal sinuses the coordinated function of cilia propels the mucus layer from the sinuses to the nasal cavity and then to the nasopharynx, where it is subsequently ingested into the gastrointestinal tract. Normal and effective mucociliary clearance is a critical component of sinonasal immunity and defence that is dependent on proper cilia function. In addition, unlike the lower airways where a compensation for decreased cilia function can be accomplished by a cough, the paranasal sinuses are solely dependent on ciliary function to propel mucus (Olbrich *et al.*, 2002).

The genetic mutations responsible for PCD have not been completely identified. The DNAI1,

DNAI2, and DNAH5 genes, for example, are all associated with outer dynein arm defects and have been implicated in the clinical manifestations of PCD. Since the protective function of cilia is hampered, viral infection further add insult to injury. Certain bacteria like *H. influenza*, *S. pneumonia*, *P. aeruginosa* release certain inflammatory factors further slowing down cilia. In case of *P. aeruginosa*, pyocyanins and 1-hydroxyphenazine which are low molecular proteins cause all the damage (Escudier *et al.*, 2009).

Nasal nitric oxide levels are usually low in PCD and its measurement is now used to screen patients for whom a diagnosis of PCD is suspected. The main disadvantage of nasal nitric oxide measurements is cooperation among younger children (Noone *et al.*, 2004).

CLINICAL PRESENTATION

Patients present to the otolaryngologist with nasal obstruction, rhinorrhoea and deafness if symptoms pertaining to the other systems have not yet manifested. Nasal polyps, by and large, are a result of allergy (Marsden, 1978), and quite common and severe in cystic fibrosis (CF) but are not often seen in PCD; tonsillar hypertrophy and obstructive sleep apnoea are also rare in these patients; OME (otitis media with effusion) is the most common otolaryngological problem in PCD but may stabilise by adolescence (Bush *et al.*, 2007).

CONCLUSION

The patient can have varied presentation which delays correct diagnosis and treatment. When young child can have recurrent chest infections not responding well to routine treatment, later, non resolving and recurrent sinusitis and bronchiec-

tasis occur. Asthma like symptoms and signs responding poorly to conventional treatment further may add to confusion. Recurrent lower respiratory tract infections causing fever, sweating and weight loss, tempting the physician to give a trial of anti tubercular drugs can equally cause dire consequences.

Patients with Kartagener's syndrome can also present with left sided appendicitis if they develop this problem at some stage in their lives. Furthermore, like in our case one child had global milestone delay, although it was a incidental finding it many a times adds to confusion.

Because of the unusual constellation of clinical features crossing various organ systems, the diagnosis is often delayed even though the first signs may present in infancy. Since the disease may not picked up early, it can lead to undue suffering of the child as the differential diagnosis include asthma and allergic rhinitis or sinusitis, neonatal respiratory distress, cystic fibrosis, or primary immunodeficiencies. Definitive diagnosis can be established by ultrastructural study of cilia by electron microscopy. Treatment is symptomatic and surgical intervention is needed very rarely in cases of otorhinological complaints (Olbrich *et al.*, 2002).

The other associated congenital or developmental variations are taken into consideration when the patient with kartageners syndrome in managed (Belaldavar, 2008).

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