Primary ciliary dyskinesia: Report of three cases in Lagos South West Nigeria.

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Abstract

Primary Ciliary dyskinesia (PCD) is rare with a prevalence of about 1:30,000 with Kartagener Syndrome occurring in about half of them. Kartagener syndrome is a subcategory of PCD which is a genetically determined syndrome said to be inherited by autosomal reccesive with incomplete penetrans. In Nigeria there exists few isolated case reports about this condition.

Three patients consisting of two females and one male were seen in the respiratory clinic of an urban tertiary health having presented with recurrent haemoptysis and recurrent lower respiratory tract infections, which dated to childhood. There was no family history.

Bronchiectasis was diagnosed in all the three cases with HRCT. Dextrocardia was present in two patients with situs inversus. Two of the patients had primary infertility. Pulmonary function test was done in two patients and was abnormal. Chronic sinusitis was also present in all patients.

We diagnosed primary ciliary dyskinesia in these three patients. PCD is rare but high index of suspicion is needed in this part of the world for early diagnosis and prevention of long-term sequelae.

All the three patients responded well to bronchodilators, broad-spectrum antibiotics and chest physiotherapy.

Key words: kartergener, ciliary dyskinesia, bronchiectasis

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Introduction

The term primary ciliary dyskinesia (PCD) is used to describe a genetic defect in which there exists an extensive genetic heterogeneity characterized by abnormal ciliary motion and impaired mucociliary clearance. This is different from the transient ciliary dyskinesia which may follow epithelia injury from viral respiratory infections or exposure to pollutants which is an acquired defect.(secondary ciliary dyskinesia)

Ultrastructural and functional defects of cilia result in the lack of effective ciliary motility, causing abnormal mucociliary clearance. This leads to recurrent or persistent respiratory infections, sinusitis, otitis media and male infertility. This is also known as immotile cilia syndrome (ICS). This is an autosomal recessive disease with extensive genetic heterogeneity. About half of these patients have kartergener syndrome charcterised by the triads of situs inversus, chronic sinusitis and bronchiectasis.[1] Afzelius later described the defects in the ultrastructure and coined the term immotile cilia however studies have showed that disorganized and ineffective ciliary beat is responsible and, hence the term ciliary dyskinesia syndrome (CDS)[2].

The basic defect is in the cilia which could be the absence of one or both rows of dynein arms, absence of spoke heads or central sheaths of the cilia. These abnormalities prevent normal transport of mucus from bronchial tree to the mouth and result in severe impairment of lungs defence system. This also affect the upper and lower respiratory, the paranasal sinuses and the middle ear. This is responsible for the various presentations. Male infertility is common and women are often sub fertile.

Cases

Case one is a 30 year old lady with 15 year history of recurrent cough with worsening of symptoms in the last three years. This was associated with sputum expectoration and episodes of haemoptysis. She had some weight loss but no drenching night sweat, no history of contact with chronic cough. She complains of recurrent nasal congestion and occasional headache.

She has had several courses of antibiotics and had completed two courses of treatment for Tuberculosis before referral. She admitted to improvement on medications but symptoms reoccur on discontinuation. She is the last of four children and others are alive and well with no similar complaint. She has been married for 12 years without any pregnancy.

On examination, she was not in any obvious respiratory distress, afebrile, anicteric, mildly pale

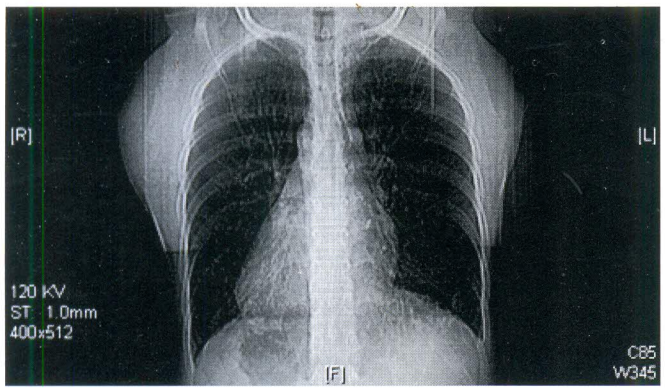


Figure 1:
Dextrocardia with normal lung fields.

and no digital clubbing. Her Respiratory rate was 20 Cycles per minutes. She had a pulse rate of 76beats per minutes, that was regular and of normal volume. The blood pressure was 110/70 mmHg. The JVP was not elevated. Her apex beat was located in the epigastrium. She had only first and second heart sound with no murmurs. The chest was symmetrical with the trachea central. She had equal chest expansion. Percussion note was dull in the left lower zone (hepatic Dullness). She had vesicular breath sound with bilateral coarse crepitations, expiratory and inspiratory Rhonchi in the middle and lower zone anteriorly and posteriorly.

At presentation she had had several investi done which included several chest xrays, n sputum examination for acid fast bacilli and done Gene xpert test for Rifampic were negative for tuberculosis. Her was also negative. Her ESR was 65mn pcv was 36% and WBC count 10,000/c liver function test, electrolyte urea and atinine were normal. Sputum microscopy showed gram positive cocci and yielded no growth on culture. Her chest xray confirmed dextrocardia (figure 1) and lower zone bronchiectatic changes while the High resolution CT showed bronchiectasis involving middle lobes, Lingula and lower lobes as well as Situs inversus Totalis (figure 2a, 2b).

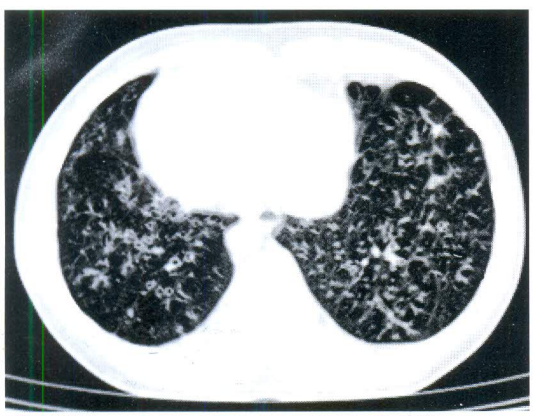


Figure 2a:
Dextrocardia with normal lung fields. There is marked peribronchial thickening and generalised linear and curvilinear hyperdensities

Pulmonary function test was not done here because the sputum remain persistently gram positive for numerous cocci, the exact organism yet to be cultured.

Case 2:
Is a 23-year-old fashion designer with 10-year history of chronic cough. No episodes of haemoptysis but cough often productive of yellowish to brown sputum with episodes of remission and exacerbation. She had recurrent rhinorhea, and stuffy nose since child hood. No history of atopic dermatitis and no itchy red eyes. She is single and had no family history of similar complaints. Physical examination revealed a young lady that was anxious, afebrile, anicteric, mildly pale and with ocular albinism.

Her pulse was 80 beat per minute regular and moderate volume. Blood pressure was 100/80 mm HG. Her apex beat was not felt. She had first and second heart sounds alone with no murmurs. Her chest was symmetrical with a central trachea. She had coarse crepitations in the middle and lower mes anteriorly and posteriorly. There were few onci.

chest xray also showed dextrocardia with ndus on the left (figure 3). Her HRCT widespread bronchiectatic changes (figure 4). She was negative for HIV 1 and 2; all her three sputa were negative for Acid-fast bacilli. The pulmonary function test showed a mixed pattern (restrictive and obstructive defect) with minimal reversibility.
The predicted FEV1 2.58 L, predicted FVC= 2.8L obtained FEV1=1.14L obtained FVC=1.77 L FEV1/FVC= 0.64 %predicted FVC=63% post bronchodilator FEV1=1.23L FVC= 1.95 L (8%)

Case 3:
46 year old man with recurrent cough associated with sputum expectoration and haemoptysis. No history of weight loss no history of contact with chronic cough an no night sweats. He has recurrent nasal congestion, no history of chronic headache. He has being married for 15 years without achieving pregnancy. His seminal fluid analysis repeatedly showed azospermia. He had serial evaluation for tuberculosis done which were all negative. His chest scannogram is as shown in (figure 5)

The X-rays of the paranasal sinuses of all cases revealed findings suggestive of sinus disease, and were referred to the ENT surgeons for further

evaluation and treatment. Case 3 s sinus xray is shown in Figure 6

His pulmonary function test showed obstructive pattern with minimal reversibility with bronchodilator. (Predicted FEV1=3.2L, predicted FVC =3.9L, obtained FEV1 =2.5L, obtained FVC 3.8L, FEV1/FVC =66% with 6% improvement with bronchodilator.

Saccharin mucociliary screening test, nasal nitric oxide and nasal biopsy were not done in any of the patients.

All the patients were all treated with broad-spectrum antibiotics, bronchodilators, Ear, Nose and Throat assessment as well as chest physiotherapy with improvement in symptoms. Case 1 and 3 have primary infertility and were referred for assisted conception, case 2 is Single and declined evaluation for this purpose.

Discussion

Siewert in 1903 first described the triads of bronchiectasis, sinusitis and situs inversus but the syndrome was named after the Swiss paediatrician who described four cases in 1932. 2,3

A hereditary disease, PCD is characterized by ciliary ultrastructural abnormalities that impair the normal ciliary activity and have direct consequences on mucociliary clearance, thus predisposing to recurrent respiratory infections. This results in chronic obstructive-suppurative disease of the respiratory tract. Found in all races and in both genders, PCD is also characterized by generalized ciliary dysfunction. Therefore, alterations can be found at the following sites: in the epithelium of the deferent ducts; in the uterine tubes; in the endometrium; in the corneal endothelium; in the ependyma; in the cilia of the olfactory epithelium mitral cells and of the crests; in the ampulla and cells of Corti of the inner ear; and in the epithelium of the respiratory tract. Consequently, ciliary function must be investigated in these organ.

In this report two of the patients presented with hemoptysis while recurrent chest infections occurred in all of them, in fact two of the three patients had been previously treated for tuberculosis despite a negative test but with recurrence of symptoms. The HRCT showed bronchiectasis in all cases and the triads of the kartergener syndrome were identified in the two females. It is of note that while the frequencies of this disease are well described elsewhere this is unknown in Nigeria and few isolated reports exists about the condition amongst Nigeria.[3,4]

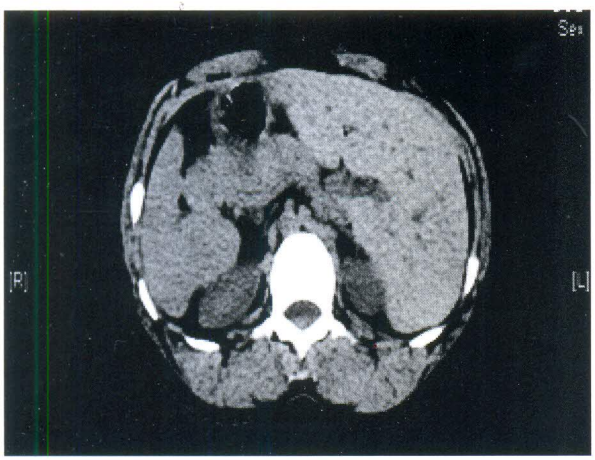
The fact that the symptoms of our patients dated to when they were young and the association of several component s of PCD made us considered primary ciliary dyskinesia as against the secondary dyskinesia which often occurred following viral respiratory infection or exposure to pollutants and is often transient. In Brazil, Ortega et al reported six cases of primary ciliary dyskinesia in which five were kartagener syndrome with one having levocardia. with a mean age of 32 years and consisting of 4 males and 2 females.[7]

It was therefore of interest to document the three cases seen in our practice to increase the awareness amongst physicians and increase surveillance for early diagnosis, which will have implications for long term management. All these patients had high resolution CT scan of the chest done which aided the diagnosis of bronchiectasis. The availability of this diagnostic tool will assist immensely in the diagnosis of those whose chest xray may appear normal and without situs inversus. It remain unclear the prevalence of this condition among Nigerians, a high index of suspicion among young children who present with recurrent respiratory tract infection will improve outcome in adulthood as early diagnosis with prompt and adequate antibiotic use may reduce the extent of permanent lung damage.

It is important to note the limitation imposed by not doing a Saccharin test to access muco ciliary activities as a screening tool in this patients. Similarly nitric oxide analyzer is not available in our centre hence nasal nitric oxide was not done in any of the patients. This is said to be low in patients with PCD. Nasal biopsy /brushing or curettage was not done in this series and this may aid diagnosis in about 20% revealing ciliary abnormalities.

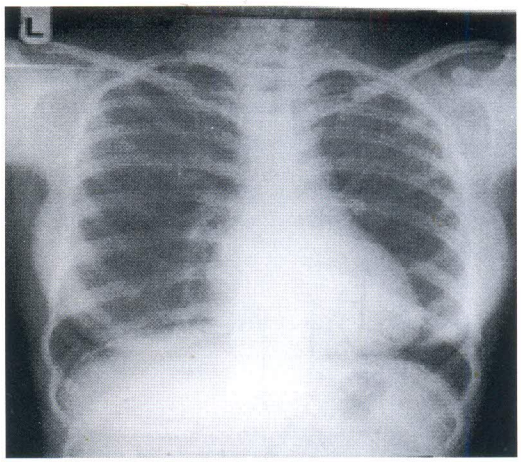
As in most developing countries, patients expect cure of their diagnosis and often live in denial of the chronic nature. These patients had counselling and input into their management from the Ear Nose and throat surgeons, physiotherapists , gynaecologist and urologist. Presently follow up for these cases appear optimal and the clinical condition much improved even though conditions such as infertility will demand increase resources for assisted conception.

Figure 2b:



The liver is seen within the left hypochondrion (Situs Inversus) Some simulating tree in bud appearance while signet ring is noted within the right lung field.

Figure 3:



There is dextrocardia seen. The lung fields are clear

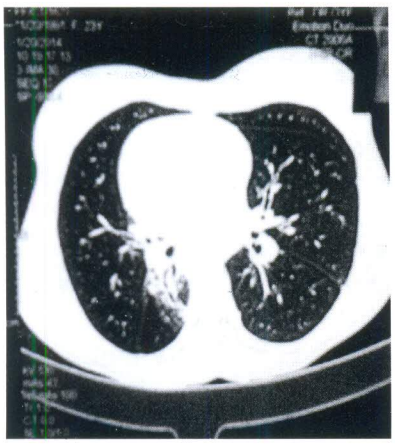


Figure 5:

There is a linear hypodense area interspersed between two linear hpyerdensities within right perihilar area inferiorly simulating rail roading' typical of cylindrical bronchiectasis.

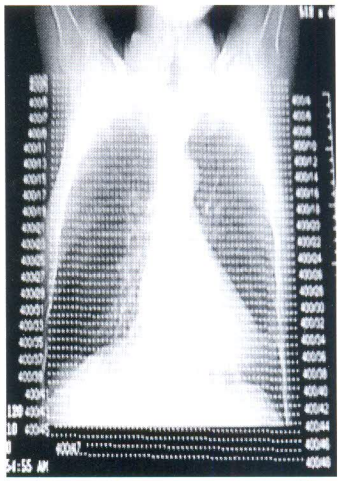
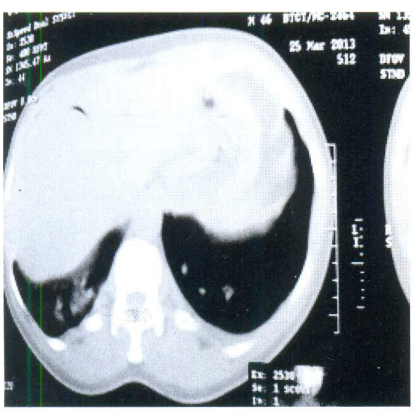
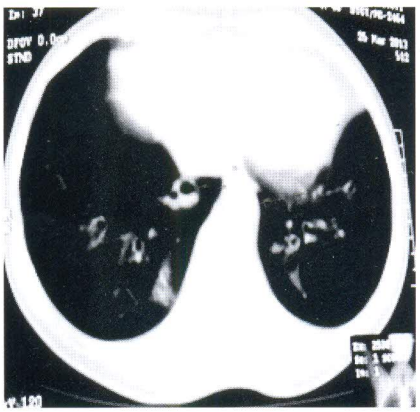


Figure 3:





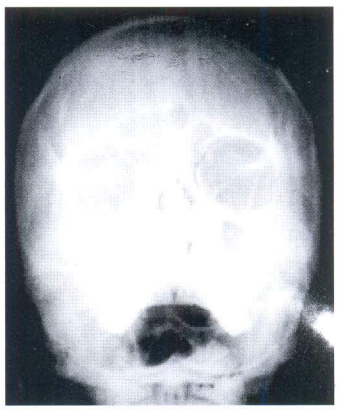


Figure 6:

There is opacity and haziness of the right maxillary antrum and right ethmoidal sinuses. Noted. This is consistent with chronic sinusitis.

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