Cor pulmonale in a case of infantile Gaucher’s disease

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ABSTRACT
Infantile Gaucher’s disease presenting as cor pulmonale is rarely reported in pediatric literature. We report a 3.3 year old boy with infantile Gaucher’s disease who presented to us as interstitial lung disease, pulmonary hypertension along with features of cor pulmonale. The high resolution CT findings were typical of interstitial and airspace disease. Cor pulmonale in this patient was a result of severe pulmonary hypertension.

Key words: Cor-pulmonale, Gaucher’s disease, infant

Introduction
With an overall incidence of approximately 1 in 50,000 to 1 in 1,00,000 live births, Gaucher’s disease is the most prevalent lysosomal storage disorder. An autosomal recessive disorder, Gaucher’s disease is caused by mutations in the glucocerebrosidase gene, leading to decreased enzyme activity and accumulation of glucocerebrosides within the reticuloendothelial system. Three clinical forms of the disease are known—the adult type (type I), the infantile (type II), and the juvenile (type III). Types II and III involve the central nervous system and are very rare. Type I, the adult type, is a non-neuronopathic form, with a later onset and milder course. Though pulmonary involvement has been widely reported in Gaucher’s disease, we report the case of a 3.3 years old boy suffering from Gaucher’s disease with interstitial lung disease, pulmonary hypertension, and cor pulmonale.

Case Report
A 3.3-year-old male child presented with progressively increasing swelling of abdomen for the last 2 years. There was history of easy fatiguability for the last 6 months and increasing respiratory distress for last 1 month. The child’s Motor and Language milestones were also found to be delayed. The boy was born out of a non-consanguineous marriage, with all the other siblings reportedly normal. Child’s weight and height were both below the 5th percentile for his age. Pallor, engorged, and pulsatile neck veins and central cyanosis were present on general physical examination. Abdominal examination revealed a firm, non-tender liver having a sharp margin, and measuring 7 cm below costal margin with a span of 12 cm, and the left lobe measuring 9 cm. The spleen measured 12.5 cm below costal margin along the splenic axis, with a firm consistency, and was non-tender. On respiratory system examination, crepitant and rales were found to be present over the middle and lower zones of both the lungs. On cardiovascular system examination, there was loud pulmonic component of second heart sound along with a pansystolic murmur suggestive of tricuspid regurgitation at a left lower parasternal area.

Blood analysis showed thrombocytopenia (platelet count 66000/µl), leucocytopenia (total leucocyte count in the range of 1700-2600/µl), and anemia (Hb 8.9 g/dl). The liver
enzyme levels were within normal range (serum bilirubin 1.2 mg/dl, SGOT 17 U/L, SGPT 25 U/L) with prolonged prothrombin and activated partial thromboplastin time (PT: control 10.1 s, test 21.0 s; aPTT: control 27.3 s, test 41.6 s). Renal function tests were found to be within a normal range. Arterial blood gas analysis showed hypoxemia (pO$_2$ - 35.4 mmHg). Abdominal ultrasonography revealed homogenous hepatosplenomegaly (liver measured 11.5 cm and spleen 13.8 cm). Chest radiograph showed cardiomegaly with normal looking lung fields. The tubercular work-up and HIV testing for this child was negative.

So, in the presence of huge hepatosplenomegaly, cardiomegaly with murmurs suggestive of tricuspid regurgitation and presence of crepitation in chest, we have thought the possibility of storage disorder – mainly Gaucher and Niemann-Pick with interstitial lung disease in mind and proceed for further investigation.

A bone marrow aspiration study revealed the presence of few large cells with abundant foamy cytoplasm and small round nucleus (Gaucher cells). An enzyme study showed very low levels of enzyme Glucocerebrosidase (<20% of the normal level) which confirmed our diagnosis of Gaucher’s disease. Although the Genetic study was planned for this patient, it couldn’t be done due to non-availability.

The high resolution CT scan [Figure 1] showed diffuse bilateral ground glass opacities with interlobular septal thickening. Diffuse thickening of central peribronchial vascular interstitium was present, the above findings reflecting the presence of interstitial and air-space disease, typical of interstitial lung disease. On electrocardiogram, there was right axis deviation, p-pulmonale, features of right ventricular hypertrophy along with presence of prominent Q waves in leads II, III and aVF. Echocardiogram showed dilated right atrium and right ventricle, severe pulmonary arterial hypertension, severe tricuspid regurgitation, and moderate pulmonary regurgitation with right ventricular systolic pressure measuring around 80 mmHg. Inter-atrial and interventricular septum was found to be bulging toward the left with paradoxical movement.

Enzyme Replacement Therapy was planned for the child, but before it could be instituted, the child succumbed to his illness.

**DISCUSSION**

Pulmonary involvement in Gaucher’s disease has been widely discussed, and reported in about one third of the patients.[3] The medical literature, though, supports the occurrence of cor pulmonale in Gaucher’s disease; reports on such involvement are very scarce and mainly in juvenile age groups.[4,5] In our case, echocardiogram findings gave conclusive evidence of the presence of cor-pulmonale in the child. As severe pulmonary involvement is reported mainly in type II and type III Gaucher’s disease, these forms are at more risk of developing cor pulmonale. The deranged coagulation profile in the presence of normal LFT may be due to early stage of liver dysfunction due to cor pulmonale.

Several patho-physiological mechanisms can contribute to the occurrence of cor pulmonale in Gaucher’s disease—firstly, the infiltration of Gaucher cells in the lung interstitium and alveolar spaces leads to hypoxemia and loss of alveolo-capillary bed, thus, leading to pulmonary vasoconstriction.[6] Secondly, the plugging of the pulmonary capillary vessels by the Gaucher cells leads to pulmonary hypertension.[7,8] One more mechanism has been postulated for the pulmonary hypertension in Gaucher’s disease i.e. increased levels of angiotensin II.[9,10] Although the precise Pathophysiology is not known, Gaucher cells are found to be rich in angiotensin converting enzyme.[9] The above mechanisms lead to an increased pulmonary vascular resistance, which, in turn, leads to an increase in after load of the right ventricle, eventually leading to the hypertrophy of the right ventricle and later cor pulmonale.

Although the improvement in the pulmonary function tests in patients of Gaucher’s disease has been modest with the institution of the enzyme replacement therapy,[11,12] the development of cor pulmonale confers a poor prognosis on such patients as once cor pulmonale sets in the efficacy of enzyme therapy is doubtful.[11] So, we suggest that in a case of Gaucher’s disease, a comprehensive evaluation
of pulmonary vascular disease should be made as soon as possible, even in the absence of clinical signs and symptoms. It should primarily include imaging studies of the lungs, pulmonary function tests, and electrocardiogram and echocardiogram to evaluate pulmonary hypertension.

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