

Down's syndrome with Ventricular Septal Defect (VSD)

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INTRODUCTION

Down's syndrome (DS) (Trisomy 21) occurs in about one in 800 live births without predilection for race or socioeconomic class with a male to female ratio of 1:1. It is the most common chromosomal abnormality in newborns and one of the most frequent genetic causes of mild to moderate mental retardation^{1,3}.

Clinical features of this syndrome include microbrachycephaly, midface hypoplasia, excess nuchal skin, small overfolded ears, generalized shortening of the limbs, small hands, clinodactyly of the 5th fingers (60%), single palmar creases (45%) and wide spacing between first and second toes (sandal toes). They have upslanting palpebral fissures, epicanthal folds and generalized body hypotonia^{1,2}.

Organ defects co-existing with Down's syndrome may include congenital heart defects (50%) (of which Endocardial cushion defects and VSD's are the commonest), gastrointestinal defects ((duodenal atresia / stenosis, traceoesophageal fistula, imperforate anus (20%), Hirschsprungs disease (10%)) are present in 5% of the infants. They are more predisposed to thyroid dysfunction (15%) (commonly hypothyroidism), hearing loss (75%), otitis media (50-75%), eye disease (60%), celiac disease and atlanto-occipital instability. Sterility is common and they have a 12-20% increased risk of getting leukemia^{1,2,3}.

In Down's syndrome, 95% of all cases are caused by non disjunction: one cell has two 21st chromosomes instead of one, so the resulting fertilized egg has three 21st chromosomes. Hence the scientific name, trisomy 21. The cause of the non disjunction error isn't known, but there is definitely connection with maternal age. At age 30, for example, a woman has less than a 1 in 1,000 chance of conceiving a child with DS. Those odds increase to 1 in 400 by age 35. By 42, it jumps to about 1 in 604. Three to four percent of all cases of trisomy 21 are due to Robertsonian Translocation which may be inherited⁵. The remainder of cases of trisomy 21 are due to mosaicism.

Recent advances in medicine have made it possible to a great degree identification of Down's syndrome in Utero. Combining maternal age with maternal serum biochemical markers (alpha fetoprotein, unconjugated

estriol and human chorionic gonadotrophin), the detection rate is approximately 60%. An additional 20% can be identified using sonographic markers like increased nuchal translucency¹.

CASE

L.L a 6 month old female was brought to MNH by her biological mother complaining of difficulty in breathing since birth, fever and cough for the past 2 months. She was a known patient with Down's syndrome with a ventricular septal defect (VSD).

The difficulty in breathing was of gradual onset, progressive and present when the child would breastfeed or cry. The mother had never noted any bluish discoloration around the lips or the fingers nor had she noticed any abnormal sounds made by the child when breathing. Initially there was no cough associated with the difficulty until around 4 months of age. The cough was dry but gradually became productive. The cough was followed by fever which would be of high grade and was not associated with any convulsions or loss of consciousness.

The patient's medical history is significant for a previous admission at MNH due to difficulty in breathing when the baby was 2 months old. She was diagnosed with Down's syndrome and an echocardiogram revealed an 8mm wide VSD. She was found to be in heart failure and anti failures were prescribed accordingly. She recovered from the pneumonia and was subsequently discharged after having been enrolled at the cardiac clinic for follow up.

The child had delayed developmental milestones and a growth pattern that had continuously been in the red zone of the Reproduce Child Health (RCH) card 1 since birth. The mother was 20 years and of good health.

On examination, the child was hypotonic and had upslanting palpebral fissures, flat nasal bridge, low set ears, a protruding tongue and sandal toes (dysmorphic features suggestive of Down's syndrome). She had lower chest indrawing and nasal flaring but was not cyanosed and did not have finger clubbing. She had a respiratory rate of 58 breaths per minute. There

was dullness on percussion and bronchial breaths were heard on auscultation. Her cardiac examination revealed a pan systolic murmur best heard over the lower left sternal border on auscultation.

Her full blood picture revealed neutrophilia (37.9%) and a normocytic hypochromic anemia (Hb 8.7g/dl, MCV 81.1fl, MCH 25.5pg). Her oxygen saturation when breathing room air was 95% and blood slide for malaria parasites was negative. Her chest x ray revealed patchy opacification with air bronchograms and an enlarged heart with a cardiothoracic ratio of 0.65.

Echocardiogram showed a large VSD (1.02cm in diameter) with normal valvular function. Thyroid function tests were within normal range (hTSH 3.034 μ U/ml (0.49-4.67 μ U/ml) and fT_4 0.98 ng/dl (0.71-1.85 ng/dl)). She tested negative to hepatitis screening but tested positive on the sickling test and was found to be Hb AS on electrophoresis. These two tests were done as part of routine screening on children with cardiac conditions being referred abroad for treatment.

The patient was started on antibiotics for severe pneumonia (ampiclox and gentamicin) and continued on anti failures (lasix, spironolactone and digoxin). She started recovering from the cough and fever subsided subsequently. She was later discharged home and the mother was advised to return a week later for the feedback about the cardiac surgery.

Down's syndrome, being a stable neurological condition, the prognosis of this patient depends on the timely correction of the septal defect and appropriate management of other complications that may arise subsequently (like heart failure, chest infections etc).

DISCUSSION

Patients with Down's syndrome, early morbidity and mortality are usually attributed to the cardiac problems. With VSD's surgical correction is usually performed in the 2nd year of life but may be deferred up 4 to 6 years if symptoms are not too disabling⁶. The patient therefore belongs to an age group where the cardiac defect could still be corrected.

Advanced age (above 35 years) is a significant finding in many mothers with children who have Down's syndrome. However this association is most significant with trisomy due to non disjunction⁴. The patients mother in this case was 20 years old making it very likely that the cause here could be a translocation rather than non disjunction and since translocations

may be inherited, the risk that this mother may give birth to another child with Down's syndrome is much greater compared to the risk attributed to a mother with an advanced age. It would be rather difficult to ascertain a Robertsonian translocation as karyotypic analyses are hardly done in our settings. The mother was therefore informed on the possibility of her next child also having the syndrome.

Despite the fact that prenatal screening for Down's syndrome is available and is highly predictive of the disease, it is hardly done in our setting. Ultrasonography may be able to pick nuchal translucency, but only in very skilled hands. Of the serum biochemical markers, alpha fetoprotein and human chorionic gonadotrophin can be measured but may be unaffordable to the majority in our setup.

Sometimes these tests may have to be requested from private hospitals which are expensive contributing further to the economic difficulty. Even if it were possible to diagnose Down's syndrome in utero, would it be ethical to terminate that pregnancy even if the parents were well informed? Even if the financial and technical hardships were to be resolved, an answer to this question must be obtained before routine screening could be initiated.

CONCLUSION

The case described above reflects one of the many associated abnormalities in Down's syndrome – in this case a VSD. Several other organ defects may be present in such infants and the overall prognosis may eventually depend on prompt correction of these defects rather than addressing the Down's syndrome itself. In order to manage the associated abnormalities in good time, early diagnosis is essential. Because of the high frequency with which this syndrome occurs, the essentials for its diagnosis must be well known to most practitioners.

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