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Case Report

Cholelithiasis and Nephrolithiasis in Two Infants with Down's Syndrome: A Case Report

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Abstract: Cholelithiasis in infants and children is rare. There are very few reports of cholelithiasis in infants with Down's syndrome. Here we are reporting two cases of Down's syndrome aged 3 months and 6 months respectively in whom cholelithiasis was detected. One of the babies had nephrolithiasis also. Down's syndrome patients are at an increased risk of developing lithiasis and should be monitored throughout the neonatal period.
Keywords: Down's syndrome, Cholelithiasis, Nephrolithiasis

INTRODUCTION

Down syndrome is the most common chromosomal disorder with an incidence of 1 in 750 live births [1, 2]. The constellation of findings in Down syndrome was found to be due to Trisomy 21 in 1959 by Lejeune and his coworkers . Although the typical phenotype of Trisomy 21 hasn't changed over years there have been some reports of rare associations like biliary sludging, cholelithiasis, Meckels diverticulum etc. with Down syndrome [3, 4, 6, 7]. We report two infants with Trisomy 21 who presented with asymptomatic cholelithiasis and one of them had nephrolithiasis too. The incidence of gallstones in Down syndrome is 3.92 %, while the incidence of nephrolithiasis in Down's is not known [3]. The associated problems in our cases were identified as a part of the diagnostic workup and there was an interesting association of Hirschsprungs disease and fenestrated interatrial septum also in one of our cases. Here we describe the major associations seen in two infants with Down syndrome.

CASE REPORT

Case 1

Ahmed, 3 months old male, the only child born to a non consanguinous marriage was diagnosed with 21 trisomy in the first week of life. His birth history, maternal history and family history were not significant. He presented to us in the 3rd month of life with short duration fever and loose stools. Clinically, he was febrile, and had respiratory distress. He also had conjunctival congestion with photophobia and bulging corneas. Chest findings were, bilateral crepitations and a fixedly split s2. The SpO2 was normal. Per abdomen examination was normal. He had developed social smile but had no neck control. Ocular examination did not reveal glaucoma or keratitis. Fundus examination was normal. All of his lab parameters were normal except for indirect hyperbilirubinemia. The usual work up for jaundice did not reveal any abnormality. His thyroid profile was normal. Chest radiograph did not reveal any significant abnormality. ECHO revealed an ostium secondum ASD with a left to right shunt (9 mm). The abdominal USG revealed multiple cholelithiasis, evidence of nephrolithiasis and cystitic changes. The X-ray KUB and the micturating cystourethrogram were normal .The cranial ultrasound was normal. He improved with supportive care. His parents were not carriers of a balanced translocation. Proper counselling regarding prenatal genetic diagnosis was given and the infant was discharged with follow up advice after a 6 day hospital stay.

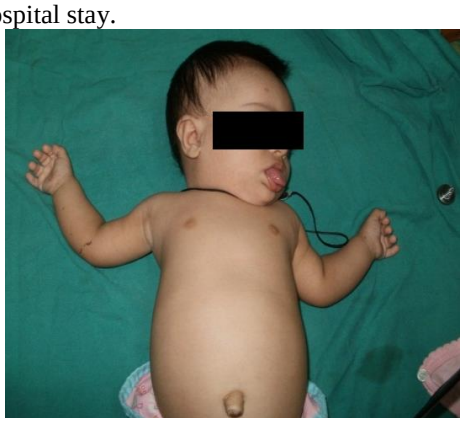

Fig. 1: Case 1

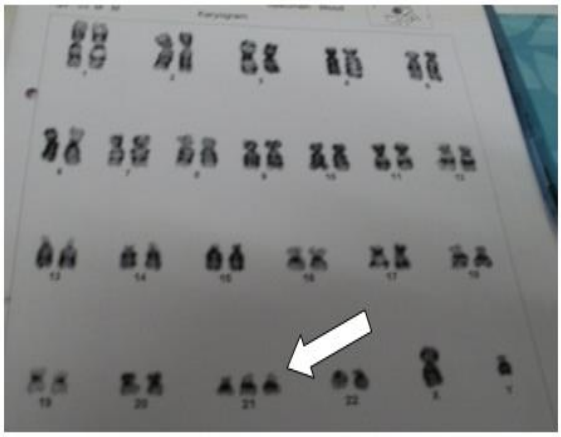

Fig. 2: Karyotyping showing trisomy 21

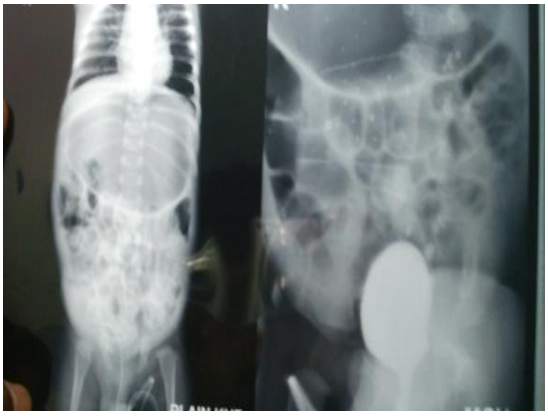

Fig 3: Normal X ray KUB and MCU

Case 2

Pooja, a 6 month old female, was diagnosed with 21 trisomy during her admission into our neonatal unit on the third day of life with deep icterus. Her birth history, maternal history and family history were not significant. Work up for jaundice did not reveal anything significant although the mothers blood group was O +ve with the baby being B +ve. Her thyroid profile was normal. Other lab parameters were normal except for indirect hyperbilirubinemia. The abdominal USG showed bilateral PUJ obstruction with mild hydronephrosis . Echocardiography showed fenestrated inter atrial septum. The parents were not carriers of a balanced translocation. The neonate was discharged on the 9th postnatal day with follow up advice. Later on from the 4th month onwards the infant had recurrent episodes of constipation. She came to our OPD in the 6th month with fever, loose stools and vomiting for one day. After stabilisation, a barium enema was done which revealed Hirschprungs disease. The abdominal ultrasound this time showed multiple cholelithiasis with no evidence of hydronephrosis . A full thickness rectal biopsy could not be done since the parents were not willing. She was discharged with suppository advice with definite surgery planned later on by the surgeon.

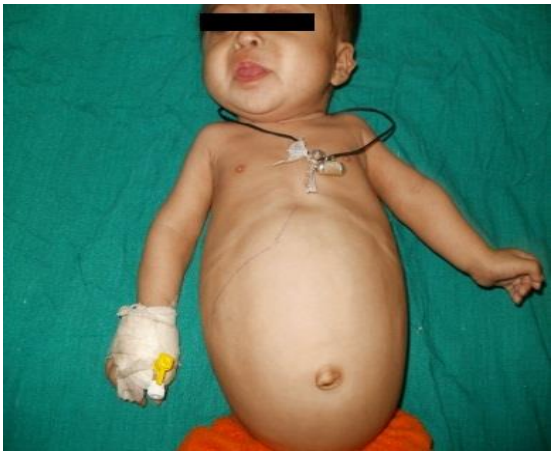

Fig. 4: Case 2

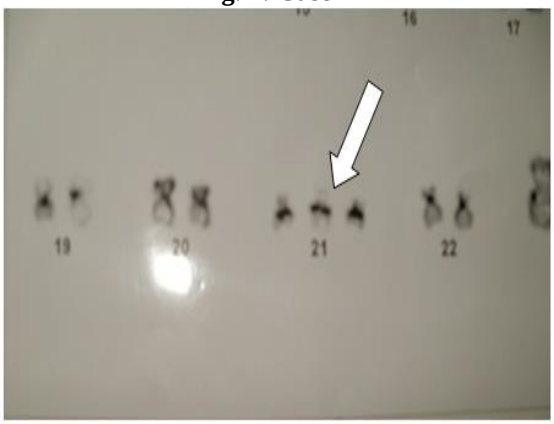

Fig. 5: Karyotype showing trisomy 21

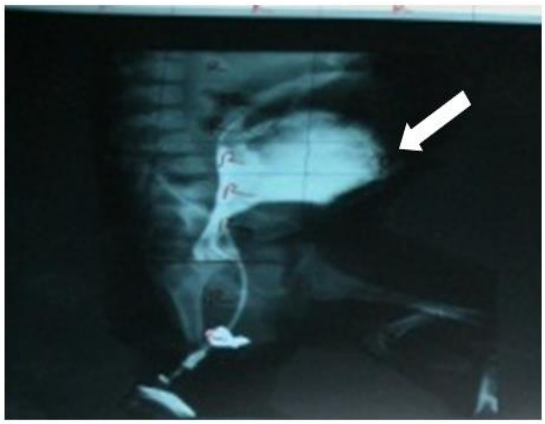

Fig. 6 : Barium enema showing distended sigmoid colon

DISCUSSION

The incidence of heart lesions in trisomy 21 is about 60 % [1, 2]. AV canal defects are more common in Downs's syndrome (40 % of all cardiac lesions in Downs). In our cases one had ostium secundum ASD while second cases had fenestrated interatrial septum. There is a 40% higher risk of a Down's child to have associated heart disease when compared to the general population. Although a thorough search for fenestrated interatrial septum in Down's sydrome did not show any result.

Table 1 : Major associations in our cases

Case 1	Case 2
> Ostium secundum ASD	> Fenestrated interatrial septum
> Multiple cholelithiasis	> Hirschsprungs disease
> Nephrolithiasis	> Cholelithiasis

The reported incidence of Downs's syndrome in Hirschsprungs disease is 2%, varying from 2 to 15% [2]. The overall incidence of cholelithiasis is found to be 6.9% in infants with Down's syndrome [3] and approx 3.92 % in the 11 to 20 yrs old patients with Down's syndrome [4]. The latter study also reported a significantly higher prevalence of obesity in these patients (83% vs 20%; $p<0.001$). Another study revealed decreased gall bladder motility in patients with Downs's syndrome [5]. A case report of two infants with Down's syndrome with gallstones was published in 1995 [6]. One association of Hirschsprungs Disease, meckels diverticulum and cholelithiasis is reported in the literature [7]. Children with Down's syndrome have a significantly higher prevalence of cholelithiasis compared with controls [8, 9].

The genetic abnormality in cases with Hirschsprungs Disease was found to be a mutation in the RET proto ontogeny [10, 11]. Polycythemia was considered to be the cause of gallstones in those two infants. Both of our infants had normal haematocrit values.

Nephrolithiasis has never been reported as an association in Down's syndrome although studies have revealed hyperuricemia in Downs's syndrome. Hyperuricemia is complicated in high frequency at Down's syndrome. The details about the origin of the hyperuricemia which complicates in Down's syndrome at high rate are unknown. With the association of RET enhancer polymorphisms with Hirschsprungs Disease in Downs it would be interesting if associated new genetic abnormalities are discovered in future in case of nephrolithiasis and cholelithiasis associated with Down syndrome [10, 11].

CONCLUSION

From our report it could be concluded that large scale studies in Downs syndrome to know the incidence of nephrolithiasis and cholelithiasis should be undertaken . Clinicians should be aware of the risk of gallstones in children with Down's syndrome and their possible complications. Ifan association of nephrolithiasis is found, appropriate investigations to rule out the cause and proper management of associated complications if any can be instituted. We also strongly believe that other finer molecular diagnostic methods in such cases could reveal a particular genotype.

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