CASE REPORT

Biliary hypoplasia in Williams syndrome

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Neonatal hepatitis and biliary hypoplasia are not recognised features of Williams syndrome. A case of Williams syndrome, presenting with neonatal conjugated hyperbilirubinaemia leading to an initial misdiagnosis is reported.

The child (RS) was born at term by spontaneous vertex delivery with a birth weight of 2580 g (9th centile). He presented at the age of 6 weeks with poor feeding. His weight was 3520 g (2nd–9th centile). He was jaundiced and had a grade 3/6 systolic murmur which was loudest in the pulmonary area. Liver function tests showed a conjugated hyperbilirubinaemia and raised transaminases (table 1).

Investigations for neonatal hepatitis, including α_1 antitrypsin phenotype were normal. An HIDA scan showed normal uptake in the liver but no evidence of tracer in the gallbladder and negligible excretion into the gut, raising the possibility of biliary atresia. Liver biopsy showed bile stasis, dilated sinusoids, and a paucity of intrahepatic bile ducts (fig 1). An echocardiogram showed bilateral pulmonary artery branch obstruction, mild supravalvar aortic obstruction, and a small atrial septal defect.

A diagnosis of Alagille syndrome was made on the basis of the liver biopsy findings, chronic cholestasis, and peripheral pulmonary stenosis; a clinical geneticist felt that the facial features were compatible with this diagnosis.[1] There was, however, no evidence of posterior embryotoxon on ophthalmological examination and no vertebral abnormalities on *x* ray examination. No mutation was identified in JAG1.[2]

The conjugated hyperbilirubinaemia gradually resolved over a period of six months (table 1) and the transaminases improved, although did not return to the normal range.

At the age of 10 months he presented with vomiting, fever, irritability, lethargy, and constipation. He was hypertensive (117/73 mm Hg) and overtly hypercalcaemic with a serum calcium level of 3.81 mmol/l.

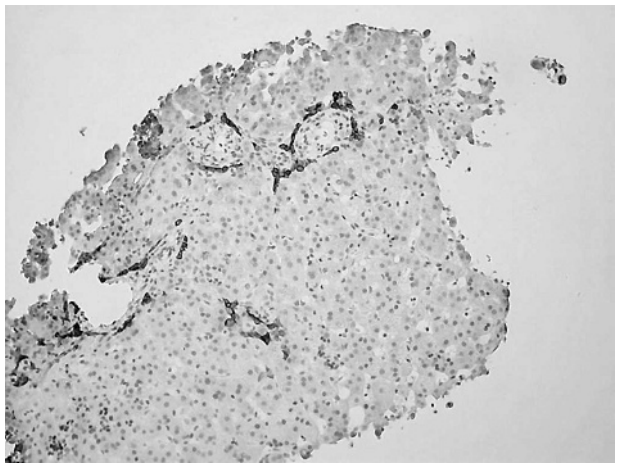

Figure 1 Liver biopsy (AE1/AE3 stain) showing biliary hypoplasia with epithelial cell recruitment at margins of portal tract.

RS now had more obvious facial features suggesting a diagnosis of Williams syndrome.[3] He was a small child with developmental delay who was unable to sit up at the age of 10 months. He now also had a number of serum calcium estimations which were borderline high (table 1). A FISH test confirmed the diagnosis of Williams syndrome with a deletion detected at the elastin gene locus 7q11.23.

RS continues to be followed up as an outpatient. His calcium levels remain stable on low calcium milk (Locasol). His bilirubin levels are normal but transaminases remain mildly elevated. A repeat echocardiogram showed moderate right pulmonary artery stenosis but no supravalvar aortic stenosis.

DISCUSSION

Conjugated hyperbilirubinaemia and biliary hypoplasia are not known to be features of Williams syndrome.

In this case, the initial presenting features were those of prolonged jaundice, biliary hypoplasia, and pulmonary branch stenosis, leading to the incorrect diagnosis of Alagille syndrome. Our attention has since been brought to other cases of Williams syndrome and prolonged conjugated hyperbilirubinaemia, one of whom was also initially thought to have Alagille syndrome (Metcalfe K; personal communication, 2005). There is some overlap between the clinical features of Alagille syndrome and Williams syndrome.[3] Both syndromes are associated with poor feeding, short stature, and developmental delay. Cardiac abnormalities occur in both syndromes, and although classically Williams syndrome is associated with supravalvar aortic stenosis, pulmonary branch stenosis is also common.[3 5] It has been suggested that Williams syndrome should be looked for in all cases of supravalvar aortic stenosis or pulmonary branch stenosis.[6] Although some minor dysmorphic features are shared by both syndromes, for example, depressed nasal bridge, the facies are described as being quite different. However, we highlight the difficulty in detecting subtle features in a baby of 6 weeks of age. In our patient the facial characteristics were much more apparent at the age of 10 months.

Mutations in the JAG1 gene on chromosome 20p12 are thought to be present in 70% of cases of Alagille syndrome,[2] but testing for mutations in the JAG1 gene is not available at all centres. The diagnosis of Alagille syndrome is often a clinical one. The FISH test for Williams syndrome is more easily accessible and shows an elastin gene deletion in over 96% of cases.[4]

In conclusion, there are clinical similarities between Williams syndrome and Alagille syndrome. In our case the presence of conjugated hyperbilirubinaemia and biliary hypoplasia, not documented as features of Williams syndrome, led to the misdiagnosis of Alagille syndrome. If we had adopted a policy of FISH test for Williams syndrome in

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; HIDA, hepatobiliary iminodiacetic acid; FISH, fluorescent in-situ hybridisation

Table 1 Liver function and calcium levels

Age (weeks)	6	8	17	22	45	57	Reference range
Total bilirubin (μmol/l)	229	257	109	20	6	<5	0–20 μmol/l
Conjugated bilirubin (μmol/l)	185	226	87	NA	<5	<5	0–20 μmol/l
AST (U/l)	178	473	148	581	134	66	15–45 U/l
ALT (U/l)	185	305	158	774	120	69	10–40 U/l
Serum calcium (mmol/l)	2.58	2.68	2.83	2.53	3.81	2.75	2.20–2.70 mmol/l
Serum albumin (g/l)	35	37	39	39	47	40	30–45 g/l

NA, not available.

all cases of supravalvar aortic stenosis or pulmonary branch stenosis, the correct diagnosis would have been established earlier. We also emphasise the importance of being aware of the calcium levels in cases of presumed Alagille syndrome, particularly those in which not all clinical features are present. In addition, our report of biliary hypoplasia in this case further extends the phenotype of Williams syndrome.

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REFERENCES

1 **Alagille D**, Estrada A, Hadchouel M, *et al*. Syndromic paucity of interlobular bile ducts. *J Pediatr* 1987;**110**:195–200.
2 **Krantz I**, Piccoli D, Spinner N. Clinical and molecular genetics of Alagille syndrome. *Curr Opin Pediatr* 1999;**11**:558–64.
3 **Winter RM**, Baraitser M. *London dysmorphology database, version 3.0*. Oxford: Oxford Medical Databases, Oxford University Press, 2001.
4 **Lowery MC**, Morris CA, Ewawrt A, *et al*. Strong correlation of elastin deletions detected by FISH with Williams syndrome: evaluation of 235 patients. *Am J Hum Genet* 1995;**57**:49–53.
5 **Eronen M**, Peippo M, Hiippala A, *et al*. Cardiovascular manifestations in 75 patients with Williams syndrome. *J Med Genet* 2002;**39**:554–8.
6 **St Heaps L**, Robson L, Smith A. Review of referrals for the FISH detection of Williams syndrome highlights the importance of testing in supravalvular aortic stenosis/pulmonary stenosis. *Am J Med Genet* 2001;**98**:109–11.

IMAGES IN PAEDIATRICS

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Pneumothorax after a roller coaster ride

Shortly after enjoying a roller coaster ride at an amusement park, this 16 year old boy felt a sharp pain in his chest and experienced some difficulty in breathing. Ten days later he was brought to the A&E department by his mother for evaluation, because of persistent pain and difficulty in breathing. He was a non-smoker and had previously been fit and healthy.

At 170.9 cm, his height was on 50th centile and he had no marfanoid features. On examination, there was no respiratory distress but the air entry was reduced on the right side. Chest *x* ray examination confirmed pneumothorax on the right side (fig 1). He was given 100% oxygen for a couple of hours to aid resolution of the pneumothorax. A week later there was little change in his chest *x* ray findings; however, by 2 weeks there was a complete resolution of the pneumothorax.

There have been no previous citations of occurrence of spontaneous pneumothorax after roller coaster rides, but occurrence of pneumothoraces in previously healthy lungs has been described in relation to sudden pressure changes[1] and exposure to loud music.[2] In our case it seems to be a combination of both.

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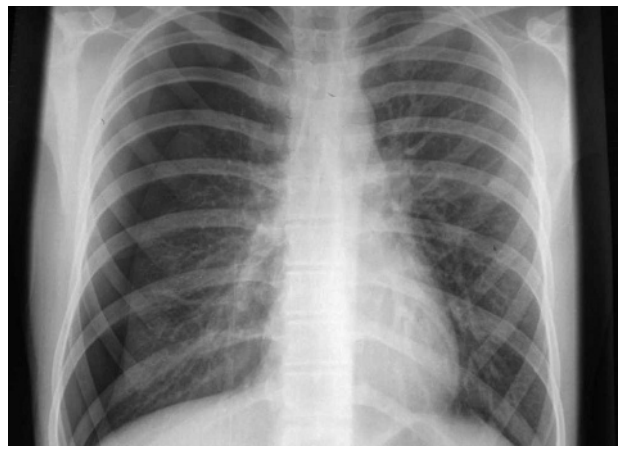

Figure 1 Chest radiograph showing pneumothorax.

References

1 **Smit HJ**, Deville WL, Schramel FM, *et al*. Atmospheric pressure changes and outdoor temperature changes in relation to spontaneous pneumothorax. *Chest* 1999;**116**:676–81.
2 **Noppen M**, Verbanck S, Harvey J, *et al*. Music: a new cause of primary spontaneous pneumothorax. *Thorax* 2004;**59**:722–4.