Clinical Quiz

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Abnormalities of the face, liver, heart, and eyes

Clinical Presentation

A 13-year-old male presented with a history of chronic itching since the age of one year. The pruritus was disturbing his sleep and daily activities, and it had not improved with antihistamine medication. During his childhood, he had jaundice associated with poor growth with anorexia. The family revealed that his cousin had chronic liver disease. His past medical history was otherwise, noncontributory. His physical examination demonstrated icteric sclera, malnourished, and dysmorphic features (**Figure 1**). Hepatomegaly was noted. Systolic ejection murmur was heard in the pulmonary area otherwise, systemic examination was unremarkable. The laboratory findings revealed a normal complete blood count. The electrolytes, renal function, and coagulation study were normal. Liver function test showed increased levels of total bilirubin 131 micromol/L (reference value 0-20 micromol/L), direct bilirubin 76 micrommol/L (<9 micrommol/L), alanine aminotransferase 163 U/L (5-55 U/L), aspartate aminotransferase 94 U/L (5-34 U/L), gamma -glutamyltransferase 347 U/L (12-64 U/L), and alkaline phosphatase 826 U/L (<500 U/L). The echocardiogram showed peripheral pulmonary stenosis. Ophthalmologic slit lamp examination demonstrated posterior embryotoxon. A liver biopsy showed portal inflammation with a few lymphocytes infiltrated and a paucity of the interlobular bile ducts. This case is presented to describe the disease featured below as it is multisystem disorder and the management of cholestasis is related to morbidity and mortality.

Figure 1 - Dysmorphic facial features.

Clinical Quiz

Questions

1. Describe the face abnormalities in Figure 1.
2. What is the diagnosis?
3. What is the treatment option of pruritus?
4. What is the long-term prognosis?

Answers and Discussion

1. ***Abnormalities.*** **Figure 1** showed face abnormalities including wispy hair, triangular face, scleral icterus, and cutaneous jaundice, broad forehead, deep set eyes, straight nose,= and pointed chin.
2. ***Diagnosis.*** The diagnosis is Alagille syndrome (AGS). The AGS is characterized by the paucity of interlobular bile ducts associated with at least 3 of 5 major criteria:[1]
   1) Chronic cholestasis
   2) Cardiac anomalies, most commonly peripheral pulmonic stenosis
   3) Butterfly vertebrae
   4) Posterior embryotoxon (prominent Schwalbe line) of the eye
   5) Dysmorphic facies, consisting of broad nasal bridge, triangular faces, and deep set eyes

   The AGS is a highly variable multisystem disorder that primarily affects the liver, heart, eyes, face, and skeleton. In addition, vascular and renal manifestations are now well described.[1] The AGS is inherited as an autosomal dominant characteristic.[2] The gene responsible for the condition (JAG-1) has been mapped to chromosome 20p12.
3. ***Treatment.*** The cholestasis in AGS is commonly profound and manifests clinically with pruritus. It is important to aggressively medically manage the pruritus in the early years, and possibly avoid liver transplantation. Bile flow may be stimulated with choleretics, and ursodiol is the most commonly used agent. Phenobarbital, cholestyramine, rifampin, and naltrexone have been shown to be effective against pruritus in cholestatic patients.[3] The treatment of AGS generally focuses on trying to increase the flow of bile from the liver, maintaining the child's normal growth and development pattern, and correcting any of the nutritional deficiencies that often develop.[3]
4. ***Prognosis.*** Liver disease contributes significantly to the morbidity of this syndrome, but mortality arises largely from cardiac and vascular disease.[4] The long-term prognosis is related to: a) the severity and duration of the early phase of cholestasis, and especially of secondary severe malnutrition and infectious complications in the youngest patients;[4] b) the severity of the complex cardiovascular abnormalities, which may lead to early death, before or after cardiac surgery; and c) liver status, since a poor status may lead to portal hypertension, or liver failure in patients with prolonged cholestasis.[4]

References

1. Subramaniam P, Knisely A, Portmann B, Qureshi SA, Aclimandos WA, Karani JB, et al. Diagnosis of Alagille syndrome-25 years of experience at King's College Hospital. *J Pediatr Gastroenterol Nutr* 2011; 52: 84-89.
2. Oda T, Elkahloun AG, Meltzer PS, Chandrasekharappa SC. Identification and cloning of the human homolog (JAG1) of the rat Jagged1 gene from the Alagille syndrome critical region at 20p12. *Genomics* 1997; 43: 376.
3. Feranchak AP, Sokol RJ. Medical and nutritional management of cholestasis in infants and children. In: Suchy FJ, Sokol RJ, Ballistreri WF, editors. Liver Disease in Children. 3rd ed. New York (NY): Cambridge University Press; 2007. p. 190-231.
4. Emerick KM, Rand EB, Goldmuntz E, Krantz ID, Spinner NB, Piccoli DA. Features of Alagille syndrome in 92 patients: frequency and relation to prognosis. *Hepatology* 1999; 29: 822-829.