Diagnosis and Management of Paediatric Autoimmune Sclerosing Cholangitis (ASC)

The purpose of this guide is to outline the diagnostic and management issues related to ASC and to provide guidance for complicated clinical scenarios.

Sclerosing cholangitis is a chronic inflammatory disorder that affects the intrahepatic and/or extrahepatic biliary tree leading to bile duct damage and progressive liver fibrosis. Although the name ASC is not universally accepted, it is becoming increasingly used by both the paediatric and adult hepatology community.

Diagnosis

The diagnosis is based on typical bile duct lesions being visualized on cholangiography. With the growing use of non-invasive biliary imaging, sclerosing cholangitis, previously considered rare in children, is diagnosed with increasing frequency in paediatric age.

Treatment

Studies indicate that if treatment is started early, the parenchymal liver damage in ASC could respond well in terms of normalisation of biochemical and immunological parameters to the same immunosuppressive treatment used for AIH, with good medium to long-term survival. Bile duct disease progresses in about 50% of patients despite treatment, particularly in those with associated difficult-to-control IBD. Immunosuppressive treatment is effective in controlling both parenchymal and biliary disease in 50% of ASC cases.

Note of caution: Standard liver function tests do not help in discriminating between ASC and AIH. IAIHG scoring systems do not discriminate between AIH and ASC. Therefore, ASC is frequently diagnosed and treated as AIH-1 and the presence of sclerosing cholangitis may be discovered during follow-up, after the appearance of an overt cholestatic biochemical profile. The differential diagnosis between AIH and ASC is achieved only by cholangiographic studies.

NOTE TO CLINICIANS

Alkaline phosphatase and gamma glutamyl transpeptidase levels—usually elevated in cholestatic disease—are often normal or only mildly increased in the early disease stages of ASC, although the alkaline phosphatase/AST ratio is significantly higher in ASC than in AIH. One-quarter of the children with ASC, despite abnormal cholangiograms, have no histological features suggesting bile duct involvement. Conversely, 27% of the patients with AIH have biliary features on histology (including bile duct damage, acute and/or chronic cholangitis and biliary periportal hepatitis).

Table 4. Proposed scoring criteria for the diagnosis of juvenile autoimmune liver disease

		Points	
Variable	Cut-off	AIH	ASC
ANA and/or SMA*	≥1.20†	1	1
	≥1.80	2	2
Anti-LKM-1* or	≥1.10†	1	1
	≥1.80	2	1
Anti-LC-1	Positive†	2	1
Anti-SLA	Positive†	2	2
PANNA	Positive	1	2
IgG	>ULN	1	1
	>1:20 ULN	2	2
Liver histology	Compatible with AIH	1	1
	Typical of AIH	2	2
Absence of viral hepatitis (A, B, E, EBV), Nash, Wilson disease and drug exposure	Yes	2	2
Presence of extrahepatic auto immunity	Yes	1	1
Family history of autoimmune disease	Yes	1	1
Cholangiography	Normal	2	-2
	Abnormal	-2	2

Juvenile ASC vs PSC

Sclerosing cholangitis in children/adolescents is widely referred to as PSC, borrowing the adult definition. There are important differences, however, between adult PSC and juvenile sclerosing cholangitis. Other inherited conditions, for example, underlying genetic defects in the ABCB4 (MDR3) gene, are being increasingly recognised as a possible cause of small duct sclerosing cholangitis in both children and adults. Sclerosing cholangitis may also complicate a wide variety of disorders, including primary and secondary immunodeficiencies, Langerhans cell histiocytosis, psoriasis, cystic fibrosis, reticulum cell sarcoma, and sickle cell anaemia. An overlap syndrome between AIH and sclerosing cholangitis (ASC) is more common in children than in adults. Only in those paediatric patients in whom sclerosing cholangitis occurs without any of the above defining features, the name of "primary" would be appropriate.

"Primary" denotes ignorance about aetiology and pathogenesis, whereas in paediatrics, there are well-defined forms of sclerosing cholangitis, including biliary atresia and autosomal recessive neonatal sclerosing cholangitis (DCDC-2 deficiency).

IBD is strongly associated with paediatric sclerosing cholangitis, and studies have shown it is associated with 60-90% of cases. IBD can precede the diagnosis of liver disease by many years, be diagnosed at the same time or during follow-up.

This advice guide is produced and published by the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and authored by members of the society's Hepatology Committee.

Full references for the advice within this guide can be found within the following paper, which this guide is based upon: Mieli-Vergani, Giorgina, et al. "Diagnosis and Management of Pediatric Autoimmune Liver Disease: ESPGHAN Hepatology Committee Position Statement." Journal of Pediatric Gastroenterology and Nutrition 66.2 (2018): 345-360.

CLINICAL FEATURES OF ASC

50% of patients are male

Abdominal pain, weight loss, and intermittent jaundice, are frequent presenting symptoms in both ASC and AIH-1

90% of children with ASC have greatly increased serum IgG levels

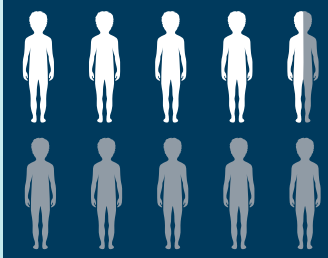
Almost all ASC patients are seropositive for ANA and/or SMA

pANCA is present in 75% of patients with ASC

compared to 45% of patients with AIH-1

and 10% with AIH-2.

IBD affects around 45% of children with ASC



and about 20% with AIH

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