Autoimmune Hepatitis - Full Clinical Guideline

Reference no.: CG-T/2014/192

Diagnosis: made on the basis of the clinical, laboratory and histological features and the exclusion of other causes of chronic hepatitis (consider drugs, Wilson's disease and viral infection).
Female:Male 3:1, Bimodal age pattern – peak in childhood/ teenage years then 4th-6th decade

Clinical features: Fatigue, general ill health, anorexia, wt loss, joint pains (swelling rare)
25% asymptomatic at Δ, 40% present as an acute hepatitis (autoantibodies may initially be negative) with jaundice
30-50% have another autoimmune disease, 30% have cirrhosis at Δ

The International Hepatitis Group have drawn up criteria for the definition of Autoimmune Hepatitis for inclusion in clinical trials (Alvarez et al, J Hepatol 1999; 31:929-938) and have also proposed simplified criteria with – sens > 80% and spec > 90% at a cut off of ≥ 7 pts (See below).

Feature/parameter	Discriminator	Score
ANA or SMA+	≥1:40	+1*
ANA or SMA+	≥1:80	+2*
Or LKM+	≥1:40	
Or SLA+	Any titre	
IgG or immunoglobulin level	>Upper limit of normal	+1
	>1.1× Upper limit	+2
Liver histology	Compatible with AIH	+1
	Typical of AIH	+2
Absence of viral hepatitis	No	0
	Yes	+2

≥6 points: probable AIH; ≥7 points: definite AIH.
*Addition of points achieved for all antibodies (maximum 2 points).
ANA, antinuclear antibody; LKM, liver kidney microsomal antibody; SLA, soluble live antigen; SMA, smooth muscle antibody.

Adapted from Hennes et al. Hepatology 2008; 48:169-76

ANA is usually of a homgeneous or speckled pattern in AIH. 9-17% of patients will have negative liver autoantibodies. They are also not specific for AIH. 20-40% of patients with ALD have low ANA/ SMA titres. 25% of NAFLD patients are positive for ANA/ SMA and 20% meet IAIHG criteria for probable or definite AIH prior to biopsy

Causes: Post viral (Hepatitis A, EBV, Human Herpes 6, Measles)
Drugs* – e.g Nitrofurantoin, minocycline, interferon α, anti TNF
*Can be difficult to distinguish drug induced AIH from DILI. Consider treating with steroids until LFTs normal, then withdrawing steroids. Treat as AIH if initial response, then relapse.

Classification:

90% Type 1, 10% Type 2

Type 3 (Anti SLA) also described but similar to type1, though may be more severe.

Overlap syndromes (PBC:AIH and PSC:AIH) **see PBC and PSC**

Feature	Type 1 AIH	Type 2 AIH
Characteristic autoantibodies	ANA ASMA Anti-actin antibody Anti-SLA/LP antibodies 25% of patients negative ANA	Anti-LKM-1 antibody Anti-LC-1 antibody
Geographical variation	Worldwide	Worldwide
Age at presentation	All ages	Usually childhood and young adulthood
Sex (F:M)	3:1	10:1
Clinical phenotype	Variable	Generally severe
Histopathological features at presentation	Broad range: mild disease to cirrhosis	Generally advanced, ↑ inflammation/cirrhosis common
Treatment failure	Rare	Common
Relapse after drug withdrawal	Variable	Common
Need for long-term maintenance	Variable	Approximately 100%

Treatment
The majority of patients need treatment. A small number of patients (usually those with co-morbidties/ advancing age) with ALT < 3 x ULN, minimal activity (Ishak HAI < 4/18) and no advanced fibrosis on biopsy can be monitored with no treatment.

Initial Treatment:
- Start the patient on **Prednisolone 30mg/day** and reduce by 5mg per week to 20mg od, and then by 5mg every 2 weeks to 10mg daily
- AdCal D3 1 tab bd (bisphosphonate in steroid treated patients > 65yrs or with history of fragility #)
- If the patient has severe steroid side effects or there is good reason to wish to avoid the systemic effects of steroids (e.g diabetes) then **Budesonide 9mg/day** is an alternative in the absence of cirrhosis
- Check TPMT levels - 1:300 homozygous for deficiency allele (avoid Azathioprine), 10% heterozygous - intermediate activity
- When ALT <2 x normal add **Azathioprine 50mg or 1mg/kg**
  (Mycophenolate Mofetil (MMF) 0.5-1g bd can be substituted in patients (10%) intolerant of Azathioprine. MMF is teratogenic. Both men and women require counselling on the risk of harm to the foetus. Patients must use effective contraception during and for 6 weeks (female)/ 12 weeks (male) after stopping treatment)

Treatment failure:
- 9% of patients have clinical, biochemical and histological worsening within 3-6 weeks
  Review diagnosis and if satisfied correct → Prednisolone 60mg for 4 weeks or Prednisolone 30mg + Azathioprine 150mg (70% improve with this strategy)

Azathioprine/ Mycophenolate monitoring:
- Initiation phase: FBC and LFTs weekly for four weeks then monthly for 3 months
- Maintenance phase: FBC, LFTs IgG levels every 3 months.

Maintainence therapy:
- Azathioprine 1-2mg/kg/day + Prednisolone 5-10mg/day or Azathioprine 2mg/kg monotherapy
- Treatment is aimed at achieving and maintaining a normal ALT and IgG
- Consider repeat liver biopsy at 12-24mths - Histological remission is usually 3-8 mths behind biochemical remission
- If persisting hepatitis on biopsy ↑ Azathioprine to 2mg/kg/day or switch to Tacrolimus
- DEXA scan every 1-5 years + advise annual optician review for cataracts/ glaucoma while on steroids
- Advise UV protection
- Ask GP to vaccinate for Hepatitis A and B and annually for influenza

Incomplete biochemical response:
- 13% of patients fail to enter remission by 36/12 – **Check compliance with therapy**
- Consider - ↑ Pred by 2.5mg/d (<10mg/d) + (Azathioprine 2mg/kg/day or switch to Tacrolimus)

Treatment withdrawal:
- The vast majority of patients will require immunosuppressive therapy for life (>70% of patients will relapse within 12 months of stopping all therapy)
- Patients with advanced liver fibrosis should not be considered for treatment withdrawal
- Consider tapering out of steroids after biochemical remission for > 12mths - reinstitute steroids or increase Azathioprine to 2mg/kg/day if relapse
- Complete treatment withdrawal should only be considered in patients with complete biochemical remission for > 3 years on monotherapy – a liver biopsy to confirm complete histological remission prior to treatment withdrawal is recommended (relapse rate reduced to 30% in this group)
- Persistent hepatitis on liver biopsy or relapse on treatment withdrawal necessitates permanent immunosuppressive therapy

Further reading

EASL Clinical Practice Guidelines: Autoimmune hepatitis 2015
AASLD Practice guidelines. Diagnosis and management of Autoimmune Hepatitis. 2010
BSG guidelines for management of autoimmune hepatitis. GUT 2011

Documentation Controls

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