JHEP|Reports

Should all pediatric patients with type 1 autoimmune hepatitis be screened for inflammatory bowel disease?

To the Editor:

The recent publication in this *Journal* by Warner *et al.* on long-term outcomes in pediatric patients with autoimmune liver disease provides key insights into the natural history of type 1 autoimmune hepatitis (AIH) in children.[1] Their findings show that in approximately 20% of pediatric patients with AIH, the disease evolves into primary sclerosing cholangitis (PSC) or an overlap syndrome of PSC-AIH over a median follow-up period of 16.7 years from the initial AIH diagnosis. Importantly, 70% of these patients were diagnosed with inflammatory bowel disease (IBD) as their disease course progressed.

These results align closely with our hypothesis that all cases of PSC may emerge from a PSC-IBD-AIH overlap syndrome, wherein PSC represents a central component, with AIH and IBD manifesting along a variable continuum unique to each patient.[2] This hypothesis is supported by Warner *et al.*'s observation that a subset of patients initially diagnosed with AIH alone may, in fact, have an underlying PSC-IBD-AIH overlap syndrome, where only AIH surpasses the clinical threshold for diagnosis at the outset. For these patients, it is likely that the "PSC subtype" of IBD,[3] typically a proximally dominant ulcerative colitis, will eventually become clinically apparent in 70% of cases. PSC-IBD can be clinically silent, both in adults,[3] and children.[4,5] Suboptimal screening for IBD may be one reason for the highly variable prevalence of IBD in patients with PSC observed across different studies (from 50% to 99%).[6] Additionally, in cases of PSC-IBD-AIH, where only the AIH is diagnosed at presentation (*i.e.* the PSC and IBD are still clinically silent), immunomodulator therapy (steroids, thiopurines) may treat/mask the IBD variably for prolonged periods of time. Therefore, we propose that all pediatric patients with AIH should be carefully screened for the presence of colitis at diagnosis, before the start of immunomodulatory therapies. Fecal calprotectin testing[7] could serve as a relatively inexpensive, sensitive, and sufficient first-line screen in our opinion. When fecal calprotectin is elevated, colonoscopic biopsies with special focus on the cecum/ascending colon[2] should be obtained to rule out both endoscopic and histologic signs of IBD. Such an approach could capture PSC-IBD at an early stage of PSC-IBD-AIH in up to 20% of pediatric patients with "AIH" based on the results of the study by Warner *et al.*

Early identification of subclinical PSC-IBD-AIH cases may allow for timely initiation of management and malignancy surveillance,[8] and open a valuable therapeutic window, potentially enabling the use of targeted treatments such as oral vancomycin[2,9] to modulate PSC-IBD progression and, possibly, mitigate associated manifestations of AIH.

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Conflict of interest

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Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) used ChatGPT in order to improve language and readability. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhepr.2024.101291.

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