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Mini Review

Hepatic Involvement in Childhood-Onset Systemic Lupus Erythematosus

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Abstract

Childhood-onset systemic lupus erythematosus (cSLE) is a chronic autoimmune disease with an incompletely understood etiology that commonly presents with fatigue, arthralgia, fever, malar rash, oral ulcers, and alopecia. Although the liver is less frequently involved than other organ systems, hepatic abnormalities are an important and under-recognized manifestation. Hepatic dysfunction in cSLE may result from immune-mediated lupus hepatitis (LH), drug-induced liver injury, infection, metabolic disease, or overlap with other immune-mediated disorders such as autoimmune hepatitis (AIH), making timely and accurate diagnosis essential. This mini-review presents recent evidence on the epidemiology, proposed pathogenic mechanisms, histopathologic features, and differential diagnosis of hepatic involvement in cSLE, and provides a diagnostic approach and management principles.

Keywords: *Childhood-Onset Systemic Lupus Erythematosus (cSLE); Lupus Hepatitis (LH); Autoimmune Hepatitis (AIH)*

Introduction

Childhood-onset systemic lupus erythematosus (cSLE) is a chronic autoimmune disease that begins before adulthood and its underlying causes are not yet fully understood. The pediatric population typically exhibits a more aggressive course and more severe clinical manifestations compared with adult population [1]. cSLE may affect any organ system, producing a broad spectrum of symptoms [2]. The liver can be involved, with abnormal liver function tests (LFTs) reported in up to 25% of patients, most often in a subclinical manner. While liver abnormalities are most commonly drug-induced, in rare cases portal and periportal hepatitis result from cSLE disease activity [3]. Lupus hepatitis (LH) is a distinct clinical entity reported to affect 3-8% of adult patients with systemic lupus erythematosus (SLE) [4]. Mariniello., *et al*. performed a retrospective chart review of 32 patients with cSLE; 6 patients had LFTs elevated 1.5 times above normal values, and in one patient liver involvement was concurrent with the diagnosis of cSLE and normalized after initiation of prednisone [3]. Clinical manifestations of hepatic involvement include fatigue, malaise, weight loss, and nausea, whereas physical examination may reveal jaundice and hepatosplenomegaly [5].

Discussion

Pathways of hepatic involvement in SLE

Because of quantitative and qualitative defects of Fc and complement receptors in SLE, immune complexes bind to tissue proteins, leading to activation of inflammatory cells, including B and T lymphocytes, release of inflammatory mediators, and consequentially tissue damage [6]. The precise mechanism of LH is not fully understood, but studies indicate complement activation and vasculitis as important

factors in liver injury. Adult patients with LH are known to have C1q, immunoglobulin G (IgG) and immunoglobulin A (IgA) deposits in the liver portal area and hepatic sinusoid walls. Furthermore, initiation of treatment negatively affects the deposition process [7,8].

Histopathologically, LH is often nonspecific and may produce hepatocellular, cholestatic, or vascular changes. Mild hepatitis may be seen in both lobular and portal zones, with mild inflammation characterized by lymphocytic infiltration [9]. Additionally, portal inflammation, interface hepatitis, cholangiolitis, cholangitis, cholestasis, and focal necrosis can occur [10]. Nodular regenerative hyperplasia (NRH) is a serious complication of LH that may result from immune complex deposition in vascular areas. This can initiate inflammation and coagulation cascades, leading to obliterative venopathy. Histologically, NRH is characterized by numerous hepatic nodules without fibrous walls, surrounded by a thin rim of flattened hepatocytes mimicking thin fibrous membranes but without significant fibrosis [11,12].

Diagnostic approach and management strategies

Along with a thorough patient history and physical examination, further investigations are required to assess liver involvement. Basic laboratory tests should include alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (GGT), bilirubin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), C3 and C4 complement components, and standard SLE serological markers [3,4]. Imaging, most commonly ultrasound, can be useful when differentiating from other diseases [3,10]. LH usually presents subclinically, with only modest LFTs elevations. When LFTs are significantly elevated, causes other than SLE should be considered [10].

The first consideration is drug-induced LFTs elevation, commonly due to aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs), or corticosteroids [13-15]. Hydroxychloroquine, an important treatment for cSLE, rarely causes hepatotoxicity [2,16]. An important differential diagnosis is autoimmune hepatitis (AIH), which causes hepatocyte destruction with inflammatory cell infiltrate, cholestasis, and hepatic fibrosis. Both LH and AIH may have elevated IgG and positive antinuclear antibody (ANA). AIH may also be associated with anti-smooth muscle antibody (ASMA) and anti-liver-kidney microsome type 1 (anti-LKM-1) autoantibodies [17]. Although anti-ribosomal P antibodies are more often seen in LH than in AIH and can help differentiate the two, liver biopsy is recommended to distinguish these conditions [10]. Histology in AIH typically shows a plasma cell infiltrate and a greater degree of interface activity, whereas C1q deposits are a feature of LH and may have prognostic value [8,10,18]. Clinicians must also exclude alcohol, viral hepatitis, metabolic and hereditary liver disease, and other immune-mediated disorders such as primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC) [10,19].

There are no standardized treatment guidelines for LH. Because it is often mild and transient, LH frequently does not require specific treatment. The first step is to exclude AIH and the other aforementioned causes [10,20]. LH usually responds to corticosteroids, but steroid-sparing agents and DMARDs (such as azathioprine) can be considered in patients with an inadequate steroid response [3,4,21]. Non-alcoholic fatty liver disease and relapse of LH after steroid discontinuation remain important concerns. In cases of persistent or severe liver involvement, consultation with a hepatologist is recommended [4,22].

Conclusion

Although LH is rare and liver involvement in cSLE is usually mild and transient, it presents important diagnostic and therapeutic challenges. Most evidence on liver injury in SLE comes from adult cohorts, and pediatric-specific data are limited [1-4]. There is a need for pediatric multicenter registries and standardized definitions of LH in children. Prospective studies are also required to define long-term fibrosis risk and to develop evidence-based guidance on the selection and duration of immunosuppressive therapy when liver injury persists.

Conflict of Interest

The author declares that there are no conflicts of interest to disclose.

Bibliography

1. Aggarwal A., *et al*. "Childhood-onset systemic lupus erythematosus (cSLE): An international perspective". *Current Allergy and Asthma Reports* 24.10 (2024): 559-569.

2. Sura A., *et al*. "Childhood-onset systemic lupus erythematosus". *Pediatrics in Review* 45.6 (2024): 316-328.

3. Mariniello G., *et al*. "Liver involvement in juvenile systemic lupus erythematosus (SLE)". *Pediatric Rheumatology* 9.1 (2011): P254.

4. Piga M., *et al*. "Liver involvement in systemic lupus erythematosus: incidence, clinical course and outcome of lupus hepatitis". *Clinical and Experimental Rheumatology* 28.4 (2010): 504-510.

5. Runyon BA., *et al*. "The spectrum of liver disease in systemic lupus erythematosus. Report of 33 histologically-proved cases and review of the literature". *American Journal of Medicine* 69.2 (1980): 187-194.

6. Tsokos GC. "Systemic lupus erythematosus". *New England Journal of Medicine* 365 (2011): 2110-2121.

7. Takahashi A., *et al*. "Liver dysfunction in patients with systemic lupus erythematosus". *Internal Medicine* 52.13 (2013): 1461-1465.

8. Zheng RH., *et al*. "Clinical and immunopathological features of patients with lupus hepatitis". *Chinese Medical Journal (England)* 126.2 (2013): 260-266.

9. Fiel MI., *et al*. "Systemic disease and the liver-part 1: Systemic lupus erythematosus, celiac disease, rheumatoid arthritis, and COVID-19". *Surgical Pathology Clinics* 16.3 (2023): 473-484.

10. Afzal W., *et al*. "Lupus hepatitis, more than just elevated liver enzymes". *Scandinavian Journal of Rheumatology* 49.6 (2020): 427-433.

11. Vaiphei K., *et al*. "Liver pathology in collagen vascular disorders highlighting the vascular changes within portal tract". *Indian Journal of Pathology and Microbiology* 54.1 (2011): 25-31.

12. Bessone F., *et al*. "Challenge of liver disease in systemic lupus erythematosus: clues for diagnosis and hints for pathogenesis". *World Journal of Hepatology* 6.6 (2014): 394-409.

13. Schmeltzer PA., *et al*. "Liver injury from nonsteroidal anti-inflammatory drugs in the United States". *Liver International* 36.4 (2016): 603-609.

14. Conway R., *et al*. "Risk of liver injury among methotrexate users: a meta-analysis of randomized controlled trials". *Seminars in Arthritis and Rheumatism* 45.2 (2015): 156-162.

15. Chertoff J., *et al*. "Azathioprine-induced hepatitis and cholestasis occurring 1 year after treatment". *BMJ Case Reports* (2014): bcr2014206859.

16. Abdel Galil SM. "Hydroxychloroquine-induced toxic hepatitis in a patient with systemic lupus erythematosus: a case report". *Lupus* 24.6 (2015): 638-640.

17. Mieli-Vergani G., *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.

18. Gurung A., *et al*. "Histologic features of autoimmune hepatitis: a critical appraisal". *Human Pathology* 82 (2018): 51-60.

19. Mori S., *et al*. "Hepatitis B virus reactivation associated with antirheumatic therapy: risk and prophylaxis recommendations". *World Journal of Gastroenterology* 21.36 (2015): 10274-10289.

20. Balbi VA., *et al*. "Autoimmune hepatitis in 847 childhood-onset systemic lupus erythematosus population: a multicentric cohort study". *Advances in Rheumatology* 58.1 (2018): 43.

21. Adiga A., *et al*. "Lupus hepatitis and autoimmune hepatitis (lupoid hepatitis)". *American Journal of the Medical Sciences* 353.4 (2017): 329-335.

22. Huang D., *et al*. "Prevalence and risk factors for liver biochemical abnormalities in Canadian patients with systemic lupus erythematosus". *Journal of Rheumatology* 39.2 (2012): 254-261.

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