Diagnostically Challenging case of SLE with Concurrent Wilson's Disease in Young Girl- A case report

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Title:

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Key Clinical Message:

Abstract: Systemic lupus erythematosus (SLE) and Wilson's disease (WD) can present similar symptoms, complicating diagnosis. This case report details a rare instance of both conditions in a 12-year-old girl, emphasizing the diagnostic challenges. It highlights the need to explore the possibility of concurrent WD in patients diagnosed with SLE.

Key words: Systemic lupus erythematosus (SLE); Wilson's disease (WD); lupus nephritis; KF rings

Introduction:

Wilson's disease (WD), also known as hepatolenticular degeneration (HLD), is a rare inherited autosomal recessive disorder. It arises from a defect in copper excretion, leading to its toxic accumulation in organs like the liver, corneas, kidneys, heart, and nervous system. This condition stems from mutations in the ATP7B gene on chromosome 13.(1–3) Systemic lupus erythematosus (SLE), on the other hand, is an autoimmune disease. In SLE, the body produces abnormal antibodies that attack healthy tissues, causing damage to various organs, including the skin, kidneys, joints, lungs, heart, digestive system, blood vessels, and the nervous system.(1–3)

The co-occurrence of WD and SLE in a patient without prior exposure to the drug d-penicillamine is a rare phenomenon reported only in a few recent cases. This case report presents a unique instance of both WD and SLE diagnosed in a 12-year-old female patient. The aim is to raise awareness among healthcare professionals about the potential for these two conditions to coexist.

Case Presentation:

A previously healthy twelve-year-old female presented to the emergency department at Patan Academy of Health Sciences, Nepal, with a five-day history of progressively worsening epigastric pain. She reported multiple episodes of non-bilious, non-bloody vomiting with radiation to the back. Four days prior, she had experienced a fever, which resolved spontaneously. On examination, the child appeared pale and icteric and was in shock with prolonged capillary refill time and hypotension. Two oral ulcers were noted on the left buccal mucosa, characterized by whitish coloration with central erythema. There was mild tenderness in the epigastric region but no organomegaly. Additionally, the patient exhibited multiple erythematous, non-blanchable petechiae on her limbs, trunk, and upper extremities.

Results:

The patient remained hospitalized for 46 days; throughout this period, clinical and hemodynamic stability was achieved, accompanied by normalization of laboratory parameters, including Complete Blood Count (CBC), renal function tests, liver function tests, and pancreatic enzymes **(Table 1).**

Subsequently, on day 46 of hospital admission, the patient was planned to be discharged. On discharge, it was planned to give monthly IV cyclophosphamide for total 6 cycle and continued oral prednisolone with a gradual tapering schedule as per KDIGO 2024 clinical practice guideline for the management of lupus nephritis, along with oral hydroxychloroquine, zinc sulphate, antihypertensives, hematinic, calcium, and multivitamins.

Over the following three months of outpatient follow-up, serum ceruloplasmin and urinary copper levels were normalized **(Table 1);** ophthalmological evaluation yielded normal findings, and the child successfully returned to school.

Discussion:

This is an unusual case of a 12-year-old patient presenting with features of acute pancreatitis. Further, the workup revealed a multisystem involvement, which led to tests specific for SLE, which turned out to be positive. Due to the renal involvement, a renal biopsy was done, which revealed diffuse lupus nephritis class IV. Findings suggestive of WD were made upon further evaluating the child.

SLE is a chronic systemic disease characterized by complex and heterogeneous clinical presentation involving multiple organs and tissues in the body. (5) One of the common and dire manifestations of SLE is the involvement of the kidneys, which typically occurs three years after and usually five years after the onset of SLE. However, in the pediatric age group, the patients can only present with isolated kidney manifestation, as a study conducted by Qiu et al. revealed that the most common manifestation was proteinuria (81.36%).(6) Diagnosis is made through laboratory findings such as proteinuria or cellular casts. However, patients with asymptomatic disease can show abnormalities like raised serum creatinine levels, hypoalbuminemia, proteinuria, or sediment indicating active lupus nephritis. Active SLE complement levels (C3, C4) are low with the presence of anti-dsDNA autoantibody. With the help of renal biopsy, the histologic form and stage of the disease are established. (1)

SLE commonly affects females in their pubertal age group; common manifestations are class III and IV lupus nephritis. These findings are consistent in our patient as our patient was 12 years-female with diffuse lupus nephritis class IV. However, our patient presented with features of pancreatitis, which is a rare presentation. Pancreatitis associated with SLE is rare and has an annual incidence of 0.4 to 1.1 per 1000 patients. The pathogenic mechanism of SLE-related pancreatitis is not well established; however, it has been associated with vascular damage. Severe hypertension or antiphospholipid syndrome, intimal thickening and proliferation, and immune complex deposition with complement activation in the wall of pancreatic arteries may lead to necrotizing vasculitis, occlusion of arteries, and arterioles by thrombi resulting in pancreatitis. (7)

SLE Is a multisystem disease that can also involve many parts of the eye. Ocular manifestations of SLE are common and may lead to permanent blindness. Keratoconjunctivitis sicca is the most common manifestation. (8) To recognize the disease early and possibly treat it, an ophthalmological examination was done, which revealed a Kayser-Fleischer ring, characteristic of WD. Additionally, laboratory results demonstrated a low ceruloplasmin level and elevated urinary copper, further supporting WD.

WD is a rare inherited autosomal recessive disorder characterized by significant copper accumulation on various tissues and organs secondary to the ATP7B gene mutation, leading to several clinical manifestations. Liver dysfunction is one of the most common symptoms associated with WD. (9) KF rings are a typical ophthalmic manifestation of WD, which are present in almost 100% of neurologic WD and 20-30% in asymptomatic WD. A prospective, observational study conducted in jaundiced patients or patients with clinically suspected WD showed Pseudo-Keyser-Flesher (PKF) rings could be present in various conditions such as Viral hepatitis, Autoimmune hepatitis, Autoimmune hepatitis-primary biliary cholangitis overlap (AIH-PBC), Alcohol-associated hepatitis, drug-induced liver injury (DILI), and other conditions. (10) The

presence of autoantibodies, including ANA, ASMA, and even anti-dsDNA autoantibodies, has been rarely reported in WD. However, its coexistence with SLE is rare. (9) Therefore, as in our case, if liver involvement is present, it is wiser to look for other evidence of WD.

Few cases have been reported on the coexistence of SLE and WD. One of the cases by Xu et al. involved the diagnosis of SLE in a 24-year-old female based on the clinical findings and laboratory results. Similar to our case, KF rings were incidentally discovered during the ophthalmic examination, and further investigations revealed low ceruloplasmin levels and high 24-hour urine copper levels. (11) Similarly, a pediatric case of a nine-year-old girl was reported by Yang Z. et al., who presented with proteinuria, hematuria, pancytopenia, hypocomplementemia, and positivity for multiple autoantibodies led to the diagnosis of SLE, and a further workup of WD was sent due to elevated liver enzymes which led to the diagnosis of the coexistence of both diseases. (9)

Treatment is challenging when there is a co-existence between SLE and WD because penicillamine use is associated with a risk of drug-induced lupus and, thereby, may aggravate the symptoms of SLE. (8) In such conditions, Zinc supplementation could be the cornerstone of WD management. (1) Therefore, our case was managed with oral zinc sulfate, guided by several kinds of literature and suggested by a pediatric gastroenterologist. Consequently, the patient responded very well.

Conclusion:

This case report highlights the rare co-occurrence of Wilson's disease (WD) and systemic lupus erythematosus (SLE). Both diseases can affect multiple organs, making diagnosis challenging. Furthermore, the use of penicillamine, a common treatment for WD, can worsen SLE. This necessitates other approaches, such as zinc supplementation alone, which may be insufficient for long-term management in patients with coexisting WD and SLE. Therefore, long-term follow-up and more studies are needed to see the response in such patients.

References:

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Tables:

Table 1: Laboratory findings:

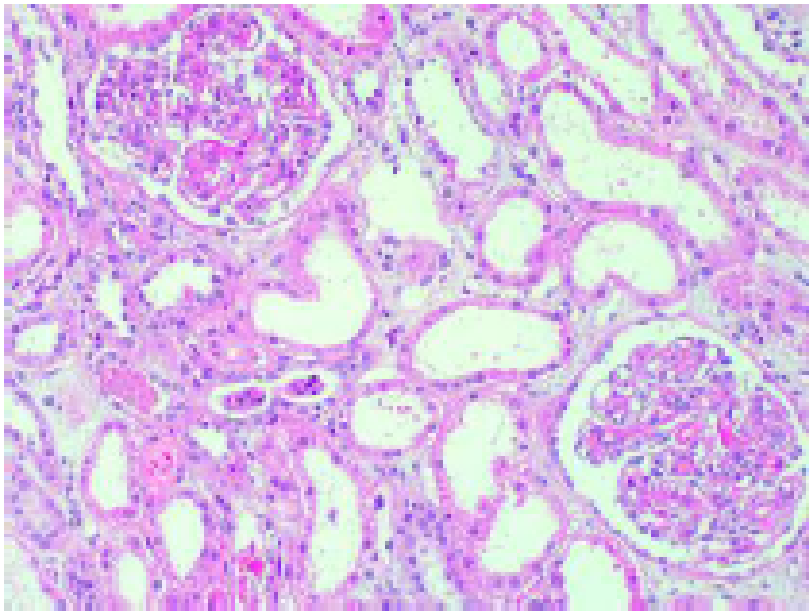
	Day 1	Day 6	Day 11	Day 15*	Day 19	Day 22#	Day 26	Day
TC (10ˆ3/mcl)	7.15	10.02	8.53	9.83	5.77	8.57	8.77	8.2
Hb (gm/dl)	8	8.1	6.7	7.3	8.2	7.4	7.7	7.6
Platelets (10ˆ3/mcl)	145	222	230	264	285	309	213	239
Urea	109	69	74	144	169	101	99	68
Creatinine	2.1	1.4	2.3	6.3	7.2	3.6	3.3	2
Total Bilirubin	5.3	5.9	6	-	-	1.6	-	-
Direct Bilirubin	4.2	3.2	2.9	-	-	0.4	-	-
ALT	124	55	40	-	-	40	-	-
AST	751	345	215	-	-	56	-	-
ALP	413	289	223	-	-	160	-	-
Albumin (g/dl)	1.9	-	-	-	-	-	3.1	-
PT/INR	14.9 /1.06	14.7 /1.05	-	-	-	-	14.5 /1.04	-
APTT	-	42	-	-	-	-	32.3	-
Amylase	648	-	-	-	157	154	-	-
Lipase	16353	-	-	-	935	797	-	-
Serum Ceruloplasmin (mg/dl)	15.22	-	-	-	-	-	-	-
Urinary copper (mcg/24 H)	104.9	-	-	-	-	-	-	-
ANA	Positive (1:200)	-	-	-	-	-	-	-
Anti-ds DNA abs	++	-	-	-	-	-	-	-
Autoimmune Hepatitis panel	Negative	-	-	-	-	-	-	-

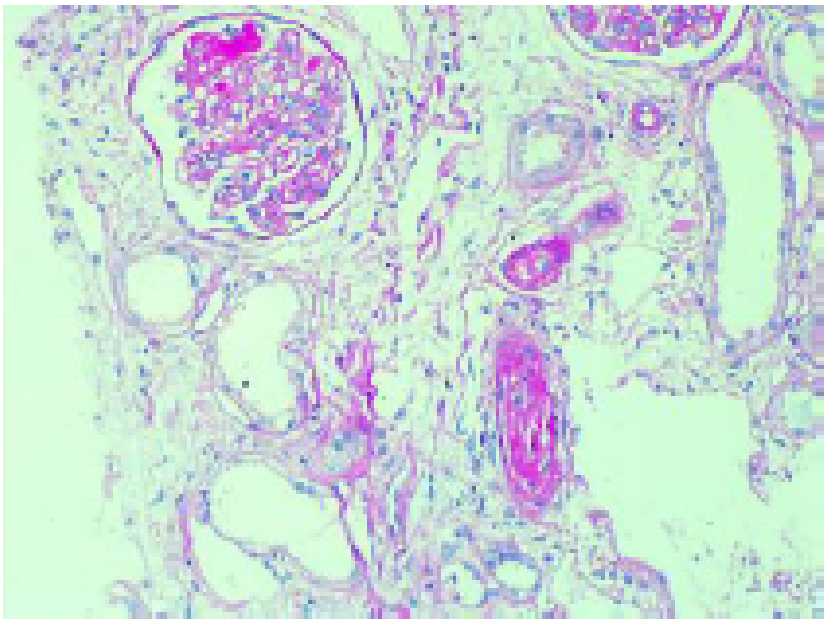
*date at which hemodialysis started

#date at which hemodialysis stopped

Figures:

Figure 1: Histopathology showing grade IV lupus nephritis





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