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WILSON DISEASE AND UNUSUAL DERMATOLOGICAL MANIFESTATIONS: A CASE STUDY ANALYSIS

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Abstract

Wilson's disease, an autosomal recessive disorder, primarily affects copper metabolism due to mutations in the ATP7B gene, leading to abnormal copper accumulation in various organs, including the liver, brain, cornea, kidneys, and joints. Despite being initially characterized by neurological and hepatic symptoms, Wilson's disease can also present with dermatological manifestations, which are less commonly discussed but equally important for comprehensive patient care. We present the case of a 22-year-old male patient with Wilson's disease who presented with painful subcutaneous nodules dispersed across his body, along with other systemic symptoms. Laboratory investigations revealed abnormalities indicative of liver dysfunction, iron excess, and anemia. Histopathological examination of a nodular biopsy demonstrated inflammatory changes consistent with Wilson's disease. Treatment included conventional therapy for Wilson's disease, dietary modifications, and antibiotic treatment for skin lesions. This case underscores the significance of recognizing and addressing dermatological manifestations in Wilson's disease, which may aid in early diagnosis and tailored treatment approaches. Further research and awareness are warranted to better understand and manage dermatological findings associated with Wilson's disease.

Keywords: *Abnormal copper accumulation, Dermatological manifestations, Liver dysfunction, Subcutaneous nodules, Wilson's disease*

INTRODUCTION

Wilson's disease is an autosomal recessive and inherited disorder that affects metabolism of copper due to mutations in the ATP7B gene, that codes for a copper transporter, which is in charge of copper's biliary excretion and ceruloplasmin's incorporation (1). Abnormal copper accumulation is caused by this transporter's dysfunction, and it mostly affects the liver and brain in addition to other organs like the cornea, kidneys, and joints. Wilson's disease was initially defined as a "progressive lenticular degeneration accompanied by cirrhosis in the liver" by British neurologist Samuel Alexander Kinnier Wilson (2).

Although Wilson's disease is not as common in all populations, estimates place the global incidence at about 1 in 30,000 (3). However, depending on a person's ethnic origin and geographic area, prevalence rates may vary. Although the disease can strike at any age, occurrences in younger children or older adults have also been documented (4). Typically, symptoms first emerge between the ages of five and thirty-five. For the first time, Rumpel reported finding extra copper in the liver of a Wilson's disease patient. Cumings confirmed this finding and demonstrated that the disease's etiological basis was copper accumulation in the liver and basal ganglia (5).

Less than 50 years after its discovery, Wilson's disease was identified as the first chronic hereditary liver disease with a specific treatment (6) that may halt the disease's destructive course and avert mortality. Even with these early developments, WD is still an underdiagnosed disease and diagnosis is still difficult. Pathophysiologically, tissue damage and malfunction result from the buildup of excess copper in different organs. Copper deposition in the liver results in hepatic damage, which subsequently advances to cirrhosis and fibrosis. Neurologically, brain accumulation of copper causes a variety of symptoms, including cognitive decline, mental issues, and movement abnormalities. A distinguishing diagnostic trait of corneal

copper deposition is the formation of the typical Kayser-Fleischer rings. Hematological abnormalities, renal failure, and bone abnormalities are additional systemic problems (7).

Copper builds up in the brain, liver, cornea, kidneys, and joints due to Wilson's disease. This can lead to conditions like brain neuronal degeneration, liver failure, Kayser-Fleischer rings at the corneal limbus, renal tubular acidosis, nephrolithiasis, arthritis, and premature osteoporosis (8). Skin-related observations represent an additional unusual yet significant manifestation. Low blood levels of copper and ceruloplasmin, increased copper excretion in the urine, and raised liver copper levels are used to diagnose Wilson disease (9). Diagnostics can also be achieved using molecular testing. These indicators aid in determining whether Wilson disease is present. We are presenting the case of a male patient, age 22, who had unique dermatological findings and was diagnosed with Wilson's disease.

CASE PRESENTATION

A 22-year-old male patient with many painful subcutaneous nodules over his body presented to Shifa International Hospitals Ltd. with a clinical diagnosis of Wilson's disease. After consulting with the dermatologist, an abdominal nodular biopsy was carried out. Pus discharge was seen during the nodule's incision. To rule out any possible infection, a sample of the pus was taken and sent for culture. One-year prior, the patient experienced fever, jaundice, and pruritus.

Table I. Case Presentation of the patient of Wilson's disease

Category	Information
Chief Complaint	Description: Subcutaneous nodules throughout his body
Present Disease	Symptoms: Fatigue etc. Onset: The symptoms were started three months before the examinations. Duration: the symptoms have been present for 6 months Severity: Severe
Medical History	Wilson's Disease No Other Relevant Medical Conditions
Family History	Hypertension

The Table I shows that the patient has been having lethargy and other symptoms for six months, with start three months previously, and now has subcutaneous nodules dispersed across the body. Severity is described as extreme. For a thorough assessment and course of treatment, additional evaluation and management are necessary.

On examination, the patient was observed to be mildly pale, moderately icteric, and had pedal edema. His vital signs were within normal limits. The patient weighed 42 Kgs with a normal body temperature. His CT scan of the abdomen showed hepatomegaly and splenomegaly. His ophthalmic report showed xerosis and night blindness. The mucous membranes, palms, soles, hair, nails, and teeth appeared to be within normal limits. Examinations of other systems did not reveal any notable abnormalities. Investigation findings are listed in Table II and Fig. 1.

The Table II and Fig. 1 show the several abnormalities. Red blood cell count (RBC) is low at 3.52 m/μL and white blood cell count (WBC) is increased at 19,830/μL. The platelet count of 366,000/μL is within the usual range. With hemoglobin level of 11.4 g/dL below normal, anemia is indicated. The increased INR of 1.35 suggests the possibility of clotting problems. Elevated ferritin and iron levels indicate a possible iron excess. Elevated values of total bilirubin and alkaline phosphatase suggest potential liver disease. Gamma G.T., however, is within the usual range. The albumin level (3.3 g/dL) is quite low. All things considered, the patient might have liver malfunction, iron excess, and anemia.

Table II. Laboratory findings of Wilson's disease

Investigations	Result	Reference Range
WBC, Total	19830	4000 - 10500 /µL
RBC, Total	3.52	4.5 - 6.5 m/µL
Platelets	366000	150,000 - 400,000 /µL
Haemoglobin	11.4	12.5 - 16.1 g/dL
INR	1.35	< 1.1
Ferritin	439	12 - 300 ng/mL
Iron	105	76 - 198 mcg/dL
Alkaline Phosphatase	220	40 - 130 U/L
Gamma G.T.	8.0	Upto 60 U/L
Total Bilirubin	26.1	Upto 1.2 mg/dL
Albumin	3.3	3.5 – 5.5 g/dL

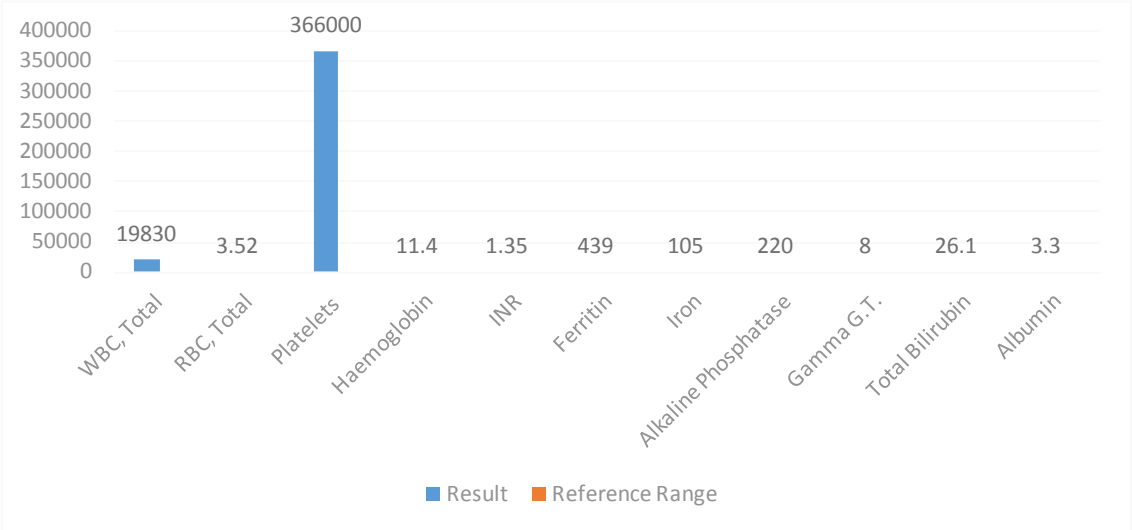

Fig. 1. Laboratory findings of Wilson's disease

DISCUSSION

Wilson's disease usually manifests as neurological and hepatic symptoms (10). It is crucial to remember that Wilson Disease can also have unusual symptoms, such as changes to the skin, and that there aren't many studies on the condition's dermatological effects.

Wilson's disease can show atypically with dermatological symptoms. The case study "Wilson Disease and Unusual Dermatological Manifestations" clarifies this unusual presentation and highlights the significance of identifying and treating such manifestations in clinical practice. Our patient revealed a few odd facts related to their skin. The patient had pus-filled, hyper-pigmented nodules, which prompted a biopsy and additional testing that revealed disease-related inflammatory alterations. Standard Wilson's disease treatments were used in conjunction with dietary changes to reduce aggravating variables and antibiotics for skin lesions. This instance emphasizes the need for a thorough approach to disease management that takes into account both frequent and uncommon signs, as illustrated in Fig. 2a and 2b. The abdominal nodule's biopsy result showed an inflammatory, ruptured cyst that was mostly composed of neutrophils, lymphocytes, and eosinophils, as well as granulation tissue and large cells that looked like foreign bodies. There was no indication of cancer.

The patient received treatment for Wilson's disease, which included the administration of a Copper Chelating Agent - Penicillamine at a dosage of 250mg three times a day (11). Additionally, they were prescribed 20mg of Zinc-sulphate orally three times a day. Ursodeoxycholic acid were given at a dosage of 500mg orally three times daily. Furthermore, the patient was prescribed 50mg of Pyridoxine once daily. The Co-Amoxiclav and Polyfax was recommended by the dermatologist for skin lesions. The patient was

advised to avoid copper-containing foods such as avocado, chocolates, nuts and oysters and report to the hospital immediately if any serious complication appears (12).

Dzieżyc-Jaworska (2019) claims that deposits of poisonous copper build up in several organs. While hepatic and neurological abnormalities are the most typical presentations of WD, there are additional, less prevalent symptoms that are equally crucial for diagnosis and management (13). Compared to healthy people, WD patients' kidney, heart, and osseous tissue had much higher copper contents.

Wilson's disease manifests neurologically and hepaticly, as Kasztelan-Szczerbinska (2021) pointed out, emphasizing the urgency of early diagnosis and treatment. Our case study, on the other hand, concentrates on the dermatological component, which is less frequently discussed but just as significant for all-encompassing patient care. It acknowledged the variety of clinical manifestations in Wilson's disease and offered an update on diagnostic workup and therapy (14).

Our case study adds to this understanding by highlighting the significance of recognizing and addressing dermatological manifestations, which are less commonly reported but crucial for comprehensive patient care. Wilson's disease commonly manifests as neurological and hepatic symptoms; however dermatological abnormalities such as pus-filled subcutaneous nodules can also appear. The significance of a multidisciplinary strategy that includes dermatology in addition to conventional disease therapy is shown by this instance. Moreover, the results of the biopsy demonstrating inflammatory cysts support the multiple organ involvement typical of Wilson's disease. Including these case study-related insights improves our comprehension of the disease spectrum and makes it easier to diagnose patients and provide individualized treatment plans.

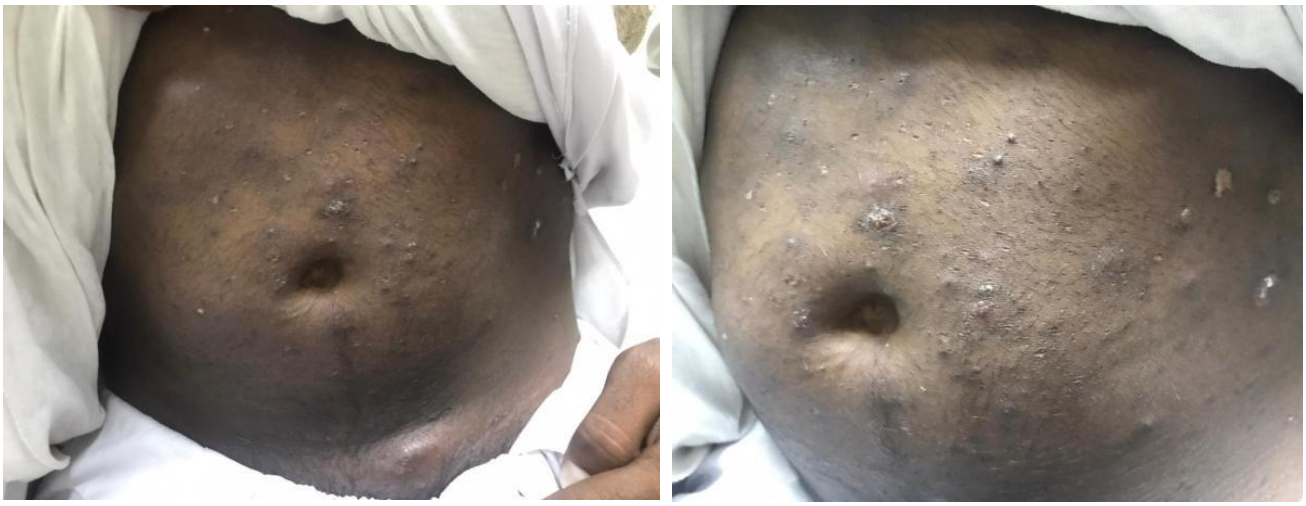

Fig. 2 (a). Abdominal nodules of Wilson's disease **(b).** Pus containing nodules of Wilson's disease

Wilson's disease dermatological features may have underlying mechanisms related to skin deposition of copper, which can cause inflammation, tissue damage, and the formation of subcutaneous nodules with pus discharge. Additionally, granulomatous diseases like sarcoidosis or infectious processes like abscesses may be included in the differential diagnosis.

Wilson's disease treatment should include dietary changes to limit copper consumption, such as avoiding foods high in copper, such as nuts and avocado. Furthermore, it's critical to regularly check liver function tests and copper levels. Changes in lifestyle may help patients reduce their exposure to copper and slow the development of neurological and hepatic symptoms. Liver transplantation can be the only choice for treatment in extreme circumstances.

CONCLUSION

This case report highlights the dermatological findings as one of the presenting features of Wilson Disease. It emphasizes the importance of considering uncommon dermatological findings in cases of Wilson Disease. Therefore, thorough diagnostic evaluation and tailored treatment approaches are needed to effectively manage patients presenting with dermatological findings of unknown etiology. Further research

and awareness are needed to better understand and address dermatological findings seen in patients with Wilson Disease.

One of the main findings, which highlights the variety of clinical presentations of Wilson's disease, is the presentation of hyperpigmented nodules with pus discharge in a male patient, age 22. These dermatological findings highlight the need of thorough evaluation in clinical practice by providing critical diagnostic cues. For prompt diagnosis and efficient treatment, it is crucial to identify and address such signs. In addition, the existence of symptoms related to dermatology implies a systemic involvement, which calls for a multidisciplinary approach to patient care.

Conflict of interest:

The authors have no conflicts of interest to declare.

Consent for Publication:

Written informed consent was taken from the patient for case report and publication. None of personal information will be disclosed in the final publication.

References:

1. Chanpong A, Dhawan A. Wilson disease in children and young Adults-State of the art. Saudi Journal of Gastroenterology. 2022;28(1):21-31.
2. Wilson GN. Wilson disease. InRosenberg's Molecular and Genetic Basis of Neurological and Psychiatric Disease 2020:601-611. Academic Press.
3. Hussein MS, Alshehri TM, Aloufi NM, Saeed A, Alghamdi I, Abdulrahman S, Alharbi FA, Alqerafi AA, Alem MA, Jamal A. Epidemiology, Evaluation and Management of Wilson Disease. Journal of Pharmaceutical Research International. 2021;33(57A):94-103.
4. Poujois A, Woimant F. Challenges in the diagnosis of Wilson disease. Annals of translational medicine. 2019;7(Suppl 2).
5. Sánchez-Monteagudo A, Ripollés E, Berenguer M, Espinós C. Wilson's disease: facing the challenge of diagnosing a rare disease. Biomedicines. 2021;9(9):1100.
6. Mulligan C, Bronstein JM. Wilson disease: an overview and approach to management. Neurologic clinics. 2020;38(2):417-32.
7. Collins JF. Copper nutrition and biochemistry and human (patho) physiology. InAdvances in food and nutrition research 2021; 96:311-364. Academic Press.
8. Haider R. Wilson's Disease. J. Cancer Research and Cellular Therapeutics. 2023;7(3):2640-1053.
9. Avan A, Członkowska A, Gaskin S, Granzotto A, Sensi SL, Hoogenraad TU. The role of zinc in the treatment of Wilson's disease. International journal of molecular sciences. 2022;23(16):9316.
10. Hedera P. Wilson's disease: A master of disguise. Parkinsonism & related disorders. 2019; 59:140-5.
11. Socha P, Czlonkowska A, Janczyk W, Litwin T. Wilson's disease-management and long term outcomes. Best Practice & Research Clinical Gastroenterology. 2022;56:101768.
12. Teufel-Schäfer U, Forster C, Schaefer N. Low Copper Diet—A Therapeutic Option for Wilson Disease? Children. 2022;9(8):1132.
13. Dzieżyc-Jaworska K, Litwin T, Członkowska A. Clinical manifestations of Wilson disease in organs other than the liver and brain. Annals of Translational Medicine. 2019;7(Suppl 2).
14. Kasztelan-Szczerbinska B, Cichoz-Lach H. Wilson's disease: an update on the diagnostic workup and management. Journal of clinical medicine. 2021;10(21):5097.