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A Diagnostic Dilemma: Wilson's Disease with Cutaneous Manifestations

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Abstract
Wilson's disease, an autosomal recessive disorder of copper metabolism, most commonly presents either with hepatic or neurological features. sometimes it may have certain atypical features like cutaneous and renal manifestations which may lead to diagnostic difficulties. we report here a case of Wilson disease who presented as Xerosis and generalised hyperpigmentation of body along with nephrotic range proteinuria. This case report is rare and highlights the fact that early recognition of skin lesions may play a role in diagnosis of Wilson's disease and specific treatment can prevent further liver injury and neurological complications in most cases.
Keywords: *xerosis, hyperpigmentation, Wilson's disease, proteinuria*

Introduction

Wilson's Disease (WD) is an autosomal recessive disorder of copper metabolism caused by mutations in a gene, ATP7B, encoding a copper-transporting, P-type ATPase which leads to progressive copper accumulation in the liver and subsequent deposition in other organs, such as brain, corneas, kidneys, bones, and joints. Hepatic and neurological symptoms are the main clinical features of the disease.[1] But, it often has certain unusual presenting features which may pose a diagnostic dilemma for the clinicians.[2] Sometimes it can present as renal tubular acidosis, nephrolithiasis, premature osteoporosis, arthritis, cardiomyopathy, pancreatitis, hypoparathyroidism, and infertility or repeated miscarriages.[3] Dermatological findings are another uncommon presentation. There are only a few case reports/case series describing cutaneous manifestations with Wilson's disease.[4-7] Here we report a case of Wilson's disease which presents with unusual cutaneous manifestations.

Case Report

A 12 year old male child presented with progressive darkening of skin over the whole body for last 3 years. Currently he came with complaints of abdominal pain for 1 month, swelling of lower limbs followed by upper limb and reddish discolouration of urine for last 15 days along with bullous lesions over right hand for last 7 days [Figure-1,2]. At the time of admission he had also oliguria and low grade fever.

He had neither history of jaundice, hematemesis, Malena, seizures, altered sensorium nor history of

blood transfusions, taking any offending drugs in past. Family history was nothing suggestive. He is the first born child to non consanguineous married parents with uneventful perinatalhistory. Developmental history was age appropriate and immunised till date according to NIS.

On examination, he had mild pallor, generalised lymphadenopathy, bullous lesions over hand and bilateral pedal edema. Her vitals were within normal limit, weight 22 kg (<-3SD W/A) and height 147 cm lies within centile chart with BMI of 22kg/m2. Physical examination showed well defined painless, brownish, dry, itchy and scaly skin lesions over whole body and some fine cracks on the skin over extensor surface of both legs and hands [Figure-3,4] The mucous membranes, palms, soles, hair, nails and teeth were normal. Examinations of other systems were un-remarkable. The child had peripheral stigmata of chronic liver disease such as clubbing, leukonychia and testicular atrophy. Lab investigations are listed in table 1

Table 1

Investigations	Values
CBC	Hb- 9.3/8.4gm/dl Plt-125/258 th/§l TLC-16.19(55/22)/19.2(78/14)
Peripheral smear	Microcytic hypochromic with neutrophilic leukocytosis
RFT	Cr-0.57/1.03/0.98 mg/dl Urea-19.7/30.2/25.2mg/dl
Total protein/albumin	Pr- 8.42/8.40/7.14gm/dl Alb- 1.48/0.78/1.39 gm/dl
Serum electrolytes	Na+/k+/ca+2-137/4.4/1.06 meq/l
LFT	Bilirubin(D/T)-0.26/0.11 SGOT - 3.4/3 SGPT - 5.9/7.2 ALP-126/66
CRP	17.70/33.3
ESR	120/125
Serology/triple screening	Negative
CBNAAT GA	Negative
Sickling test	Negative
Dengue/scrub IgM	Negative
SR amylase, lipae	Normal
Urine routine and microscopy	Albumin ++
ANA screening	Negative
Sr ceruloplasmin	11.8mg/dl
24hr urinary copper	153mcg/day(before penicillamine challenge test) 2341.8mcg/day(after test)
Kf ring	Absent
Sr ferritin	243.2 ng/ml
Sr c3	1.27gm/l
USG	Hepatomegaly with periportal cuffing
FNAC of inguinal LN	Reactive hyperplasia of lymph nodes

The child was diagnosed as a case of WD and was started copper restricted diet and oral Penicillamine (20 mg/kg/day in two divided doses). Dermatological consultation was taken and emollient with antihistamine were given. Hepatology consultation also taken and MRI, liver biopsy were planned for future.

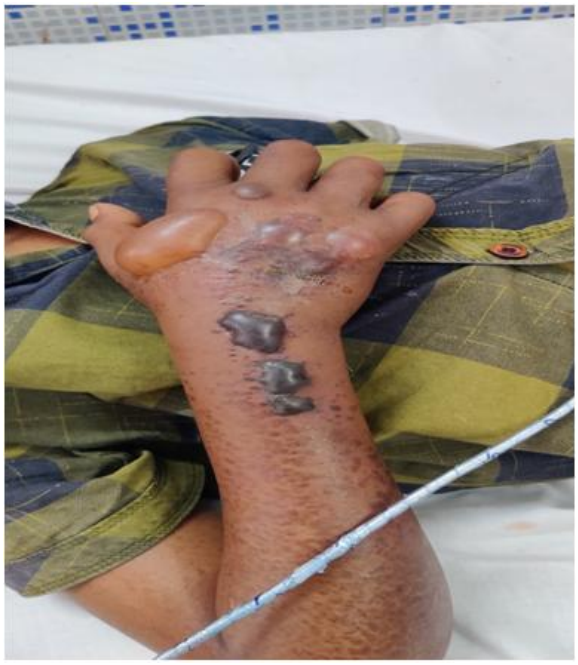

Figure 1

Figure 2

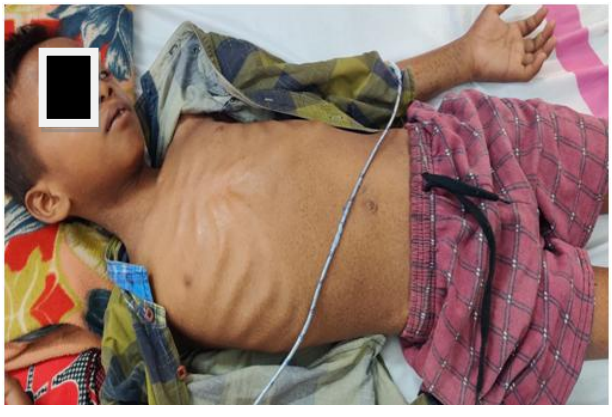

Figure3

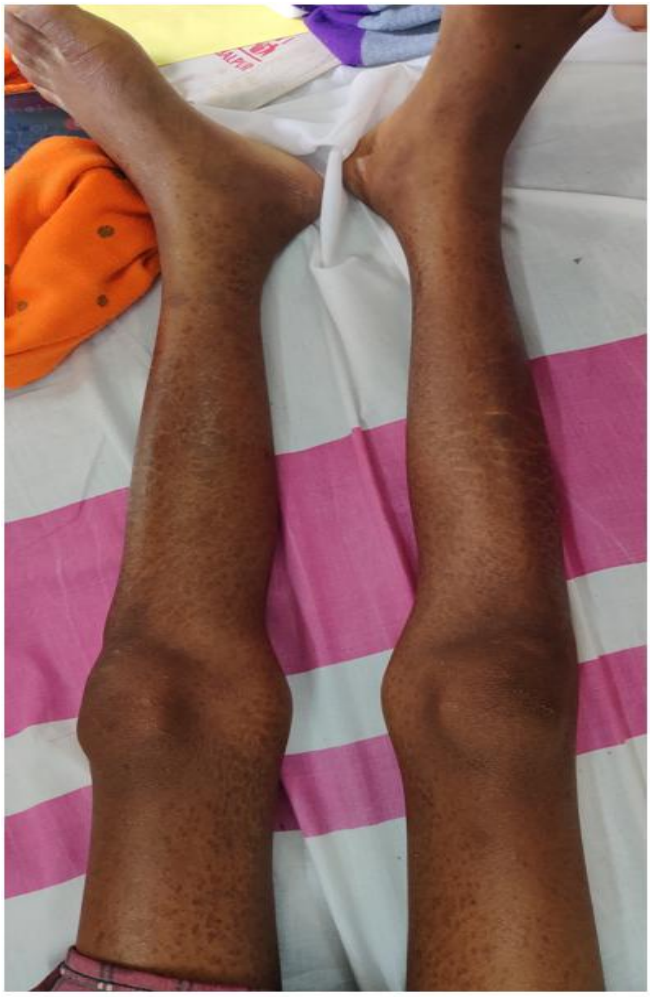

Figure 4

Discussion

Wilson's disease in children is the most common inherited disorder of copper metabolism in India with varied clinical manifestations secondary to deposition of copper in various organs including skin. Correct diagnosis is important because it is a treatable condition, but often presents with diagnostic dilemmas especially when it presents with atypical features.[2]

The association of xerosis, hyperpigmentation in Wilson's disease has rarely been reported in literature. Dermatological changes in WD are very rare and there are only a few published reports (Mainly in the form of case reports). Out of many large series published on Wilson's disease, we could find only one research article in which the authors have reported the incidence of dermatological signs in WD. Seyhan et al in a study of 37 children with WD have shown that 70.3% had at least one dermatological finding[4].

They also showed that 67.5%, 13.5% and 24.3% patient had at least one skin, mucosal and nail finding respectively and most common finding was xerosis of skin (45.7%)[4]. Xerosis of skin was the clinical diagnosis in our case. In our case dermatological findings were not associated with any drug usage, disease severity, malnutrition or duration of disease. Gurubacharya et al. reported a case of Wilson's disease in a 9- year- old child with generalized hyperpigmentation but with liver disease.[5] Steiner et al. reported a case of a 16- year- old adolescent who presented with signs of hypersplenism due to cirrhosis and neurological disturbances but with hyperpigmentation of only lower legs, unlike our case who had generalized skin darkening.[6] Another case report from India described a patient of Wilson's disease in a 9year-old boy with generalized hyperpigmentation with neurological involvement unlike our patients and who had hepatic manifestations only[8]. Remarkably, almost all the cases reported previously in literature had hyperpigmentations on lower limbs unlike our case who has generalised hyperpigmentation all over body along with xerosis, cellulitis and bullous lesions over right hand which are very rare in Wilson's disease.

It has been speculated that the cause of these melanindeposits is increased activity of the enzyme tyrosinase as body copper is high. Copper is essential for the activity of this enzyme.[9]

Conclusion

Diagnosis may be delayed because of wide spectrum of symptoms in patients with WD. Dermatological manifestations, though uncommon, may be the presenting feature of WD. The need to highlight the importance of hyperpigmentation as a pointer to the diagnosis of Wilson's disease prompted us to report this case.

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