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ATYPICAL CEREBRAL IMAGING FINDINGS IN WILSON'S DISEASE

Radiodiagnosis

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ABSTRACT

Wilson's disease is a rare hereditary disorder of copper metabolism which affects multiple organs, the central nervous system being a predominant participant. The disorder usually presents with neuropsychiatric manifestations and metabolic disturbances. Typically, the corpus striatum is particularly vulnerable, with involvement of caudate nuclei, putamina, thalami, along with brainstem involvement. Atypical imaging findings in such inherited metabolic disorders may cause hindrance in reaching the correct diagnosis, as multiple metabolic disorders show overlapping imaging findings. Hence, correlation between radiological and biochemical parameters is of paramount importance. The authors report a case of two biologically related brothers who presented with neurological and metabolic disturbances and atypical cerebral imaging findings of Wilson's disease.

KEYWORDS

Wilson's disease, atypical imaging findings, cortical grey, subcortical white matter.

INTRODUCTION

Wilson's disease is a rare hereditary disorder of copper metabolism. It is characterised by abnormal accumulation of copper in both the liver and brain, causing cirrhosis and neuronal degeneration. Copper is also accumulated in cornea and kidneys.

The pattern of inheritance is autosomal recessive in nature. In most populations the frequency of this disease is about 1 in 30,000–40,000, with a carrier rate of 1 in 90 [1]. The primary genetic defect is caused by mutations in the ATP7B gene located on the long arm of chromosome 13. The accumulated copper is deposited primarily in the Golgi bodies and mitochondria, resulting in oxidative damage. This causes symptoms related to neurological, hepatobiliary and musculoskeletal systems.

In Wilson's disease, copper excretion through biliary route is impaired. Hence, excessive copper resides in the plasma and urine and serum ceruloplasmin shows a low value. Clinical presentations include neuropsychiatric and metabolic disturbances along with acute haemolytic crisis and cardiac arrythmias.

In the brain, the caudate nuclei, putamina, ventrolateral thalami and the brainstem show predominant involvement [2]. Two brothers with Wilson's disease were treated and we discuss their clinical, metabolic and neuroimaging findings.

CASE HISTORY

A 14-year-old boy presented with complaints of excessive salivation for the past 5 years. It progressed to slurring of speech with decreased communication and interest in surroundings. 4 years later, his younger brother presented with abnormal posturing of hands with difficulty in writing. There was persistent flexion of both upper limbs with fisted hands. The younger brother also had gait abnormalities with drooling from mouth and abnormal movements like lip smacking and neck twisting. Both brothers, in their respective disease course, showed anger outbursts and inappropriate laughter.

On examination, the older brother had dysarthria and an expressionless face. Ophthalmological examination revealed bilateral Kayser-Fleischer (KF) ring present with a normal fundus. His MMSE score was 30/30. The younger brother had persistent posture of adduction of bilateral arms and flexion at elbow , with fisting of bilateral hands. His lower limbs remained extended. He, too, had bilateral Kayser-Fleischer ring, with a normal fundus.

Their biochemical and sonological parameters were as follows-

TABLE 1

	PATIENT 1 (VALUES ON ADMISSION)	PATIENT 2 (VALUES ON ADMISSION)
SERUM BILIRUBIN	0.9 mg%	1.15 mg%
SERUM CERULOPLASMIN	1.5 micromole/l	4.23 micromole/l
FREE SERUM COPPER	22.4 microgram/dl	20.2 microgram/dl
KF RING	positive	positive
COPPER IN URINE(24 h)	42 microgram	36.1 microgram
ABDOMINAL ULTRASOUND	Liver – 14 cm Spleen – 12.5 cm	Liver – 14.5 cm Spleen – 13.6 cm

Both the brothers were referred to the radiology department where they underwent magnetic resonance imaging. The T1-weighted images of the **older brother (hereby referred to as PATIENT 1)** showed altered signal on **bilateral basal ganglia** regions with **mild caudate atrophy**. T2/FLAIR images showed **bilateral symmetrical increased signal in ventral nuclear mass of thalamus and in the outer ring of putamen and brainstem**. No abnormal enhancement was noted on contrast study.

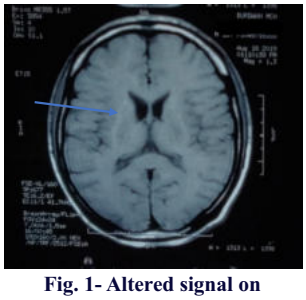

Fig. 1- Altered signal on bilateral basal ganglia regions and thalamus on T1-w; PATIENT 1.

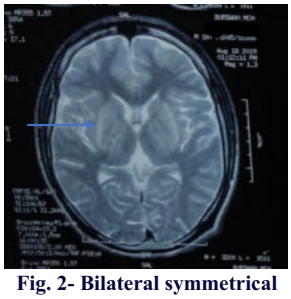

Fig. 2- Bilateral symmetrical increased signal in ventral nuclear mass of thalamus and in the outer ring of putamen on T2-w image; PATIENT 1

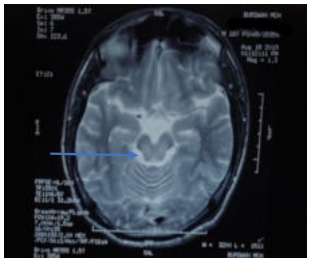

Fig. 3- Brainstem involvement on T2-w image; PATIENT 1

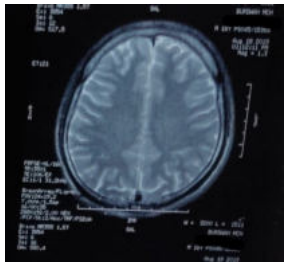

Fig. 4- No cortical grey matter involvement; PATIENT 1

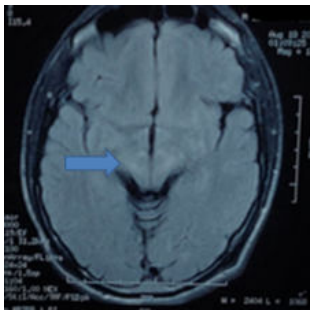

Fig. 5- FLAIR HYPERINTENSITY IN BRAINSTEM; PATIENT 1.

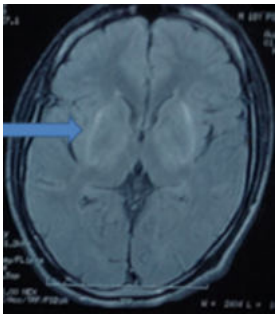

Fig. 6- FLAIR HYPERINTENSITY IN PUTAMINA; PATIENT 1.

The MRI evaluation of the **younger brother (hereby referred to as PATIENT 2)** revealed altered signal intensity changes on basal ganglia and thalamus, on T1-w images, similar to the findings of PATIENT 1. **T2/FLAIR images showed increased signal on bilateral fronto-parietal regions, left temporal and left occipital regions with involvement of both cortical grey and subcortical white matter at centrum semiovale and periventricular levels.** No abnormal enhancement was noted on contrast study.

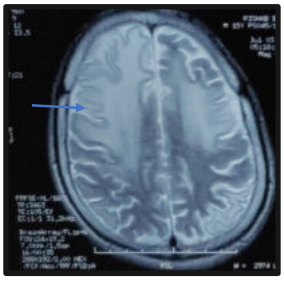

FIG. 7- T2 HYPERINTENSITY SHOWING FRONTO-PARIETAL CORTICAL GREY AND SUBCORTICAL WHITE MATTER INVOLVEMENT; PATIENT 2

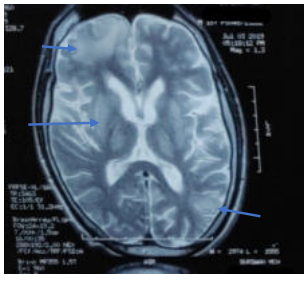

FIG. 8- BASAL GANGLIA AND THALAMUS T2 HYPERINTENSITY; RIGHT FRONTAL AND LEFT OCCIPITAL REGION INVOLVED

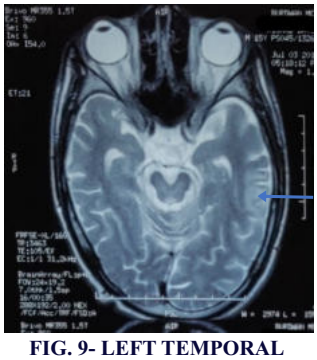

FIG. 9- LEFT TEMPORAL INVOLVEMENT

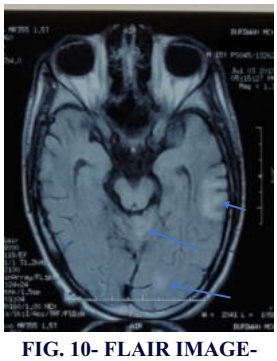

FIG. 10- FLAIR IMAGE- Hyperintensity on left cerebellar hemisphere and vermis, left temporal region.

FIG. 11 – KF RING OF PATIENT 1.

FIG. 12- KF RING OF PATIENT 2.

DISCUSSION

Diagnosis of Wilson's disease is mainly based on clinical and biochemical data, supplemented by radiological evaluation. There has not been much discussion in previous literature regarding the presence of white matter abnormalities in Wilson's disease. Grey-white matter abnormalities, in MRI, manifest as hypointensities on T1-weighted images and hyperintensities on T2/FLAIR images.

The largest percentage of patients showing white matter signal intensity changes was reported by van Wassenaer-van Hall *et al*. in 1995 (41%) [3]. They postulated that the white matter abnormalities mainly involved three tracts: Dentatorubral, thalamopontocerebellar, and corticospinal. In contrast to grey matter lesions which were mostly symmetrical, white matter lesions in patients with Wilsons's disease are usually asymmetrical. [4] Our case report is in agreement with the nature of the findings mentioned above.

In a study performed in 2006 by Grover et al, they concluded that the hyperintense appearance is possibly the result of edema, gliosis, necrosis and cystic degeneration [5]. A study performed by Shetty et al reported extensive cortical cystic lesions due to cortical cystic necrosis in Wilson's disease [6].

In our report, PATIENT 2 showed asymmetrical cortical-subcortical abnormalities or altered signal intensity in bilateral fronto-parietal, left temporal and left occipital regions. History of seizures clinically was also present with respect to the second patient. This type of rare MR spectrum has been explained by previous investigators as possibly occurring due to demyelination, softening, spongy degeneration and cavitation [7].

Differential diagnosis of such white matter abnormalities, in this age group, includes acute disseminated encephalomyelitis, HIV encephalopathy and post-hypoxic encephalopathy [8]. All the conditions were confidently excluded on the basis of history, clinical and biochemical parameters.

No significant correlation has been noted between neuroimaging findings and clinical prognosis and post-therapeutic response of the patient till date; Through the report, it is emphasised that patients of Wilson's disease should not only be evaluated for basal ganglia and brainstem lesions, but also for **extensive grey matter pathology and white matter defects.** It is imperative that neuro-physicians and radiologists be more observant about the **clinical relevance of such findings** and attempt to draw an inference regarding the management of the same. Follow-ups and further studies may be undertaken to establish clinical importance.

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