Rolandic Epilepsy as a Heraldic Manifestation of Wilson Disease in a 6-Year-Old Girl

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Objective: Wilson disease (WD) manifesting as seizure is rare. Rolandic epilepsy as presenting feature of WD has been reported only once before. **Methods:** A 6-year-old girl of nonconsanguineous parentage presented with focal seizures. There was associated fatty hepatomegaly and elevated aminotransferases. **Results:** Brain magnetic resonance imaging (MRI) was unremarkable. Electroencephalogram demonstrated bilateral centrottemporal spike classical of Rolandic epilepsy. Serum ceruloplasmin was low and 24-h urinary copper levels were elevated. Genetic mutational analysis showed she carried the rare homozygous p.Asn1270Ser genetic mutation. Administration of D-penicillamine gradually halted seizure activity together with near normalization of serum aminotransferases. **Conclusions:** Rolandic epilepsy associated with elevated liver enzymes should undergo evaluation for WD. Chelators have a salutary effect on seizure activity, as well as elevated serum aminotransferases. (J CLIN EXP HEPATOL 2020;10:633–635)

Seizures are rare in Wilson disease (WD), and in large series, it was described in up to 7.5%.¹ However, rolandic epilepsy as a presenting feature of WD is even rarer and has been reported only once.² Presence of abnormal liver tests, in any seizure setting should arouse a suspicion of WD regardless of age and consanguinity. We describe a case of rolandic epilepsy in a 6-year-old girl whose final diagnosis of WD was confirmed by a rare genetic mutation. Written informed consent was obtained from the girl's parents and was approved by institution review board.

A 5-and-half-year-old girl of nonconsanguineous parentage presented in 2015 with high fever and vomiting of 1 day duration. Physical examination was unremarkable. Laboratory evaluation was significant for elevated aspartate aminotransferase (AST) to be 374 U/L and alanine aminotransferase (ALT) to be 464 U/L and normal bilirubin. All acute viral markers for hepatitis A, B, E, and antibodies for autoimmune hepatitis were negative. Raised transaminases were ascribed to a probable viral illness.

A year later at 6-and-half years of age she developed vomiting followed by up rolling of eyes, twitching movements of right hand and face followed by stiffness which lasted 1–2 min. Consciousness was preserved throughout

the seizure episode. Examination was unremarkable except for hepatomegaly. Liver tests were significant for elevated AST 131 U/L and ALT 312 U/L. Magnetic resonance imaging (MRI) brain was unremarkable for patients' age, and ultrasonography of abdomen revealed an enlarged fatty liver. An electroencephalogram showed right and left centroparietal and temporal high amplitude bifid spikes highly suggestive of Rolandic epilepsy (see Figure 1). She was started on oxcarbazepine 450 mg in divided doses which was switched to clobazam 5 mg at night. Work-up for liver disease included negative serological tests for hepatitis A, B, E, and autoimmune hepatitis. Work-up for WD yielded a negative result for Kayser Fleischer ring. Serum ceruloplasmin was very low (0.03 g/L), and 24 h urine copper was 112 µg/24 h. A liver biopsy was recommended which was declined by the parents. A diagnosis of WD was made (3 points on the original Leipzig score³ suggestive of possible WD and 5 points on modified Leipzig score⁴) and oral zinc was initiated. However, rolandic epilepsy episodes continued to occur once every few weeks while her aminotransferases continued to remain abnormal (see Table 1). Mutation test for WD by exon sequencing demonstrated ac.3809A > G; p.Asn1270Ser (p.N1270S) homozygous pathogenic mutation at ATP7B gene. The child was initiated with zinc sulfate which she continued to take for 3 years. Clobazam was continued. Despite regular intake of antiepileptic drug and zinc she continued to develop rolandic epilepsy once every 2–3 months. Coincidentally her liver test remained abnormal (Table 1). Zinc was stopped and D-penicillamine was initiated at 250 mg orally once a day and dose gradually titrated to 250 mg thrice a day. Over a period of 8 months, the rolandic epilepsy episodes ceased and transaminases gradually declined (Table 1). She continues to remain free from further epilepsy.

Keywords: transaminase, centrottemporal spikes, focal seizure, copper

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Abbreviations: AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; EEG: Electroencephalography; GGT: Gamma glutamyl transferase; WD: Wilson disease

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Figure 1 Electroencephalography demonstrating bilateral centroparietal and temporal high amplitude bifid spikes highly suggestive of rolandic epilepsy.

Table 1 Serial Liver Biochemistry Tests.

DATE	Total Protein (gm/dl)	Serum Albumin (gm/dl)	Total Bilirubin (IU/L)	Direct Bilirubin (IU/L)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	GGT (IU/L)
08.2016	6.4	3.9	0.2	0.1	131	312	175	52
09.2016	8.1	4.4	0.3	0.1	178	532	258	82
05.2017	7.6	4	0.2	0.05	55	125	375	72
08.2017	7.3	3.8	0.34	0.1	99	225	337	62
01.2018	7.3	3.5	0.38	0.05	55	115	407	44
07.2018	7.7	3.8	0.24	0.08	92	222	408	70
06.2019	7.4	4.2	0.5	0.2	71	147	387	39
11.2019	6.6	4.3	0.25	0.12	47	108	298	52

AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; GGT, gamma glutamyl transferase.

DISCUSSION

Seizures are seen in 7.7% of patients with WD. (1) Rolandic epilepsy has only been described once in WD literature. But as a presenting feature of WD this is very rare. Our case with WD had several unique features: (1) Young age of presentation of WD. (2) Rolandic epilepsy as a heralding manifestation of WD. (3) Persisting transaminase elevation as an early sign of WD. (4) p.N1270S mutation which was first detected in Europeans and less commonly described in Indians. (5). Persistence of elevated transaminases and rolandic epilepsy despite antiepileptic drug and zinc which was controlled

only after initiation and continuation of D-penicillamine indicating the importance of chelators in halting and reversing the course of WD including seizure manifestation.

CONFLICTS OF INTEREST

The author has none to declare.

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