Case Report

An unusual case of steroid unresponsive Hashimoto's encephalitis in Indian under-5

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ABSTRACT

Hashimoto's encephalopathy (HE) is a rare entity in children. Usually, it responds very well to steroids. We report a case of steroid-unresponsive HE in a 4-year-old male child presenting with acute encephalitis syndrome with raised intracranial pressure. Serum anti-thyroid peroxidase antibody was high. He was refractory to intravenous immune globulin and steroids. He underwent plasma exchange therapy which had a dramatic response with marked clinical improvement.

Key words: Child, Hashimoto's encephalopathy, Plasma exchange, Steroid

Hashimoto's encephalopathy (HE) is a rare demyelinating autoimmune meningoencephalitis occurring in 2.1/100,000 population and even rarest in children [1]. HE is mostly associated with euthyroid conditions. Most patients (90–98%) respond to steroids with clinical and electroencephalogram (EEG) normalization; hence, a favorable prognosis [2]. Delay in diagnosis and refractory to steroid therapy results in adverse sequel.

CASE REPORT

A 4-year-old male child presented in a tertiary pediatric center with complaints of sudden onset of fever with vomiting and altered level of consciousness for 24 h. There was no history of head trauma, loose stools, rash, bleeding spots, or unknown substance intake. The child was developmentally normal with no previous history of seizures.

At the time of presentation, the child was stuporous, with the glasgow coma scale of 8/15 (E_2 V_1 M_4), an axillary temperature of 101.6°F, heart rate of 92/min, respiratory rate of 24/min, and blood pressure of 118/72 mm of Hg (>95th percentile for age and height). There were generalized hypertonicity, exaggerated deep tendon reflexes, and bilateral extensor plantar reflex. Pupils were bilaterally equal and reacting to light. There was lateral rectus palsy in the right eye. There was no other obvious cranial nerve involvement, nor any signs of meningeal irritation. Other systemic examinations were unremarkable and no obvious neck gland enlargement was seen. Arterial blood gas parameters and blood glucose were within normal limits. He was provisionally diagnosed with acute encephalitis syndrome along with raised intracranial pressure.

The patient was shifted to the pediatric intensive care unit and started on a combination of intravenous (IV) fluids, a cocktail of antibiotics (ceftriaxone, vancomycin), anti-viral (acyclovir) and anti-malarial agents (artesunate), injection mannitol, and other supportive treatment. Vitals were monitored strictly. However, soon he started having generalized tonic-clonic seizures controlled with phenytoin sodium. Along with this, there was occasional decerebrate posturing associated with bruxism (Fig. 1). Repeated convulsions occurred, necessitating the use of injection phenobarbitone followed by an injection of levetiracetam.

Blood counts, liver function test, renal function test, and electrolytes were all normal (Table 1). The malaria parasite was absent and the dual antigen test was negative; hence, anti-malarial agent was withdrawn. The cerebrospinal fluid (CSF) study showed no cells, with normal sugar, but the protein level was 120 mg/dL (increased). Blood and CSF were negative for antibodies against Dengue, Japanese B encephalitis, and herpes simplex virus; hence, acyclovir was discontinued. Magnetic resonance imaging (MRI) of the brain was done which showed small areas of hyperintensities involving bilateral centrum semiovale, corpus callosum, and periventricular regions which were showing restricted signals. Considering the possibility of acute disseminated encephalomyelitis, IV immune globulin (IVIG) was given @2 g/kg. However, there was no improvement and dystonic movements of eyes and limbs continued.

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Anti-nuclear antibody was negative. Anti-N-methyl-D-aspartate antibody was normal, but the anti-thyroid peroxidase (anti-TPO) antibody in serum was markedly increased (181.90 U/mL [$n \leq 60$ U/mL]). Serum thyroid stimulating hormone and free T4 were in the normal range, and so also the antinuclear antibodies profile. EEG showed generalized slowing. This gave a diagnosis of HE. There was no family history of auto-immune disease. Ultrasound of thyroid gland was normal. Anti-thyroglobulin antibody level was 204.30 U/mL (N≤60 U/mL).

The patient was then given IV methylprednisolone @30 mg/kg/day for 5 days, followed by oral prednisolone, but there was no significant improvement. Hence, he was considered to be steroid-resistant HE. The patient was then subjected to five cycles of single-volume plasma exchange therapy (Fig. 1). The child started showing significant improvement from the second plasma exchange cycle, with improved sensorium and gradual reversal of neurological symptoms and signs. During discharge after 40 days of hospital stay, his cognitive function and orientation to time, place, and person were normal, with near-normal power in all four limbs, the speech was restored to a remarkable extent, the vision was 6/6, the visual evoked potential and brainstem evoked response audiometry were normal and repeat MRI was suggestive of sequelae of encephalitis, showing generalized widening of cerebral sulci and Sylvian fissure (cerebral atrophy) with mild hyperintensities in periventricular area.

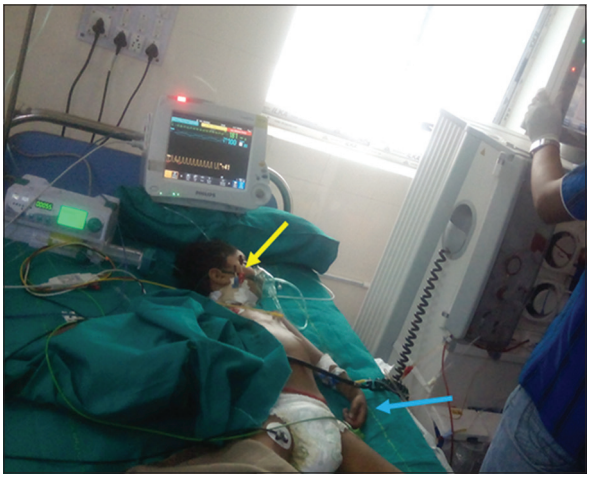

Figure 1: Hashimoto's encephalopathy child undergoing first plasma exchange therapy. Double lumen dialysis catheter at right internal jugular vein (yellow arrow); hypertonic limbs (blue arrow)

On follow-up at 1 month, he was neurologically normal with no sequelae. Repeat MRI at 3 months showed mild cerebral atrophy only. The oral steroid was gradually tapered off over a period of 3 months. At 1-year follow-up, the child was neurologically well, started non-formal education in school, power 5/5 in all four limbs, jerks and tone in all four limbs being normal. Repeat thyroid function was again normal and anti-TPO was improved to 43 U/mL without any thyroxin supplements.

DISCUSSION

HE is a rare condition with a wide range of clinical presentations. It is a subacute disease process that responds to immunosuppression and not to thyroxine replacement. Some other names for this disease are steroid-responsive encephalopathy associated with autoimmune thyroiditis, non-vasculitic autoimmune meningoencephalitis, and encephalopathy associated with autoimmune thyroid disease [3]. The first case of HE was described by Brain *et al*. in 1966. The patient was a 48-year-old man with hypothyroidism, multiple episodes of encephalopathy, stroke-like symptoms, and Hashimoto's thyroiditis confirmed by elevated anti-thyroid antibodies [4].

Being a rare disease even in adults, the incidence and prevalence in children are not well known [1,5,6]. To the best of our knowledge, this is the first case report of refractory HE in an Indian child of under 5 years of age receiving plasma exchange to date. The incidence is probably underestimated because of the low overall awareness of the disease and the lack of investigation facilities [7,8]. Thus, there is a high risk that patients with this serious disease will remain undiagnosed and thus untreated. Two

Table 1: Laboratory parameters of the patient

Routine blood counts	LFT	RFT	Electrolytes	Sugar	infection screen	CSF	Immune markers	Thyroid profile
Hemoglobin:11.28 g%	Total Bilirubin: 0.9	BUN: 15 mg/dL	Na: 138 meq/L	RBS: 109 mg/dL	Malarial antigen: neg	Cell: 0	ANA: neg	TSH: 2.5
Total leucocyte count: 8900/ Cmm	Direct bil: 0.2	Creatinine: 0.6 mg/dL	K: 4.6		Malarail slides: neg	Protein: 120, Sugar: 56	Anti-NMDA:neg	FT4: 8.3
Differential count: N67 L32 E1	SGOT: 32		Ca^{++}: 0.9		CRP: 4 mg/L	Antibodies for dengue, JE and HSV: neg	Anti-TPO: 181.90 U/mL (N≤610 U/mL)	Anti-TG antibody: 204.30 U/mL (N <60 U/mL)
Platelet: 1.8 L/cmm	SGPT: 44				ESR: 32 mm 1^{st} h			
Smear: normocytic normochromic, no toxic granules	ALP: 12KA							

LFT: Liver function test, RFT: Renal function test, BUN: Blood urea creatinine, RBS: Random blood sugar, CSF: Cerebrospinal fluid, ANA: Antinuclear antibodies, TSH: Thyroid stimulating hormone, Anti-NMDA: Anti-N-methyl-D-aspartate, SGOT: Serum glutamic-oxaloacetic transaminase, CRP: C-reactive protein, Anti-TPO: Anti-thyroid peroxidase, SGPT: Serum glutamic-pyruvic transaminase, ALP: Alkaline phosphatase, ESR: Erythrocyte sedimentation rate

possible mechanisms were suggested in the development of HE. The first suggests that it might be the result of edema and reduction in the vasculature due to autoimmune-mediated central nervous system vasculitis together with impairment of the microvascular structure [9,10]. The second proposes the formation of anti-neural antibodies and cross-reaction due to a common antigen of both the thyroid gland and the brain [1].

The accepted diagnostic criteria include a variable spectrum of clinical features, presence of thyroid antibodies (TPO or microsomal), euthyroid or mild hypothyroid state, exclusion of infective, neoplastic, structural, or vascular etiology, and responsiveness to steroid therapy [11,12]. Although the majority of described cases showed neurological symptoms for months before the acute onset, in some cases, a dramatic acute onset appeared [3]. Our patient had an acute onset. CSF is abnormal in approximately 80% of patients, usually revealing an elevated CSF protein level. EEG abnormalities seen in HE vary from epileptiform abnormalities, and generalized slowing to normal findings. MRI brain usually shows non-specific findings, such as bilateral subcortical high signal lesions on T2-weighted images or mild cerebral atrophy with a temporal predominance [13]. Many authors have reported focal lesions simulating cerebral tumors, granuloma, infection, ischemic stroke, or even a degenerative process. Others have reported diffuse white matter involvement resembling leukodystrophy, which normalizes following treatment [14]. The MRI features are usually reversible with the treatment [15]. Our patient had elevated anti-TPO, anti-TG antibodies, with abnormal CSF, EEG, and reversible MRI findings. The high effectiveness of corticosteroid treatment in most patients strongly suggests a common autoimmune origin [10]. Although the current accepted diagnostic criteria include corticosteroid responsiveness, in rare steroid non-responders other immunomodulatory therapies such as IVIG or plasmapheresis could be applied [16,17]. Plasma exchange or plasmapheresis should be used whenever the patient is unresponsive or poorly responsive to corticosteroid treatment [5,18-20]. Our patient was unresponsive to steroids and IVIG but responded very well to plasma exchange with favorable medium-term neurological outcomes.

CONCLUSION

Considering its reversible course, HE should always be in the differential diagnosis in any patient presenting with acute or subacute unexplained encephalopathy and seizures. Diagnosis of HE requires a high index of suspicion. In rare situations of steroid non-responsiveness, plasma exchange may provide a favorable outcome.

REFERENCES

1. Ferracci F, Bertiato G, Moretto G. Hashimoto's encephalopathy: Epidemiologic data and pathogenetic considerations. J Neurol Sci 2004;217:165-8.
2. Mattozzi S, Sabater L, Escudero D, Ariño H, Armangue T, Simabukuro M, *et al*. Hashimoto encephalopathy in the 21st century. Neurology 2020;94:e217-24.
3. Payer J, Petrovic T, Lisy L, Langer P. Hashimoto encephalopathy: A rare intricate syndrome. Int J Endocrinol Metab 2012;10:506-14.
4. Brain L, Jellinek EH, Ball K. Hashimoto's disease and encephalopathy. Lancet 1966;2:512-4.
5. Yu HJ, Lee J, Seo DW, Lee M. Clinical manifestations and treatment response of steroid in pediatric Hashimoto encephalopathy. J Child Neurol 2014;29:938-42.
6. Farrell RM, Foster MB, Omoruyi AO, Kingery SE, Wintergerst KA. Hashimoto's encephalopathy: A rare pediatric brain disease. J Pediatr Endocrinol Metab 2015;28:721-4.
7. Erol I, Saygi S, Alehan F. Hashimoto's encephalopathy in children and adolescents. Pediatr Neurol 2011;45:420-2.
8. Barseem NF, Helwa MA. Hashimoto's encephalopathy presenting with acute confusional state in a patient with hypothyroidism. Egypt Pediatr Assoc Gaz 2015;63:69-73.
9. Mocellin R, Walterfang M, Velakoulis D. Hashimoto's encephalopathy: Epidemiology, pathogenesis and management. CNS Drugs 2007;21:799-811.
10. Schiess N, Pardo CA. Hashimoto's encephalopathy. Ann N Y Acad Sci 2008;1142:254-65.
11. Kothbauer-Margreiter I, Sturzenegger M, Komor J, Baumgartner R, Hess CW. Encephalopathy associated with hashimoto thyroiditis: Diagnosis and treatment. J Neurol 1996;243:585-93.
12. Chaudhuri A, Behan PO. The clinical spectrum, diagnosis, pathogenesis and treatment of Hashimoto's encephalopathy (recurrent acute disseminated encephalomyelitis). Curr Med Chem 2003;10:1945-53.
13. Chen HC, Marsharani U. Hashimoto's encephalopathy. South Med J 2000;93:504-6.
14. Song YM, Seo DW, Chang GY. MR findings in Hashimoto encephalopathy. AJNR Am J Neuroradiol 2004;25:807-8.
15. Bohnen NI, Parnell KJ, Harper CM. Reversible MRI findings in a patient with Hashimoto's encephalopathy. Neurology 1997;49:246-7.
16. Mijajlovic M, Mirkovic M, Dackovic J, Zidverc-Trajkovic J, Sternic N. Clinical manifestations, diagnostic criteria and therapy of Hashimoto's encephalopathy: Report of two cases. J Neurol Sci 2010;288:194-6.
17. Jacob S, Rajabally YA. Hashimoto's encephalopathy: Steroid resistance and response to intravenous immunoglobulins. J Neurol Neurosurg Psychiatry 2005;76:455-6.
18. Nagpal T. Hashimoto's encephalopathy: Response to plasma exchange. Neurol India 2004;52:245-7.
19. Hussain NS, Rumbaugh J, Kerr D, Nath A, Hillis AE. Effects of prednisone and plasma exchange on cognitive impairment in Hashimoto encephalopathy. Neurology 2005;64:165-6.
20. Boers PM, Colebatch JG. Hashimoto's encephalopathy responding to plasmapheresis. J Neurol Neurosurg Psychiatry 2001;70:132.

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