Case Report

DOI: 10.7860/JCDR/2025/79511.22124

Parkinsonism as a Rare Manifestation of Hashimoto Encephalopathy Associated with Autoimmune Polyendocrine Syndrome: A Case Report

Internal Medicine Section

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ABSTRACT

Hashimoto's encephalopathy is a rare manifestation of a common autoimmune disease, characterised classically by its association with autoimmune thyroid disease and responsiveness to steroids. Usual clinical manifestations include a relapsing-remitting course of seizures, stroke-like episodes, cognitive decline, neuropsychiatric symptoms and myoclonus. Diagnosis requires raised Thyroid Peroxidase (TPO) antibody titre and exclusion of other encephalopathies, including neuronal surface and paraneoplastic antibodies. Here, we delve into a case of Hashimoto's encephalopathy for: 1) its rare linkage to an Autoimmune Polyendocrine Syndrome (APS); and 2) an uncommon manifestation in the form of Parkinsonism. We report a case of a 45-year-old male with previously diagnosed hypothyroidism, vitiligo and likely adrenal tuberculosis. The current presentation included a fluctuating sensorium with gradually declining mobility and all classical features of Parkinsonism. Investigations revealed hyponatraemia owing to decreased morning serum cortisol levels, normal thyroid profile, and a normal Cerebrospinal Fluid (CSF) analysis. The Electroencephalogram (EEG) showed generalised slowing. The autoimmune and paraneoplastic encephalitis panel was negative. A raised anti-TPO antibody level clinched the diagnosis of Hashimoto encephalopathy associated with APS (Autoimmune thyroid disease, vitiligo and autoimmune adrenalitis). He showed remarkable improvement with steroids, thyroxine and levodopa-carbidopa. On follow-up, the patient showed marked improvement in bradykinesia, tremors and rigidity. This rare case underscores the importance of suspicion of rare manifestations in relatively common and potentially reversible disorders.

Keywords: Altered sensorium, Anti-thyroid peroxidase, Hyponatraemia, Polyendocrine

CASE REPORT

We report a case of a 45-year-old male farmer who presented to the medical emergency unit with chief complaints of fluctuating consciousness, tightness of limbs with decreased mobility, and tremors for two years.

The patient was apparently asymptomatic two years back when he started having recurrent episodes of acute to sub-acute onset of fluctuating sensorium, with tightness of limbs and body leading to decreased mobility. The patient also had bilateral resting tremors with a pill-rolling character, which improved with attempts at voluntary movements. There was no history of seizures or altered behaviour during periods of normalcy, and no history suggestive of any cranial nerve involvement. There was no history of any positive or negative sensory symptoms. No h/o bowel or bladder incontinence or retention, abnormal sweating, postural giddiness or abnormal awareness of heartbeat. Moreover, the patient had no history of headache, projectile vomiting, fever, or photophobia. There was no history of any head trauma, joint pain, oral ulcers, photosensitivity or hair loss.

The patient was a known case of vitiligo since he was 10 years old, and hypothyroidism, for which he was under treatment. The patient had also been diagnosed with cervical tuberculous lymphadenitis and had completed anti-tubercular therapy for 6 months. There was, however, no history of diabetes or hypertension.

During previous hospital admissions with fluctuating sensorium, the patient was found to have hyponatraemia. On a thorough investigation of the cause, he was found to have decreased serum cortisol levels with elevated Adrenocorticotropic Hormone (ACTH) levels. Thyroid profile previously showed a decreased free T3 and T4, and an elevated Thyroid Stimulating Hormone (TSH) level [Table/Fig-1]. Considering the high incidence of tuberculosis in the region and the presence of a tuberculous focus in the cervical lymph nodes, the possibility of adrenal tuberculosis had been considered. Whole body Fluorodeoxyglucose-Positron Emission Tomography (FDG-PET) done previously had shown metabolically active areas in the cervical lymph node region and bilateral bulky adrenals.

Previous investigations:	
Serum soldium	120-124 mEq/L
Serum potassium	3.5-4.5
Urinary sodium	>20 mEq
Plasma cortisol levels	1.20 mcg/dL
Plasma ACTH levels	1288
Serum TSH levels	12.2 mIU/mL
Serum T3	0.24 ng/mL
Serum T4	3.85 ng/mL

[Table/Fig-1]: Initial thyroid and adrenal function tests.
ACTH: Adrenocorticotrophic hormone; TSH: Thyroid stimulating hormone; T3: Triiodothyronine; T4: Tetraiodothyronine

The patient, despite having completed anti-tubercular therapy, currently presented with a similar history of fluctuating sensorium. On examination, the patient was vitally stable, with normal blood sugars. On general examination, the patient had patchy vitiligo, mask-like facies, with a positive glabellar tap, hypomimia, and a hypophonic monotonous voice [Table/Fig-2].

Cranium and spine examination were normal. Central nervous system examination revealed altered behaviour, with a normal cranial nerve examination. Motor system examination showed hypertonia, with lead pipe and cog wheel rigidity. Froment's sign was found to be positive. However, the patient had normal power in all limbs. Patient had a shuffling, short-stepped, festinant gait with stooped

[Table/Fig-2]: Clinical photograph of the patient showing mask-like facies, patchy vitiligo.

shoulders and decreased arm swing. He had difficulty taking turns. He was also found to have pill rolling tremors, symmetrical, reduced with voluntary movements. The rest of the systemic examination was found to be normal.

Features of Parkinsonism in a middle-aged male prompted a differential diagnosis of secondary Parkinsonism, like osmotic demyelination syndrome or metabolic encephalopathy. Myxoedema coma was also considered, keeping in mind the history of hypothyroidism. With the co-existence of vitiligo, hypothyroidism and primary adrenal insufficiency, an autoimmune aetiology could explain all of the above. Hence, a differential diagnosis of autoimmune encephalitis was also sought after.

Diagnostic analyses revealed mild hyponatraemia, decreased cortisol levels, but a normal thyroid profile [Table/Fig-3].

Remaining investigations, including renal function, liver function, serum electrolytes [Table/Fig-4,5], Electrocardiogram (ECG) [Table/Fig-6] and chest X-ray were normal.

Parameter	Values
Serum T3	13.4 mcg/dL
Serum T4	9.3 mcg/dL
Serum TSH	2.69 mcg/dL
HbA1c	5.6%

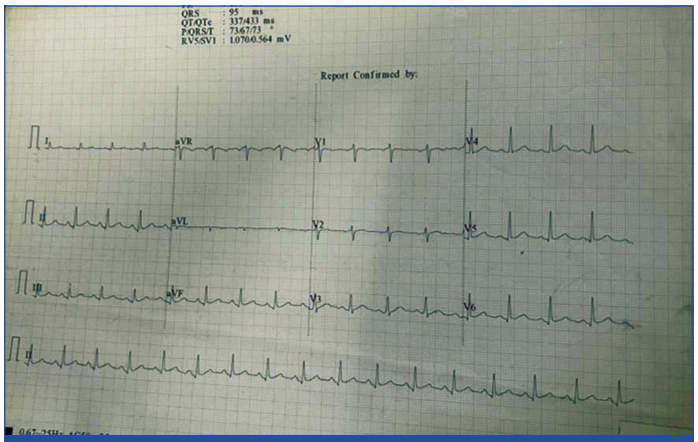
[Table/Fig-3]: Follow-up thyroid function tests and Glycosylated Haemoglobin (HbA1c) at current presentation.

Parameters	Day 1	Day 4	Day 7	Day 10
Haemoglobin (g/dL)	11.6	11.5	11.5	11.8
WBC (mm3)	5.2	6.3	6.4	5.8
Platelet (mm3)	228	278	302	300
Sodium (mEq/L)	121.7	130.2	138.2	137.4
Potassium (mEq/L)	3.93	3.98	4.02	3.94
Creatinine (mg/dL)	1.14	0.98	1.03	1.01
Urea (mg/dL)	23.8	20.2	21.2	20.9

[Table/Fig-4]: Serial haematological and metabolic parameters during hospital admission.
WBC: White blood Cell count

Parameter	Values
Calcium	9.20 mEq/L
Phosphate	3.20 mEq/L
Aspartate transaminase	28.2 IU/L
Alanine transaminase	30.2 IU/L
Alkaline phosphatase	36.5 IU/L
Total bilirubin	0.36 mg/dL
Direct bilirubin	0.08 mg/dL
Total proteins	5.97 g/dL
Albumin	3.50 g/dL
Globulin	2.47 g/dL
Lactate dehydrogenase	187 IU/L

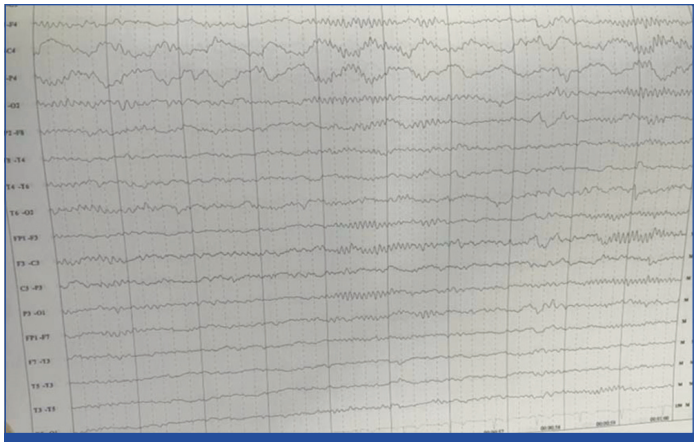
[Table/Fig-5]: Additional serum biochemical parameters.



[Table/Fig-6]: Electrocardiogram (ECG) tracing.

The EEG revealed a generalised slowing of theta waves [Table/Fig-7]. CSF analyses were found to be normal [Table/Fig-8]. Magnetic Resonance Imaging (MRI) brain showed medial temporal lobe atrophy with mild hippocampal T2 hyperintensity. An autoimmune encephalitis panel on CSF and serum was sent and found negative. After excluding the above differentials, anti-Thyroid Peroxidase (TPO) antibodies and anti-thyroglobulin antibodies were found to be positive. Hence, a diagnosis of APS (Vitiligo, autoimmune adrenalitis causing primary adrenal insufficiency, and autoimmune thyroiditis) with Hashimoto's encephalopathy presenting as secondary Parkinsonism was considered.

After initial attempts at gradually correcting the sodium levels, mild improvement in sensorium was observed. The patient was started on intravenous corticosteroids and symptomatic management for Parkinsonism, including Levodopa-Carbidopa (100+25 mcg) TDS and Trihexiphenidyl 2 mg TDS. Thyroxine 50 mcg/day was continued as before. The patient showed improvement in symptoms within a week. Steroids were then tapered and Fludrocortisone 100 mcg/day was added to the treatment. The patient was gradually weaned off of nasogastric feeding and intravenous fluids and discharged after four weeks of hospital stay on anti-Parkinsonian drugs, tapering doses of steroids, Fludrocortisone and thyroxine.



[Table/Fig-7]: Electroencephalogram (EEG) findings.

Parameter	Values
Appearance	Clear, colourless
Cobweb	Absent
Deposits	Absent
Proteins	30.90 g/dL
Glucose	52 mg/dL
Red blood cells	Absent
Total leukocyte count	2/high power field
Polymorphs	Absent
Lymphocytes	100%
Mesothelial/Macrophages	Absent

[Table/Fig-8]: Cerebrospinal Fluid (CSF) analysis results.

On follow-up after four weeks, the patient had significant improvement in rigidity, with improved ambulation. Gradually, the steroids and fludrocortisone were withdrawn. The patient did not need additional immunosuppression and was asymptomatic at the subsequent follow-ups.

DISCUSSION

Hashimoto's encephalopathy, with a presumed autoimmune origin characterised by high titres of anti-TPO antibodies, is classically characterised by its steroid responsiveness [1]. Although, like most autoimmune diseases, it is more common in women, we have described a middle-aged male with the disease. The clinical presentation may involve a relapsing and remitting course and include seizures, stroke-like episodes, cognitive decline, neuropsychiatric symptoms and myoclonus. Diagnosis must be considered in cases of 'investigation negative encephalopathies' by excluding other toxic, metabolic, infectious, autoimmune and paraneoplastic causes of encephalopathy with neuroimaging and CSF examination [2]. In our case, we found the patient had a normal thyroid profile, metabolic parameters and CSF picture, including the autoimmune encephalitis panel. Hence, after excluding all other encephalopathies, a diagnosis of Hashimoto's encephalopathy was considered.

However, there are varied presentations of Hashimoto's encephalopathy, but Parkinsonism is a rarely reported manifestation of the same. Isolated cases of Hashimoto's encephalopathy presenting with acute neuropsychiatric disturbances, rapidly progressive dementia, seizures, and extrapyramidal failure have been reported previously [3]. The rarity of Hashimoto's encephalopathy in this case is further exemplified in the extremely rare manifestation of Parkinsonism in the disease.

Another special feature of this case report is the linkage of Hashimoto's encephalopathy to an APS. Considering the high incidence of Tuberculosis (TB) in India (199 per lac population in 2022 as per the recent India TB report) [4], the patient was initially suspected to have adrenal TB. However, lack of response to antitubercular drugs, bulky adrenals on PET scan, and associated autoimmune phenomena like thyroiditis and vitiligo guided us towards an autoimmune adrenalitis and hence an APS.

An isolated case wherein an APS (type 3B) affecting the gastroduodenum in addition to the thyroid gland has been reported in association with Hashimoto encephalopathy, causing delirious mania [5]. Another case of a 29-year-old male with APS 3 with vitiligo, pernicious anaemia and autoimmune thyroid disease with severe neurological symptoms and sub-acute encephalopathy has been reported. However, the severity of neurological symptoms in the case was contributed to by both Hashimoto's encephalopathy and vitamin B12 deficiency secondary to pernicious anaemia [6].

A case of APS associated with autoimmune encephalitis has been reported wherein NMDA-receptor encephalitis, known to cause seizures, memory impairment and altered mental status, was postulated to be caused by autoimmune antithyroid antibodies reacting with neurons, causing widespread central nervous system inflammation [7]. Another case reported a 39-year-old patient with APS type 3 (APS-3) complicated by anti-NMDA-R encephalitis developing schizophreniform symptoms and seizures following a viral-like illness [8]. However, our case showed a negative autoimmune encephalitis panel, including NMDA-R antibodies. Hence, an association of APS with Hashimoto encephalopathy is unique.

Neuroimaging findings studied in the disease show increased T2 hyperintensities in the medial temporal lobe, similar to that seen in our case [9]. Normal neuroimaging findings can also be seen. Elevated CSF protein levels are frequently reported in patients with Hashimoto encephalopathy, but a normal CSF picture does not exclude the diagnosis, as seen in our case [9].

In a meta-analysis of 251 patients, the first-line treatment was steroids in 193 patients and other immunosuppressive drugs in 10 cases [10]. Corticosteroids are the cornerstone of treatment with the occasional need for alternative therapies such as azathioprine, methotrexate, or cyclophosphamide, Intravenous immunoglobulins or plasmapheresis in steroid-refractory cases [9]. In the case described above, however, corticosteroids were found to be sufficient.

CONCLUSION(S)

This case highlights the rare presentation of Hashimoto's encephalopathy with Parkinsonism in the context of APS. Despite its rarity, Hashimoto's encephalopathy should be considered in patients presenting with unexplained encephalopathy or extrapyramidal symptoms, especially when accompanied by autoimmune markers such as anti-thyroid peroxidase antibodies. Early recognition and prompt initiation of corticosteroid therapy can lead to significant neurological recovery and prevent permanent neurological disability. Additionally, this case emphasises the need to consider autoimmune aetiologies in patients with multisystem involvement and underscores the clinical utility of maintaining a high index of suspicion for reversible causes of secondary Parkinsonism. Hence, in this case of Hashimoto Encephalopathy, a rare manifestation of Parkinsonism as well as a rare association with APS makes it a diagnostic goldmine for physicians, making it a challenge as much as a dilemma.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: May 05, 2025
- Manual Googling: Aug 21, 2025
- iThenticate Software: Aug 23, 2025 (9%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Apr 01, 2025**
Date of Peer Review: **Jul 26, 2025**
Date of Acceptance: **Aug 26, 2025**
Date of Publishing: **Dec 01, 2025**