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SHORT COMMUNICATION

An insight into anti-thyroid peroxidase (TPO) positive cognitive impairment: Analysis of four unusual cases and plea for pragmatism

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Abstract Cognitive impairment and varied psychiatric manifestations are common in thyroid disorders. But autoimmune thyroid disorders masquerading as dementia or psychotic disorders without other overt systemic features of dysthyroidism are rare. Here we are presenting a detailed analysis of four heterogeneous cases of thyroid related cognitive impairments mimicking and fulfilling criteria of known psychiatric diagnosis for a brief period of time, requiring multiple psychotropic medications without any significant improvement. Cognitive impairment and behavioral abnormalities with a known psychiatric diagnosis, with unknown temporal profiling of anti-thyroid peroxidase (TPO) positivity, without encephalopathy and subsequent complete or partial responsiveness with levothyroxin, point towards a possible new entity not well explored so far.

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Introduction

Cognitive impairments and behavioral abnormalities are well known symptoms in both hypothyroidism and hyperthyroidism.[1,2] While some researchers hypothesized that altered milieu of thyroid hormones and thyroid stimulating hormone (TSH) are the reasons for these manifestations, other school of thought implicated autoimmunity as the central pathogenic trigger.[3] Thyroid hormone supplementation not only recovers neuropsychiatric symptoms among overt or subclinical hypothyroidism, but also when used in supraphysiological dose, it ameliorates long-standing refractory mood disorders[4] On the other hand, the role of thyroid autoantibodies, other non-thyroidal neuronal antibodies and cytokines, in the pathogenesis of neuropsychiatric symptoms gained huge attention in the past decade after recognizing patients with autoimmune thyroiditis (AIT) in euthyroid state that scored less than those with non-autoimmune thyroid disorders in certain domains of cognitive evaluation. Hashimoto's Encephalopathy (HE), one of the most dramatic neurological manifestations of underlying autoimmune thyroid disorder is known for its exquisite steroid responsiveness, thus recognized as Steroid-Responsive Encephalopathy associated with Autoimmune Thyroiditis (SREAT).[3] While neuropsychiatric features such as psychosis, mood disorders, cognitive deterioration, and sleep disorders are common in HE or SREAT,[3,5] isolated cognitive impairments masquerading as psychiatric problems (ranging from depression or bipolar affective disorder to psychosis, schizophrenia and schizophreniform illness) with anti-thyroid peroxidase (TPO) positivity have been sparsely reported so far.[6–12] Here we are presenting four heterogeneous cases of thyroid related cognitive impairments mimicking and fulfilling criteria of known psychiatric diagnosis for a brief period of time, requiring multiple psychotropic medications without any significant improvement.

In the past 2 years, in our cognitive clinic, we encountered 12 cases of cognitive impairment (with or without other neurological features) with anti-TPO positivity. Out of them, 8 cases were classical HE. In this series we are reporting 4 cases which did not meet the diagnosis of HE. These were heterogeneous cases of thyroid related cognitive impairments mimicking and fulfilling criteria of known psychiatric diagnosis for a brief period of time, requiring multiple psychotropic medications without any significant improvement. These peculiar four cases have been thoroughly investigated to identify any secondary causes. The cognitive status has been evaluated by the following tools: Neuropsychiatric Inventory (NPI), Frontal Assessment Bat-

Table 1 Brief case description and outcome.

Case	Age (years)/sex	Duration of illness	Neuropsychiatric diagnosis	Thyroid status	Anti-TPO level (IU/mL)	Outcome and present status
1	52/F	1 year	BPAD (d/d-bv-FTD)	Initially euthyroid, then thyrotoxic due to subacute thyroiditis, finally became hypothyroid	800	Good. Patient is only on levothyroxine, without any psychotropic medications.
2	28/F	1 month	BPAD (d/d-frontal dysexecutive syndrome)	Initially subclinical hyperthyroidism due to subacute thyroidits, then returned to euthyroid status	660	Good. Not on any medication at present.
3	45/F	6 months	Fv-AD (d/d-NAMCI)	Initially euthyroid, later became subclinical hypothyroid	1100	Marginal improvement. Patient is on levothyroxine and psychotropics
4	22/M	6 months	BPAD (in depression)	Initially euthyroid, later became hypothyroid	653	Marginal improvement. Patient is on levothyroxine and psychotropics

Key: TPO: thyroid peroxidase; d/d: differential diagnosis; BPAD: bipolar affective disorder; bv-FTD: behavioral variant of frontotemporal dementia; Fv-AD: frontal variant of Alzheimer's disease; NAMCI: non-amnestic mild cognitive impairment.

tery (FAB), Montreal Cognitive Assessment (MoCA test), Addenbrooke's cognitive test, and Kolkata Cognitive Screening Battery (KCB) whenever appropriate.

In Table 1 are summarised the main clinical features of the four patients.

Case reports

Case 1

A fifty two year old housewife graduate woman was referred to the cognitive clinic with a diagnosis of bipolar affective disorder (BPAD), diagnosed by two psychiatrists for exclusion of any underlying neurological disorder. He was on quetiapine 50 mg, divalproate sodium 500 mg, clonazepam 0.5 mg once daily (OD) for last 8 months, but without improvement of her psychiatric ailments. The caregiver (husband) complained of progressive behavioral abnormalities for the last 1 year along with intermittent anger outbursts, disinhibited behavior in form of making nonsense jokes frequently, using abusive words and unnecessary prolonged gossiping with unknown persons. Then she developed the habit of buying things of little use in her activities of daily living randomly. She also became talkative with flight of ideas and tangentiality, had decreased sleep, and lost of empathy to family members, but she did not have shameless bladder incontinence. Detailed history was also suggestive of interim loss of interest in all activities, fatigability, and desire to stay alone without any verbal communication with family members. These periods were brief and staying for 5–6 days intermittently. The caregiver also complained that for last 3 months that she engaged herself in doing things repeatedly without any relevance, some repetitive movements involving bilateral upper limbs and throat clearing. Family members noticed difficulty in execution of complex household activities like cooking, and problem solving obviously day by day. There was no history suggestive of any language deficit, paraphasias, calculation difficulties, apraxia, agnosia or forgetfulness. There were no episodes of delusions or hallucinations. The patient had no psychiatric or neurological morbidity before this episode. There was no family history of similar kind of illness.

From clinical record we learned that she showed behavioral disinhibition, apathy, stereotyped motor behavior, and executive dysfunction. So, apart from changes in food habits or history of hyperorality, all the other features closely resembled a behavioral variant of frontotemporal dementia (bv-FTD). The patient scored 12/18 on Frontal Assessment Battery (FAB), highly suggestive of frontal lobe dysfunction. All other systemic examinations were within normal limits. Importantly, the patient did not have any history of birth complications, developmental delay, fever, altered sensorium, seizures, abnormal movements, headache, focal neurological deficits, gait abnormality or use of any substance abuse. There was no history of neuropsychiatric or thyroid disorders in her family.

Disinhibited behavior, impulsivity and stereotyped movements suggested dysfunction in the orbitofrontal cortex (OFC). Interim short periods of apathy, which were considered as episodes of depression by psychiatrist, might be due to involvement of the anterior cingulate cortex (ACC) of the frontal lobe. Executive dysfunction might be due to involvement of the dorsolateral prefrontal cortex (DLFPC). Loss of concern to family members i.e., loss of empathy, points also to frontal lobe dysfunction. Abnormal vocalization (throat clearing, probably vocal tics) was due to either frontal lobe dysfunction or involvement of its subcortical network. Relative sparing of calculation, language, praxis, gnosis and memory indicate lack of involvement of parietal, temporal and occipital lobes and their connections.

Further investigations were undertaken to rule out focal frontal pathology (space occupying lesions, vascular malformations), HIV associated frontal dysfunction, immune mediated encephalopathy, neurosyphilis, deficiency of vitamin B complex and bv-FTD. Brain Magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) analysis, and repeated electroencephalogram (EEG) disclosed no relevant abnormalities. All relevant blood investigations (complete hemogram, metabolic profile, anti-nuclear antibody profile, anti-neutrophil cytoplasmic antibodies, antibodies against neuronal cell surface antigens, antibodies against intracellular onconeural or synaptic antigens, viral serology including HIV) were of no help except a high titer of anti-TPO positivity (800 IU/mL; normal: <35), in spite of euthyroid status [free tri-iodothyronine (FT_3)-3.8 pmol/L, free tetra-iodothyronine (FT_4)-10 μIU/mL, TSH-3 μIU/mL; n, FT_3-3–7, FT4-9–23, TSH-0.4–5.5). The same treatment was continued as before, but there was no significant improvement. The patient was followed-up regularly every 6 weeks without any significant appearance of new symptoms.

Eight months later (since her first visit to us) the patient presented with complaints of shortness of breath, and physical examination revealed she had tachycardia, raised jugular venous pressure, and bibasal crepitus. 2-D Echocardiography showed high output state with ejection fraction (EF) of 72% (normal range: 55–75%). TSH came out to be undetectable (<0.001 μIU/mL), with raised FT_4 (55 μIU/mL) and FT_3 (14 pmol/L), anti-TPO 756 IU/mL. Radio immune assay of thyroid gland was suggestive of thyroiditis. The case was diagnosed as Hasimoto thyroiditis (HT), currently in thyrotoxic state. Patient was stabilized with medications for heart failure and thyrotoxicosis (torasemide 10 mg once daily, and carvedilol 3.125 mg twice daily). The patient subsequently improved from the hemodynamic standpoint (repeated echocardiography after 1 month showed EF of 55%) without any significant improvement of cognitive function. Patient was again regularly followed-up at an interval of 3 weeks and her TSH levels sequentially rose to 10 μIU/mL, while FT_3, FT_4 remained within normal range, and anti-TPO level was 750 IU/mL. She was put on levothyroxin 50 μgr daily for 1 month, then 75 μgr. After 4 months her cognitive deficit started to improve (anti-TPO: 653 IU/mL) and after 6 months (anti-TPO: 658 IU/mL), with no need of further psychotropic medications. Currently she is on levothyroxin 75 μgr/day and doing fine.

Case 2

A 28-year-old female teacher presented with subacute onset-progressive mood changes such as frequent irritability, emotional outbursts, and occasional crying spell with intervening period of elated mood, inappropriate laughter

and unnecessary talkativeness for the last month. She also had history of decreased concentration on single concerns and frequently switched to different topics within very short periods of time. In the same time period she had developed forgetfulness of recent events (partially retrieved with cues) evident by frequent misplacement of objects and denial of any conversation. She often forgot to add important ingredients during making food, and also took more time to complete cooking associated with difficulty in maintaining its sequential steps. For the last week she also lost her concern about her only 3-year-old son. She had no history of any language problem or difficulty in word finding, naming, face recognition, calculation, manipulation of real objects, navigation or visuo-spatial orientation. She had no problems regarding sleep and appetite. She did not have any premorbid neuropsychitric or behavioral abnormalities. The family history was also unremarkable. Her Mini Mental Status Examination (MMSE) score was 27/30, with 2 marks in recall and 1 mark in three-step command. The MMSE score did not suggest either dementia or minimal cognitive impairment (MCI). Systemic examination was within normal limits.

Mood fluctuations can be the manifestation of either BPAD or frontal lobe dysfunction. Symptoms of elated mood can be localized in OFC and depressive spells can be localized over ACC. However, she did not have other symptoms of apathy which usually occur due to lesion in ACC. The attention deficit and execution problem can be related to frontal lobe involvement and its subcortical network. Recent memory impairment can be related with medial frontal lobe, Papez circuit, or subcortical frontal network dysfunction. To sum up, this patient had frontal sub cortical network involvement (with/without frontal lobe involvement) with medial temporal lobe involvement or connections of Papez circuit, with relative sparing of parietal lobe, occipital lobe and their connections.

In a young female presenting with subacute onset of psychiatric manifestations, the possibility of autoimmune encephalopathy was suspected first. However, the autoantibody panel, brain MRI, CSF analysis, and EEG failed to yield abnormalities. All other blood investigations were unremarkable, except a TSH level of 0.023 μIU/mL, with normal FT_3 (4.8 pmol/L) and FT_4 (16 μIU/mL) levels; anti-TPO antibodies were positive at 660 IU/mL level. As there was no encephalopathy and no other physical signs and symptoms of thyrotoxicosis, specific drugs were not prescribed, except propranolol 10 mg BD, keeping subacute thyroiditis as possible diagnosis. Quetiapine 50 mg OD was started and the patient was kept in close follow-up. Cognitive symptoms started to improve within 2 weeks, and within 3 months quetiapine, and propranolol were discontinued. The TSH level became normal (1.5 μIU/mL) within 4 months. After 8 months of follow up the patient was still positive for anti-TPO (550 IU/mL) with complete euthyroid status and normalization of cognitive symptoms.

Case 3

A 45-year-old housewife graduated woman presented with chief complaints of poor concentration in daily living activities, difficulty in maintaining conversation, and frequent distractions during conversation for 6 months. Her caregiver (husband) also complained that she started to forget things of recent days or hours; this was also associated with frequent misplacement of objects. Detailed history revealed she had difficulties in keeping pace with regular household activities, making decisions, planning, and maintaining sequence of complex activities. The aforementioned problems were of subacute onset and slowly progressive in nature. Detailed history however failed to reveal any difficulty in naming, visuo-spatial orientation, calculation, language functions, object or facial recognition, dressing, manipulation of real objects, reading, understanding (though a bit taking more time than usual) and writing. There was no history of hallucinations and delusions of any kind. However, she suffered from significant chronic low mood (also evident during conversation), as stated by the caregiver. She had no personal or family history suggestive of prior neurological or psychiatric comorbidities. MMSE score was 22/30. Detailed cognitive evaluation [FAB, Montreal Cognitive Assessment (MoCA test) and Addenbrooke's cognitive examination] revealed gross frontal dysfunction in attention, executive function, and abstraction tasks. Motor function and language were preserved. Temporal lobe dysfunction was detected by deficiencies in the word list recall test. The Clock drawing test showed a marked planning abnormality. The rest of the nervous system and other organs were absolutely normal.

Poor concentration and lost of track during conversation indicated problems of attention, particularly selective, and divided attention governed by frontal and its subcortical connections. In more detail, it could stem from problems in phonological loop, visuo-spatial sketch pad or central executive circuit, which are the three dominant pillars of attention. Problems in recent memory were ascribed to medial temporal lobe (dominant left or bilateral) or Papez circuit dysfunction. Difficulty in organizing, planning, sequencing, and executing complex activities may result from DLFPC involvement. Mood changes (depression) can be localize on sub frontal cortical network or ACC. So, to sum up, our patient had history suggestive of involvement of frontal and subcortical frontal connections, medial temporal lobe and Papez circuit, with relative sparing of bilateral parietal lobe as evidenced by intact visuospatial orientation, dressing, and no neglect (right parietal), intact calculation, language and praxis (left parietal), and sparing of bilateral occipito-temporal and occipito-parietal cortex. As more than two cognitive domains were involved, a diagnosis of dementia was done, with predominant anterior cortical and subcortical involvement. As clinical history started with clinical features of subacute onset and suggestive of frontotemporal involvement, we kept the possibility of reversible dementia (such as immune mediated, vitamin B_{12} deficiency dementia, small vessel dementia, hypothyroid dementia, infection or inflammation, granuloma or space occupying lesion). Among irreversible dementia causes, a frontal variant of Alzheimer's disease was suspected.

Brain MRI, CSF analysis, and EEG were normal. All blood investigations (including autoimmunity, viral serologic tests, and metabolic panel) were negative. The anti-TPO were positive (1100 IU/mL) in a background of euthyroid status (FT_3-4.2 pmol/L, FT_4-12 μIU/mL, TSH-1.5 μIU/mL). The patient was followed-up regularly in the outpatient clinics. At that point, aripiprazole 5 mg, sertraline 50 mg, clon-

azepam 0.5 mg once daily were prescribed, and partial improvement was observed within 2 months. After 6 months she became subclinically hypothyroid (TSH 10.8 μIU/mL, FT_3-3.8 pmol/L, FT_4-11.2 μIU/mL) with an anti-TPO level of 864 IU/mL. Levothyroxine 62.5 mg was started for 2 weeks, then we increased the dose to 75 mg daily. Very little improvement of symptoms were noted, without any further deterioration. Currently the patient is on sertraline 50 mg and levothroxine 75 mg OD. The TSH and anti-TPO levels are 2 μIU/mL and 455 IU/mL respectively.

Case 4

22-year-old male student presented with complaints of irritability and fatigability for the last 6 months. He was already diagnosed with bipolar disorder by a psychiatrist and put on divalproate sodium 500 mg twice daily, quetiapine 50 mg daily, olanzapine 5 mg daily, sertraline 100 mg daily, and clonazepam 0.5 mg twice daily, without satisfactory improvement. As narrated by his father, the patient, who had had so far a good academic performance, developed a progressive deterioration of his academic performance. His father stated that his son developed lack of concentration in daily living activities and in academic activities as well. In the recent days he became more ritualistic and involved in bizarre activities most of the day time. He started moving on to different topics after unusual delay in single topic without making the first one complete. He had difficulty in verbal reciprocation with family members and peers. He also took unusual time to solve sums, and to write texts (without any grammatical error or naming problems). He developed forgetfulness of recent events and misplacement of objects, difficulty in learning recent lessons, without difficulty in remembering things of remote past. He was not able to do his bank tasks in a proper way, and faced significant distress in opening a new account. There was no history of any language problems (e.g. comprehension, fluency (though unusual delay to start response), naming, repetition, paraphasias) visuospatial deficit, apraxia, agnosia, or behavioral disinhibition. He had a normal sleep with slightly decreased appetite. He had no history of prior neuropsychiatric illness. There was no history of psychiatric or neurological problems in his family, except autoimmune hypothyroidism in his mother (case 3). The MMSE score was 21/30, with predominant problem in registration and recall, and mild difficulties with calculation. However, considering hid educational background, it was significant. Detailed cognitive assessment by means of the Addenbrooke's cognitive test revealed poor performance in word recall test. The Clock drawing test was normal. In the FAB-test he scored 13 points. The examination of organs other than the CNS revealed no abnormalities.

Attention deficit and execution problems in this patient suggested frontal lobe dysfunction. Difficulty in calculation tasks suggested left parietal (angular gyrus). Impaired complex attention and decreased speed on information processing pointed to frontal lobe circuitry dysfunction. Recent change in personality towards ritualistic behavior suggests problems in the cortico-striato-thalmo-cortical (CSTC) loop. Forgetfulness of recent events, with sparing of remote memories, are suggestive of involvement of left dominant (or bilateral) medial temporal lobe or Papez circuit. To sum up, the neuropsychological analysis concluded that the patient had involvement of the frontal lobe and its subcortical connections, with possible involvement of Papez circuit and dominant medial temporal lobe involvement.

Given that more than two cognitive domains and daily living activities (DLA) were impaired, a diagnosis of dementia was made. Again, considering the age and pattern of cognitive involvement, a reversible dementia was considered as our first diagnosis. Among reversible dementias, we took into account infections, inflammation, space occupying lesion, vascular malformations, vasculitis, immune and endocrine disorders. All the relevant tests (including MRI brain, EEG, CSF, autoimmune profile, metabolic study) were normal except high anti-TPO (653 IU/mL), with background euthyroid status (FT_3-4.1 pmol/L, FT_4-11 μIU/mL, TSH-4.2 μIU/mL). The same treatment, as previously advised by the psychiatrist, continued at that time. Patient was closely followed-up thereafter and, after 6 months, we found high plasmatic TSH (12 μIU/mL) levels with decreased FT_3 (2.5 pmol/L), FT_4 (9 μIU/mL) and anti-TPO (345 IU/mL) levels. He was put on levothyroxine 100 μgr/day, and closely followed up. However, after 8 month period under treatment, he only showed marginal improvement regarding cognitive function; the anti-TPO level was 434 IU/mL, with normal FT_3, FT_4 and TSH levels.

Discussion

Although the above reported four cases were heterogeneous in terms of their clinical presentation and therapeutic outcome, they were unique in their sharing characteristics of cognitive impairment, which at the same time met the criteria of degenerative dementia and a well known psychiatric condition. Each case was thoroughly evaluated clinically, biochemically and radiologically to search for other secondary co-existent morbidities which might explain those neuropsychiatric features. Brain MRI, CSF analysis, EEG, metabolic profile, and autoimmune panel were all essentially normal except the thyroid panel.

Thyroid related cognitive impairments are usually subcortical in nature affecting attention and executive function, and there is delayed information processing speed.[12,13] However, in these four cases, presentation was with behavioral abnormalities. Diagnosis of SREAT was not ascribed to those cases, as the EEG failed to demonstrate any diffuse slowing typical of encephalopathy, and neither the CSF analysis nor imaging studies were supportive of it. Cognitive impairments as isolated symptoms of SREAT seemed unlikely because in all cases there was no encephalopathy at presentation or at follow-up as well. In consequence, a trial for steroid responsiveness did not seem necessary in our patients. Interestingly, the cases shared striking similarities of anti-TPO positivity, and overt hypo or hyperthyroidism developed later on subsequent follow-up with variable gap. Patients were responsive to thyrotropic medications, and 3 out of 4 cases showed improvement, which obviated the need for psychotropic medications.

The decision to administer immunosuppressive therapy in the presence of organ-specific autoantibodies should take into account other organic alterations, such as EEG and

MRI findings, or blood–brain barrier dysfunction. The CSF abnormalities suggestive of blood–brain barrier dysfunction in over 80% of HE patients,[14] were absent in all of our patients. Speculations about the pathogenesis of cognitive impairment in thyroid disorders include autoimmune cerebral vasculitis, neurotoxic effects of TSH or autoantibodies. Although spontaneous resolution of HE has been reported previously,[15] our study of these 4 cases unmasked that behavioral presentations and cognitive impairment were due probably to immune alterations. The responsiveness to L-thyroxine is a remarkable finding that support the use of L-thyroxin to treat immune-mediated cognitive impairments. Evidence showed that thyroid hormone supplementation not only resolved neuropsychiatric symptoms in overt or subclinical hypothyroidism, but also, when used in supraphysiological dose, it ameliorated long-standing refractory mood disorders.[4] Temporal relationship between anti-TPO positivity, cognitive impairments, and later overt hypothyroidism with response to L thyroxin needs further explanatory studies.

Conclusion

Cognitive impairments mimicking behavioral abnormalities with a known psychiatric diagnosis, the unknown temporal profile of anti TPO positivity without encephalopathy, and subsequent responsiveness with L-thyroxin during overt hypothyroid states, point towards a new entity not well explored in literature so far. We propose the term ''immune mediated cognitive impairments sine encephalopathy with L-thyroxin responsiveness'' for such clinical situations. Moreover, we recommend routine screening for autoimmune thyroid disorders among patients attending psychiatric or cognitive clinic, even if their thyroid function test suggests euthyroid state.

Ethical considerations

Written informed consent was taken from all the four patients regarding academic usage (teaching, presentation and publication) of their case histories while maintaining unanimity.

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Conflict of interest

The authors have no conflict of interest.

References

1. Gan EH, Pearce SH. Clinical review: the thyroid in mind: cognitive function and low thyrotropin in older people. J Clin Endocrinol Metab. 2012;97(10):3438–49.
2. Rieben C, Segna D, da Costa BR, Collet TH, Chaker L, Aubert CE, et al. Subclinical thyroid dysfunction and the risk of cognitive decline: a meta-analysis of prospective cohort studies. J Clin Endocrinol Metab. 2016;101:4945–54.
3. Montagna G, Imperiali M, Agazzi P, D'Aurizio F, Tozzoli R, Feldt-Rasmussen U, et al. Hashimoto's encephalopathy: a rare proteiform disorder. Autoimmun Rev. 2016;15:466–76.
4. Bauer M, Goetz T, Glenn T, Whtbrow PC. The thyroid-brain interaction in thyroid disorders and mood disorders. J Neuroendocrinol. 2008;20:1101–14.
5. Laurent C, Capron J, Quillerou B, Thomas G, Alamowitch S, Fain O, et al. Steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT): characteristics, treatment and outcome in 251 cases from the literature. Autoimmun Rev. 2016;15:1129–33.
6. Segers K, Braconnier P, Corazza F, Divano L, Mabrouk A, Robberecht J, et al. Subacute cognitive deterioration with high serum anti-thyroid peroxidase antibodies: two cases and a plea for pragmatism. Psychogeriatrics. 2013;13:175–9.
7. Endres D, Perlov E, Stich O, van Elst T. Steroid responsive encephalopathy associated with autoimmune thyroiditis (SREAT) presenting as major depression. BMC Psychiatry. 2016;16:184.
8. Endres D, Perlov E, Riering AN, Maier V, Stich O, Dersch R, et al. Steroid-responsive chronic schizophreniform syndrome in the context of mildly increased antithyroid peroxidase antibodies. Front Psychiatry. 2017;8:64.
9. Endres D, Vry MS, Dykierek P, Riering AN, Lüngen E, Stich O, et al. Plasmapheresis responsive rapid onset dementia with predominantly frontal dysfunction in the context of Hashimoto's encephalopathy. Front Psychiatry. 2017;8:212.
10. Haider AS, Alam M, Adetutu E, Thakur R, Gottlich C, DeBacker DL, et al. Autoimmune schizophrenia? Psychiatric manifestations of Hashimoto's encephalitis. Cureus. 2016;8:e672.
11. Guirgis H, Amar C. A case of Hashimoto's encephalopathy presenting with acute psychosis. J Neuropsychiatry Clin Neurosci. 2014;26:E1–2.
12. Samuels MH. Psychiatric and cognitive manifestations of hypothyroidism. Curr Opin Endocrinol Diabetes Obes. 2014;21:377–83.
13. Grigorova M, Sherwin BB. Thyroid hormones and cognitive functioning in healthy, euthyroid women: a correlational study. Horm Behav. 2012;61:617–22.
14. Leyhe T, Müssig K. Cognitive and affective dysfunctions in autoimmune thyroiditis. Brain Behav Immun. 2014;41:261–6.
15. Querol Pascual MR, Aguirre Sánchez JJ, Velicia Mata MR, Jimenez CG, Duran-Herrera F, Dorrego G. Hashimoto's encephalitis; a new case with spontaneous remission. Neurologia. 2000;15:313–6.