CASE REPORT

Polyglandular autoimmune syndrome disguised as mental illness

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SUMMARY

Our case acts to highlight the numerous presentations of polyglandular autoimmune syndromes. A 62-year-old Taiwanese woman with a history of schizophrenia presented to our emergency department with a brain tumour causing her headaches. She was admitted due to severe anaemia, and after further investigation, the patient was discovered to have pernicious anaemia and autoimmune thyroiditis—consistent with the diagnosis of polyglandular autoimmune syndrome IIIb. Her underlying primary psychiatric diagnosis was then questioned. The diagnosis of her endocrinopathies were likely delayed for many years due to the psychiatric disorder which may have been due to her long-standing autoimmune hypothyroidism and/or vitamin B_{12} deficiency. Initial treatment brought about major behavioural improvement, and encourages physicians to investigate secondary causes of psychosis and other coexisting autoimmune diseases when a patient presents with one endocrinopathy.

BACKGROUND

Patients with psychiatric conditions can be thought of as a burden. When there is a possibility of an underlying diagnosis, which may unlock the door to freeing the patient of this burden it is of utmost importance to try and discover it. In our patient, she was initially only admitted because she thought she had a brain tumour. And it was only due to an initial random workup by the emergency room physician that she was admitted at all and then further worked up.

CASE PRESENTATION

A 62-year-old Taiwanese woman presented to UCI Medical Center's emergency department (ED) with dizziness and right temporal headaches for 3 weeks. The patient said she wanted to get an MRI of her head to rule out a brain tumour and was unable to make an appointment with an oncologist so she came to the ED. She refused to answer questions until an MRI of her brain was performed but allowed us to speak to her son. The patient's son said she has always had a strange personality, which resulted in her being divorced from her husband and distanced from her friends and family. Additionally, she reported hearing from spirits and has severe mistrust of Western medicine because 'thyroid medication caused me to have psoriasis and it killed my mother.' Her son stated she had been eating a strict vegetarian diet since she immigrated from Taiwan 30 years ago. He also denied any family history of endocrine disorders or thyroid disease, saying there is only a family history of hypertension and diabetes and no mental illness.

INVESTIGATIONS

After physical examination the patient appeared pale and fatigued, but was alert and oriented to person, place and time. The patient had very disorganised thoughts, poor insight, delayed and circumferential thinking. She also endorsed auditory hallucinations. The patient had dry skin, dry mucous membranes, decreased skin turgor, brittle hair and cold intolerance. Additionally, she was noted to have psoriasis on both feet and a wound on her left foot, which was wrapped in Vaseline covered towels and which patient refused to let anyone see. She did not have gait abnormalities or loss of vibration or positional sense. She had 1+ biceps and patellar reflexes but no extrapyramidal symptoms.

Complete blood counts revealed the patient to be extremely anaemic on admission with a wide RDW. Initial laboratory results showed a haemoglobin (Hgb) and haematocrit (Hct) 7.2 g/dl and 21.9 g/dl, respectively, with a mean corpuscular volume (MCV) 76.4. Iron studies showed iron 21 (normal range 37–170 μg/dl), TIBC 395 (normal range 250–450 μg/dl) and ferritin 20 (normal range 20–107 ng/ml). Guiac test was negative for occult blood and reticulocyte count was 1.5%. The initial results presented a mixed picture of iron deficiency anaemia and anaemia of chronic disease. To further clarify the patient's anaemia, a soluble transferrin receptor was measured at 18.1 (normal range 1.9–4.4 mg/l), which definitively showed that the patient had a severe iron deficiency anaemia. Because of the patient's eating habits, vitamin B_{12} and folate levels were measured and determined to be 76 (normal range 180–1241 pg/ml) and 41.3 (>5.9 ng/ml). A methylmalonic acid level was measured for further confirmation and was found to be elevated at 5.21. Homocysteine levels were found to be elevated at 32 (normal range 5–15 μMol/l). The diagnosis of pernicious anaemia was then confirmed with the detection of antiparietal cell and antiintrinsic factor antibodies in the patient's serum.

Since hypothyroidism can also be a cause of anaemia, we interrogated the patient's thyroid function. Thyroid stimulating hormone (TSH) was measured to be 51.6 (normal range 0.5–5.0 μIU/ml) with a free T4 of 0.4 (normal range 0.8–1.9 ng/dl); thus confirming the diagnosis of hypothyroidism. We then searched for antibodies against thyroid peroxidase (TPO) and TSH receptors; both of

which were positive at 502 IU/ml and 3.52 IU/l, respectively, consistent with Hashimoto's thyroiditis. Her cortisol was tested and found to increase from 10 to 32 μg/dl with cosyntropin stimulation, eliminating the possibility of underlying adrenal insufficiency. Based on the above results, the patient had a diagnosis of Hashimoto's thyroiditis and pernicious anaemia without adrenal disease, consistent with polyglandular autoimmune syndrome (PAS IIIb).

Additionally, the patient's serum electrolytes showed that she was hyponatremic with a sodium of 125 (normal range 135–145 mEq/l). On initial presentation she was found to be hypovolemic with a serum osmolality of 267 mOsm/kg (normal range 278–305 mOsm/kg), and urine sodium at borderline low of 33 mEq/l. Initially we considered that the hyponatremia caused the patient's apparent psychosis. However, the hyponatremia responded to intravenous normal saline and the patient continued to have paranoid ideations saying that the levothyroxine is causing her psoriasis.

TREATMENT

Despite these multiple endocrinology abnormalities and severe deficiencies, the patient refused all oral and intravenous medications. Psychiatry and the primary internal medicine team met with the patient and found her unable to respond knowingly and intelligently to questions about the recommended treatment, and unable to understand the nature and seriousness of the illness and comprehend the consequences of lack of treatment. The medical team concluded that the patient lacked capacity to make medical decisions and was harming herself by refusing treatments. Despite scoring 27 of 30 on her Mini Mental Status Examination (MMSE), the patient scored 22 of a possible total 30 points on the Montreal Cognitive Assessment demonstrating mild cognitive impairment possibly associated with her condition.

Once the patient was found incompetent to make medical decisions, the patient's son consented to transfusion of packed red blood cells. Her iron stores were replenished with intravenous iron and then oral ferrous gluconate. Her hypothyroidism was treated with levothyroxine 100 μg daily for the first 7 days and then switched to her calculated dose of 88 μg.

OUTCOME AND FOLLOW-UP

She did well on her in-house treatment, however she continued to refuse to manage her disease as an outpatient claiming that the vitamin B_{12} injections would result in developing cancer. The patient was transferred to behavioural health in stable medical condition for further treatment of her severe vitamin deficiencies and hypothyroidism.

Unfortunately this patient did not continue taking her medications. She eventually was discharged home from behavioural health after a short stay and when following up with her son 2 months after discharge he told us she had stopped taking her medications. Likely due to her longstanding distrust of physicians, it appears that unless the patient remains under supervised care she is not likely to be compliant. So we will never know how much of her psychiatric condition is treatable.

DISCUSSION

Our patient demonstrated characteristics of pernicious anaemia and Hashimoto's thyroiditis, consistent with PAS type IIIb. There are three different types of PAS. PAS I usually manifests in infancy or adolescence with a combination of mucocutaneous candidiasis, Addison's disease and hypoparathyroidism. PAS type II is characterised by Addison's disease along with autoimmune thyroid disease and type 1 diabetes mellitus (or other autoimmune process). PAS III involves autoimmune thyroid disease along with another organ-specific autoimmune disease not including adrenal disease. It is further subdivided into three groups: IIIa involves type 1 diabetes mellitus, IIIb with pernicious anaemia and IIIc with vitiligo or alopecia.[1] Patients who have a single autoimmune disorder are roughly 30–50 times more likely to develop another.[1] This is mainly due to genetic susceptibility leading to the loss of immunological self-tolerance to antigens from multiple tissues. While diagnosing one type of autoimmune disease, it is important to have a high index of suspicion and screening for antibodies associated with additional autoimmune disorders.

From our interview with the patient, it was easily noted that the patient showed signs of acute psychosis; however, the aetiology remained unknown. Vitamin B_{12} deficiency is a common cause of neurological, cognitive and psychotic symptoms. It has been reported that cobalamin deficiency may lead to the symptoms of auditory hallucinations, suspiciousness and disorganised mentation.[2 3 4] this patient presented with psychiatric symptoms similar to those noted with vitamin B_{12} deficiency, and with repletion of her vitamin B_{12} stores her acute psychosis improved to the point where we did not require physical intervention when giving her medication. However, she still required persistent coaxing by nursing staff to remain compliant.

In this patient, a score of 22 in the Montreal Cognitive Assessment (MoCA) demonstrated mild cognitive impairment. Compared with the MMSE, MoCA is much more sensitive in detecting cognitive impairment with its sensitivity being 90%.[5] Previously, the patient had been given a diagnosis of schizophrenia, but upon presentation the patient only had delusions that her headaches were caused by brain cancer. It is important to understand that PAS may play an additional role by affecting the mental health of some patients. It is possible that her true diagnosis of PAS may have been masked by the misdiagnosis of schizophrenia and further studies should be performed to detect a link between autoimmune syndromes and psychosis. Thus, psychiatrists routinely screen all new admissions of psychiatric patients for Vitamin B_{12} and folic acid deficiency regardless of age or previous state of health.[6]

Interestingly, this patient also had severe vitamin D deficiency, which may have resulted from her diet. The patient stated that she did not eat any type of animal or dairy product. Vitamin D is a fat soluble vitamin that plays an essential role in bone metabolism and has immune-modulating properties.[5 7] Vitamin D affects the differentiation and growth of various immune modulator cells, which may lead to the failure to maintain self-tolerance noted in the various forms of PAS.[8] This vitamin D deficiency may have exacerbated her disease state, and so she was also given high dose of vitamin D to correct her deficiency. A correlation between vitamin D deficiency and multiple sclerosis, an autoimmune disease involving antibodies directed against the myelin sheath in the CNS, has been shown in a clinical case report.[9] It is suspected that loss of immunological self-tolerance involved in multiple sclerosis may be related to the antibodies produced in PAS.

In conclusion, PAS can vary in its clinical presentation and involves a wide constellation of numerous autoimmune diseases. We reported a patient with PAS IIIb presenting with hallucinations, delusions and thought disorders, which improved gradually with vitamin B_{12} and thyroid hormone replacement. One must be aware that patients with autoimmune disorders are prone to psychiatric conditions.[10] An organic cause for a patient's psychiatric symptom must be exhaustively ruled out before attributing it to an underlying psychiatric disorder.

Learning points

- Polyglandular autoimmune syndrome can vary in its clinical presentation and involves a wide constellation of numerous autoimmune diseases.
- One must be aware that patients with autoimmune disorders are prone to psychiatric conditions.[10]
- An organic cause for a patient's psychiatric symptom must be exhaustively ruled out before attributing it to an underlying psychiatric disorder.

Competing interests None.

Patient consent Obtained.

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