Autoimmune thyroiditis presenting as acute onset pure chorea without encephalopathy

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Introduction

Chorea is a hyperkinetic movement disorder, characterized by involuntary movements or movement fragments, with unpredictable timing and duration with involvement of different anatomical locations[1]. Aetiological factors of chorea are varied, and hyperthyroidism is one common acquired cause of childhood-onset chorea[2,3]. However, autoimmune thyroiditis presenting with pure chorea without encephalopathy is extremely rare[4].

Case report

A previously well 9-year-old girl presented with choreiform movements in limbs and face of 5 days duration with preserved awareness without features of lower respiratory tract infection, meningeal irritation, photosensitivity, or skin rash. Neither personal nor family history revealed features suggesting connective tissue disorders, thyroid dysfunction, or neurological diseases. Her birth and development histories were normal. There was no evidence of drug and substance misuse. On admission, she was afebrile, had a Glasgow Coma Scale (GCS) score of 15/15, with a pulse rate of 108/minute, blood pressure of 95/65mmHg, respiratory rate of 30/min and 99% oxygen saturation on air with no abnormal auscultatory findings. Initial neurological examination revealed generalized chorea with facial and ocular dyskinesia, truncal ataxia, bruxism, darting tongue, and milkmaid grip but no signs of lateralization. She was conscious with preserved cognition. There were no features of encephalopathy. The rest of the examination was normal.

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Her full blood count was normal [white blood cell count 11,400/cu mm (N 52%, L35%), haemoglobin 12.6g/dl and platelet count 317,000/cu mm]. Her liver and renal function tests were also normal (aspartate transaminase 22U/L, alanine transaminase 23U/L, serum alkaline phosphatase 96IU/L, total serum bilirubin 8.7µmol/L, serum albumin 4.6 g/dL, blood urea 20mg/dL, serum creatinine 46µmol/L, with serum sodium 137mmol/L and serum potassium 4.3mmol/L). She had a normal coagulation screen (activated partial thromboplastin time 21 seconds, prothrombin time 12.6 seconds and international normalised ratio 1.1) along with normal inflammatory marker levels (erythrocyte sedimentation rate 16 mm/hour and C-reactive protein <5 mg/dL). Urinalysis showed no cells with a negative culture. She had a normal anti streptolysin 'O' titre of 106 U/mL with normal electrocardiogram and echocardiogram. CSF evaluation showed normal findings (0 lymphocytes, 0 polymorphs, 10 red blood cells/ cu mm, protein 15.8 mg/dL and sugar 155mg/dL) and a negative culture. Electroencephalogram revealed no evidence of encephalopathy or non-convulsive status epilepticus. Contrast-enhanced computerized tomography, magnetic resonance imaging and magnetic resonance angiogram of brain were normal. Her ultrasound scan of thyroid gland showed no features of thyroid atrophy or hypertrophy and that of abdomen showed no evidence of ovarian masses. Anti-nuclear antibodies were positive in a titre of 1:80 but anti-double-stranded deoxyribonucleic acid antibody was negative. Her serum complement levels were normal for age (C3 102 mg/dL and C4 30 mg/dL). CSF for anti-N-methyl D-aspartate (NMDA) receptor antibodies was negative. Ophthalmologic examination, 24-hour urine copper excretion (22µg/24 hours) and serum caeruloplasmin levels (30mg/dL) were normal. Thyroid function tests revealed high free thyroxine (fT4) of 43/1 nmol/L with normal thyroid stimulating hormone (TSH) level of 1.31 mIU/L with subsequent high fT4 with low TSH. Afterwards fT4 decreased to normal levels followed by normalization of TSH. Her initial anti-thyroid peroxidase level was 54 IU/ml (normal <5.6 IU/ml) and anti-thyroglobulin antibodies was 106.5 IU/ml (normal <4.11 IU/ml) which were significantly high (Figures 1 and 2).

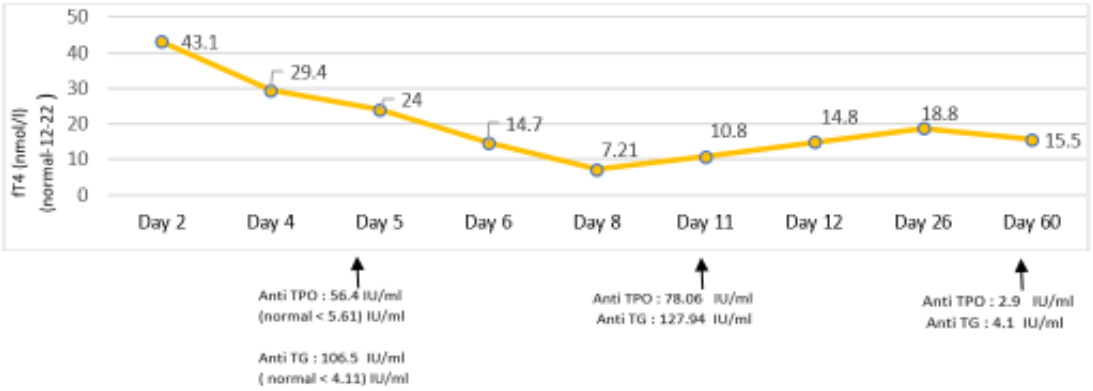

Figure 1: ***Free thyroxine and anti-thyroid antibody changes with the course of the disease***

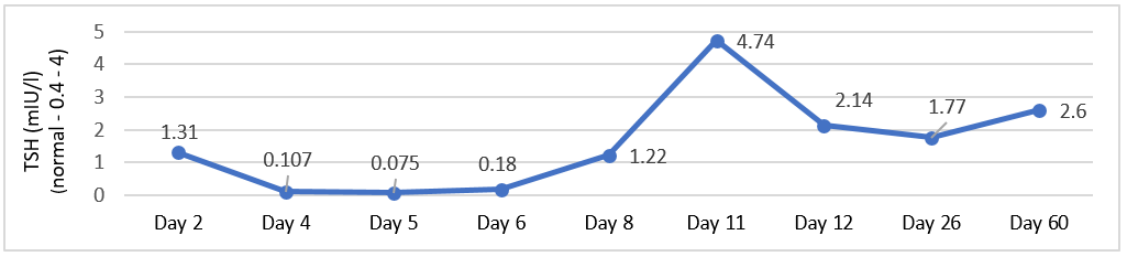

Figure 2: ***Thyroid stimulating hormone (TSH) changes with the course of the disease***

Initial symptomatic management with haloperidol, benzhexol, phenobarbitone and levetiracetam failed to control her symptoms while her creatine phosphokinase levels rose from 110 to 380 U/L (normal range 26–192 U/L) with persisting chorea severely affecting sleep and feeding. Mechanical ventilation with muscle paralysis which was initiated to avoid respiratory compromise and progression to rhabdomyolysis, controlled chorea but it recurred upon tailing off relaxants. Intravenous (IV) clonidine, IV midazolam and tetrabenazine were used in combination to control recurring chorea. Immunomodulation with IV methyl prednisolone pulses of 40mg/kg, started on day 2 for 7 days followed by therapeutic plasma exchange 6 cycles started from day 7 of illness were not effective as well. IV immunoglobulin, (total dose 2g/kg) was ineffective at chorea control as well. Cyclophosphamide 750mg/kg/m^2 and 2 doses of rituximab 750mg/m^2 were able to control chorea by day 21 and allowed extubation after 24 days of mechanical ventilation. Subsequently, hydroxychloroquine 3mg/kg/day, oral prednisolone 2mg/kg/day and tetrabenazine were continued for varying lengths and tailed off. Mycophenolate mofetil 10mg/kg twice daily was started after weaning from ventilation and escalated up to 20mg/kg. With effective neurorehabilitation she recovered without any residual neurological weakness. After 2 months, her thyroid functions remained normal with negative antithyroid antibodies and antinuclear antibodies. Mycophenolate mofetil was given for 6 months and tailed off after careful evaluation of her clinical condition.

Discussion

The word 'chorea' is derived from the Latin 'choreus' meaning 'dance'[1]. Chorea refers to irregular, flowing, non-stereotyped, random, involuntary movements that often possess a writhing quality referred to as choreoathetosis[5]. Current evidence suggests that chorea results from the imbalance in the direct and indirect pathways in the basal ganglia circuitry[5]. The disruption of the indirect pathway causes a loss of inhibition on the pallidum, allowing hyperkinetic movements to occur[5]. In addition, enhanced activity of dopaminergic receptors and excessive dopaminergic activity are proposed mechanisms for the development of chorea at the level of the striatum[5]. Common acquired causes of childhood chorea can be divided as structural abnormalities related to basal ganglia, post-infectious causes with autoimmune aetiology, immunological causes, infectious causes, vascular causes, metabolic derangements, drug-induced, and toxin-induced causes[1,2].

Hyperthyroidism is a known cause of acquired chorea[1,2]. Anti-TPO/TG antibody-related neurologic disorders responsive to steroid (ATANDS) have been reported rarely in the literature[3,4]. Chorea was the predominant movement disorder in the hyperthyroid ATANDS cohort[4]. Proposed pathogenic mechanisms are hypersensitivity of dopaminergic receptors to dopamine due to a thyrotoxic state, changes related to cerebral perfusion, autoimmune-mediated vasculitis in the central nervous system and anti-thyroid antibody-mediated effects on the nervous system[4]. Persistence of chorea despite euthyroid state suggests that these antibodies have a direct effect on chorea but there is no proven correlation between antibody titres and disease severity[4].

Chorea has been treated successfully with drugs that interfere with central dopaminergic function with tetrabenazine providing the most effective symptom relief with minimal dose related side effects[1]. However, there is no consensus as to the optimal management of autoimmune chorea, in which immunosuppressants including steroids, plasmapheresis and anticoagulation are utilized with variable success[1]. According to the literature, anti-thyroid treatment (methimazole, carbimazole, propyl thiouracil or thiamazole) beta-adrenergic blockers, medication to alleviate chorea and immunomodulation had been tried to treat patients with anti-TPO/TG antibody-related neurologic disorders[4]. As our patient was clinically euthyroid, anti-thyroid medications or beta-adrenergic blockers to control symptoms were not warranted.

Complications of chorea include rhabdomyolysis due to prolonged abnormal involuntary movements which may lead to myoglobinuria and acute renal failure[6,7]. Furthermore, orofacial dyskinesia can cause difficulty in swallowing and poses a risk of aspiration pneumonia leading to significant morbidity and mortality[8].

In conclusion, we suggest performing thyroid function tests and anti-thyroid antibody testing during the initial aetiological workup of acquired chorea as thyroid disorders presenting as movement disorders are not uncommon and should not be missed. Treatment of such a patient requires early immunomodulation as necessary along with meticulous monitoring for complications of chorea.

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