

Relapsing myelitis in patients with anti thyroid antibodies –Steroids may not be enough

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Abstract

Autoimmune thyroiditis has been seen to be associated with other autoimmune neurological disorders. More over biopsy studies of patients with steroid responsive encephalopathy has shown that antithyroid antibodies (anti thyroid peroxidase-TPO antibodies) can lead to central nervous system demyelination. We are reporting two such cases. A 32 year female presented with longitudinally extensive transverse myelitis(LETM) with negative workup for other demyelinating and autoimmune diseases, and positive for anti TPO antibody. She was started with steroids and azathioprine and recovered completely over one month period, stopped treatment herself after 5 months, had relapse of myelitis and was put on immunosuppressive treatment, showing improvement. The second patient a 52 year female had recurrent attack of LETM with negative workup for other causes of LETM except positive anti TPO antibody. In her first attack she was given only steroids pulse. After relapse she was treated with steroids and cyclophosphamide pulse, and patient remained relapse free thereafter. So it suggests that in myelitis patients associated with anti TPO antibody steroids alone may not be sufficient and, such patients require long term immunosuppression. So anti TPO antibody may predict recurrence and may be considered an independent marker for relapsing disease though it require further studies.

Keywords: Myelitis, Anti-TPO, antibodies, Recurrent myelitis, Longitudinally extensive transverse myelitis (LETM).

Introduction

Hashimoto's disease has been seen to be associated with other autoimmune diseases like Guillain Barre syndrome,¹ myelopathy,² myeloneuropathy³ and steroid responsive encephalopathy associated with autoimmune thyroiditis (SREAT).⁴ Previous studies have demonstrated that thyroglobulin and thyroid peroxidase have several autoantibody binding sites.⁵ Thus molecular mimicry between the thyroid and myelin epitopes may lead to binding of myelin basic protein to anti thyroid antibodies leading to demyelination. The studies have shown that NMO-SD is associated with other autoimmune antibodies like antithyroid antibodies,⁶ anti nuclear antibodies and Sjogren syndrome A (SSA) antibodies.⁷ but there are very few case reports of transverse myelitis associated with anti-thyroid antibody alone^{2,3} and very few cases of isolated longitudinally extensive transverse myelitis(LETM).⁸

Case 1

A 32 year old female, known case of hypothyroidism for 5 yrs, presented with 15 days history of difficulty in walking with no preceding illness. There was no previous history of similar illness or vision loss in the past. On neurological examination she was found to have symmetrical paraparesis with Medical Research Council (MRC) grade 4 power in bilateral lower limbs at all joints and sensory spinal level at T8, brisk deep tendon reflexes in lower limbs and bilateral extensor plantar response.

On investigations, complete blood count, renal function tests, liver function tests, serum vitamin B₁₂, folate levels, erythrocyte sedimentation rate, and serum C-reactive protein levels were normal. Cerebrospinal fluid examination showed 04 cells(all lymphocytes), mild increased protein

(65mg/dL) and normal glucose levels. Serum TSH 3.09µIU/ml, free T₃ 2.9 ng/dL, free T₄ 20.12 ng/dL, and serum anti TPO antibody was 377 U/ml(raised). Serologic screening for autoimmune diseases (antinuclear antibodies, anti ds DNA, anti smith, anti Ro, anti La and ACE levels was negative), serum anti AQ4 antibody, paraneoplastic and infectious diseases workup was negative. The CECT abdomen and chest were normal, VEP and MRI brain was also normal. MRI dorsal spine showed patchy central and eccentric intramedullary T₂ hyperintense signals from D2-D11 appearing isointense on T₁ weighted image.

Patient was given iv methylprednisolone for 5 days followed by oral azathioprine 100mg/day and patient recovered completely over 1 month period. The patient took azathioprine for 5 months and then left on her own considering her alright; then 3 months after drug default, patient had another relapse, which was treated by intravenous methyl prednisolone pulse and azathioprine and patient recovered completely with no relapse for last one year.

Case 2

A 50 year old female presented with 10 days history of gradually progressive difficulty in walking which progressed over 10 days to an extent that she couldnot stand without support of two person, and it was associated with numbness of bilateral legs but no bladder or bowel disturbance. There was history of gradual onset of vision loss in right eye but on evaluation it was ascribed as a result of cataract. The patient also had past history of similar attack 6 months back which was treated elsewhere with intravenous methylprednisolone pulse and she recovered completely over a period of 15 days.

Neurological examination during this attack revealed proximal muscle power in both lower limbs MRC grade 3/5 at hip and knee joint and 4/5 at bilateral ankle joint along with mild truncal weakness and normal power in bilateral upperlimbs. Sensory spinal level was at T4 level and bladder bowel were normal. Deep tendon reflexes were brisk in lower limbs and normal in bilateral upper limbs. There were no signs suggestive of optic neuritis and brainstem involvement or any signs of meningeal irritation. On further evaluation, the investigations were normal like case 1 and CSF examination had normal sugar(93 mg/dl), normal cells(03/cumm), mildly increased proteins(82 gm/dl) anti TPO antibody was also raised(89.0 U/ml). MRI dorsal spine in previous attack had intramedullary hyperintense signals on T2W images from D2 to D4 vertebral levels. During recurrence lesion extended and MRI dorsal spine showed confluent central intramedullary signals from mid thoracic cord between D5 and D9 vertebral levels which were hyperintense on T₂ weighted and mildly hypointense on T₁ weighted images. Previously noted intramedullary signal abnormality between D2 and D4 was substantially reduced and represented only subtle increased T₂ weighted and STIR signals at D3 level. So patient was diagnosed as a case of recurrent transverse myelitis and was given intravenous methylprednisolone pulse followed by oral steroids and intravenous cyclophosphamide pulse. within one month period patient recovered completely and no further relapse was noted.

Discussion

Steroid responsive encephalopathy associated with autoimmune thyroiditis (SREAT) is a well known entity. There are biopsy proven reports of cases of SREAT, which showed primary CNS demyelination and radiological evidence of steroid responsiveness, identifying CNS demyelination as a complication of autoimmune thyroiditis(9). Our two patients who presented with transverse myelitis with negative workup for all other causes of transverse myelitis and no history suggestive of preceding infection, autoimmune /connective tissue disorders or malignancy were found to be anti TPO positive. The first patient had recurrence of myelitis after defaulting immunosuppressive drug and second patient had relapse because she was not prescribed long term immunosuppression except for pulse methyl prednisolone, and did well after long term immune-suppression with no recurrence. Co-occurrence of autoimmune antibodies with Neuromyelitis Optica Spectrum disorder (NMO-SD) is a well known entity but recurrent Isolated transverse myelitis with positive anti TPO antibodies has not been emphasized much. Kimbrough et al published a study in 2014(10) about characteristics that predict recurrence following an acute transverse myelitis event, they have mentioned CSF pleocytosis at onset >05 white blood cells / μ L, positive oligoclonal band testing, vitamin D insufficiency,

longitudinally extensive transverse myelitis(LETM), presence of antinuclear antibody titre(ANA) titre >1:160 and presence of antibodies to Ro/SS-A antigen were associated with recurrence. Our emphasis is that anti TPO may also predict recurrence and may be an independent marker of recurrence in patients with isolated transverse myelitis which need further studies to confirm.

Conclusion

These case reports show that anti-thyroid antibody-TPO (Thyroid peroxidase) was associated with recurrent longitudinally extensive transverse myelitis(LETM) and had good response to steroids and required long term immunosuppression, so we can conclude that anti thyroid antibodies may be an independent marker of recurrence of myelitis.

Conflict of Interest: None.

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