

## Anti-Yo antibody associated paraneoplastic cerebellar degeneration in a patient with a metastatic carcinoma -A case report

Jithin Raj. P<sup>1,\*</sup>, Nikhil Gladson<sup>2</sup>, Kabeer KA<sup>3</sup>, Shaji CV<sup>4</sup>, Prasanth SR<sup>5</sup>

<sup>1,2</sup>Senior Resident, <sup>3</sup>Associate Professor, <sup>4</sup>Professor and HOD, <sup>5</sup>Assistant Professor, <sup>1-5</sup>Dept. of Neurology, <sup>1-5</sup>Government T D Medical College, Alappuzha, Vandanam, Kerala, India

\*Corresponding Author: Jithin Raj. P

Email: jjjrrrr49@gmail.com

### Abstract

**Introduction:** Paraneoplastic cerebellar degeneration (PCD) is a collection of neurological disorders resulting from tumor induced autoimmunity against cerebellar antigens. There are multiple antibodies associated with PCD. Of these Anti Yo antibody is considered as one of the most important antibodies. Between 90 and 98% of patients with cerebellar ataxia and anti-Yo antibodies have a cancer detected.<sup>3,4</sup> The vast majority of which are pelvic and breast cancers.

**Case Report:** 47 year old lady presented with symptoms suggestive of subacute onset pancerebellar degeneration. The evaluation showed the positivity of Anti Yo Antibody in her and on extensive evaluation, she was found to be having a lymph node metastasis from a probable ovarian malignancy without the evidence of the primary in the ovary.

**Keywords:** Paraneoplastic cerebellar degeneration, Anti Yo antibody, lymph node metastasis.

### Introduction

Paraneoplastic cerebellar degeneration (PCD) is a collection of neurological disorders resulting from tumor induced autoimmunity against cerebellar antigens. There are multiple antibodies associated with PCD.<sup>1</sup> Of these Anti Yo antibody is considered as an important one. Between 90 and 98% of patients with cerebellar ataxia and anti-Yo antibodies have a cancer detected.<sup>3,4</sup> The vast majority of which are pelvic and breast cancers. The main modalities for the treatment of PCD include the treatment of the primary malignancy and the immunotherapy. But the overall survival rate is very minimal in these patients. Detailed evaluation for the primary malignancy should be done in all patients with PCD. If the primary malignancy is not obvious from other investigations, the staging laparotomy is recommended in these patients along with the immunotherapy.

### Case Report

47 year old female presented with gradually progressive walking difficulty in the form of swaying to both sides while walking for past 4 months. She was also noticed to have inability to negotiate narrow passages with swaying to either side. Now for the last 1 month, she is able to walk only with the support of one person. It was not associated with any weakness of upper limb or lower limbs or sensory symptoms anywhere in the body. She was having difficulty in taking food to the mouth as there was smearing of food which was present for past 1 month. She had inability to pour water from a glass without spilling. Along with these symptoms she was also noticed to have tremulousness of upper limbs especially when she was bringing food to mouth.

She developed slurring of speech since last 1 month in the form of undue separation of syllables with occasional explosive quality of speech. For the past 1 month, she also has difficulty to sit up without support with swaying

anteriorly and posteriorly while sitting. She also developed repeated episodes of vomiting for past 2 weeks. She had loss of appetite and loss of weight.

No history of cognitive symptoms in the form of misplacing things, repeatedly asking for things, forgetting names of people, losing way, inability to recognise people or objects.

No history of cranial nerve symptoms. No history of slowness in activities, posturing of limbs, recurrent falls, bowel or bladder dysfunction or features suggestive of raised intracranial tension

No history of systemic symptoms, cold intolerance, constipation, loose stools, drug or toxin exposure. No history of similar illness in her family.

On examination she was moderately built and nourished. She was able to sit with support only. No neurocutaneous markers. BP- 110/80 mm Hg

Mini Mental status examination was normal 29/30. Cognitive function examination were normal.

Speech was scanning with staccato quality. Cranial nerve examination was normal. Fundus examination was also normal. Motor system examination showed normal bulk with hypotonia of all 4 limbs and grade 5 power and normally elicited deep tendon reflexes. Sensory system examination was normal. Cerebellar system examination showed a pancerebellar syndrome with impaired finger nose test, disidiadochokinesia, rebound phenomenon, truncal ataxia, titubation, impaired heel shin test and toe finger test. Oculomotor system examination showed slow and hypometric saccades with broken pursuits and gaze evoked nystagmus.

Extrapyramidal system examination was normal. She could walk only with the support of two persons. Systemic examination was normal.

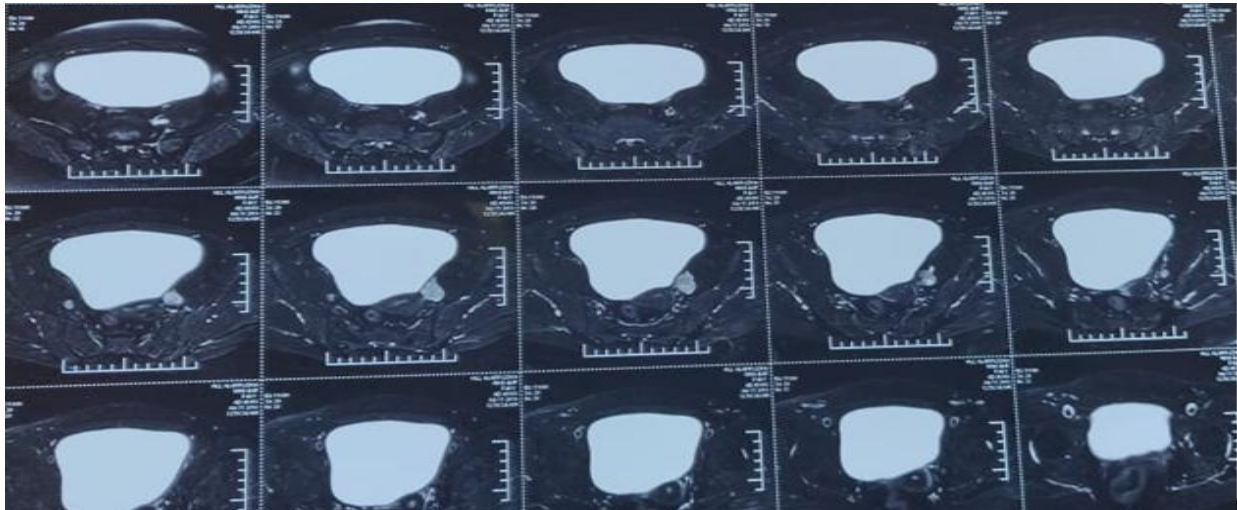
Her routine lab parameters were normal. Thyroid function test was normal, anti TPO antibody was negative, Anti Gliadin antibody, Anti GAD antibody were negative.

MRI Brain with Spinal cord with contrast was normal  
Paraneoplastic antibody panel was sent which showed positive Anti Yo Antibody.

Workup for Primary malignancy was carried out with CT Thorax and Abdomen with contrast showed only a

calcified non enhancing lesion in spleen possibly dermoid cyst.

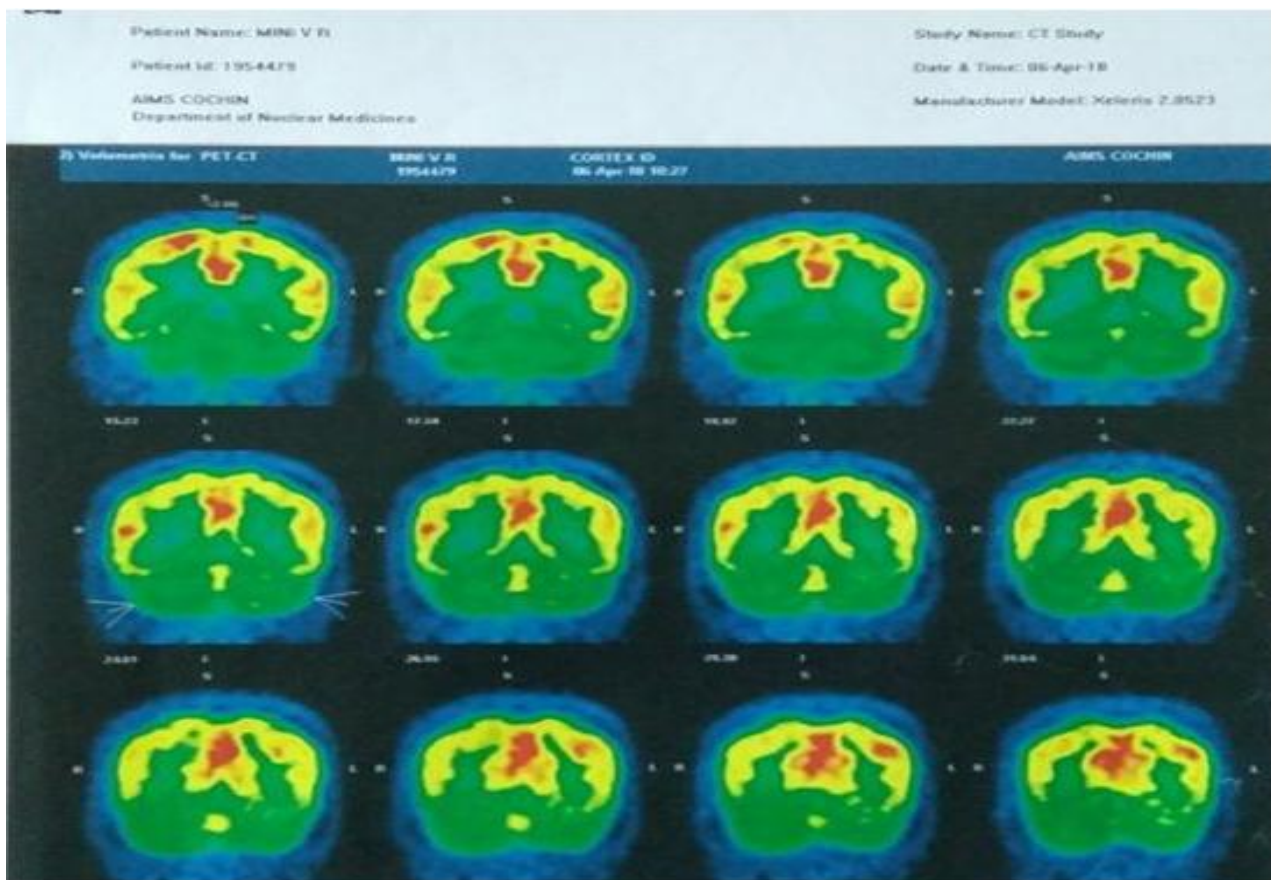
MRI Abdomen and Pelvis showed above splenic lesion to be possible dermoid cyst and enlarged left internal iliac node with diffusion restriction.



**Fig. 1: MRI Pelvis showing enlarged internal iliac lymph nodes**

Whole body FDG PET CT was done which showed severe hypometabolism of bilateral cerebellar hemisphere

and FDG avid and non avid minimally enlarged left external iliac lymph nodes-possibly inflammatory.



**Fig. 2: PET scan showing severe bilateral cerebellar hypometabolism**

She underwent 4 sessions of Plasma exchange but had no improvement in symptoms. Following that, she was given a course of Intravenous immunoglobulin 2 gram /kg over 5 days.

After that, 4 doses of Rituximab (500 mg each) was given weekly over 1 month. She was kept under follow up for 2 months but did not show much improvement. Staging laparotomy with bilateral salpingo oophorectomy was performed.

The biopsy specimen of bilateral salpingo oophorectomy did not show any evidence of malignancy on histopathologic examination. But the dissected lymph nodes showed the evidence of metastatic adenocarcinoma probably from the ovary.

## Discussion

Paraneoplastic cerebellar degeneration (PCD) is a collection of neurological disorders resulting from tumor induced autoimmunity against cerebellar antigens. There are nearly 30 different antibodies associated with this condition.<sup>1</sup>

In multiple studies, it was shown that 36% of 137 patients with a definite PNS presented with subacute cerebellar ataxia, indicating that PCD is a common presentation of Antibody associated paraneoplastic syndrome. While anti-Hu was the most frequent paraneoplastic Ab detected (66% of 137 patients), only 18% presented with PCD. In contrast, 100% of anti-Yo, anti-Tr and anti-mGluR1, and 86% of anti-Ri patients presented with PCD. In PCD patients, anti-Yo (38%) was detected most frequently, followed by anti-Hu (32%), anti-Tr (14%) and anti-Ri (12%) Antibodies.

Between 90 and 98% of patients with cerebellar ataxia and anti-Yo antibodies have a cancer detected.<sup>3,4</sup> The vast majority of which are pelvic and breast cancers. A few cases with lung cancers have been reported.<sup>5</sup>

In general, PCD predates the cancer diagnosis. In approximately 30% of patients, the ataxic symptoms occur when the cancer is in remission.<sup>6</sup> Clinically, it is difficult to differentiate anti-Yo PCD from other subacute cerebellar ataxias. As a pancerebellar syndrome, the ataxia affects both the trunk and limbs, but onset can be asymmetric in a subset of patients.<sup>2,7</sup>

Extracerebellar involvement such as limbic encephalitis and peripheral neuropathy is less severe and less common in anti-Yo PCD than in anti-Hu syndrome.

Early on, magnetic resonance imaging of the brain in the anti-Yo syndrome can be normal,<sup>7</sup> and cerebellar atrophy is usually seen only after the disease is well established.<sup>8</sup> FDG PET can show reductions in mean metabolic rate in the cerebellum.

Our patient presented with a pancerebellar syndrome which was symmetric from the onset. MRI Brain of the patient was normal and PET showed severe bilateral cerebellar hypometabolism.

## Diagnostic Criteria

The current scientific consensus includes subacute cerebellar degeneration among the “classical” paraneoplastic syndromes.<sup>3</sup>

The commonly used diagnostic criteria, based on the guidelines set forth by an international panel supported by the Paraneoplastic Neurological syndrome Euro network in 2004, require

1. The development of a severe pancerebellar syndrome in <12 weeks,
2. No MRI evidence of cerebellar atrophy, other than what would be expected given the patient's age.
3. A Rankin score of at least 3 (indicating moderate disability, requiring some help but able to walk unassisted) is required, where symptoms significantly interfere with the lifestyle or prevent independent existence.
4. Clinical evidence of truncal and hemispheric cerebellar involvement
5. Noncerebellar findings do not rule out the diagnosis.

Our patient fulfilled the diagnostic criteria of PCD.

Three of the largest case series dealing with anti-Yo PCD have reported that immunotherapies, such as corticosteroids, plasma exchange (PLEX), and intravenous immune globulin (IVIG) to be largely ineffective.<sup>2,7</sup>

Candler et al.<sup>10</sup> reported that only tumor therapy was effective in stabilizing or improving neurological outcomes. In cases where a tumor is found at the same time as the PCD is diagnosed, using immunosuppressive drugs and monoclonal antibodies is controversial, but is often attempted in conjunction with antitumor approaches. Two of six patients reported by Shams'ili et al.<sup>6</sup> improved or stabilized with a combination approach.

Progression of disability leads to <10% of patients able to ambulate without assistance over the long term, with the majority left bedridden. Long-term survival rates were reported less than 25%.<sup>6</sup>

Our case was also a pancerebellar degeneration due to Anti Yo antibody. But the rarity in our case is that with extensive interventions, we could find out the presence of malignancy in a lymph node in our patient without the evidence of a proper primary malignancy. This type of paraneoplastic presentation of a metastatic malignancy without the evidence of primary malignancy in the corresponding organ is rare.

**Conflict of Interest:** None.

## References

1. Jarius S, Wildemann B. 'Medusa-head ataxia': the expanding spectrum of Purkinje cell antibodies in autoimmune cerebellar ataxia. Part 1: Anti-mGluR1, anti-Homer-3, anti-Sj/ITPR1 and anti-CARP VIII. *J Neuroinflammation* 2015;12:166.
2. Shams'ili S, Grefkens J, De Leeuw B. Paraneoplastic cerebellar degeneration associated with antineuronal antibodies: analysis of 50 patients. *Brain* 2003;126(Pt 6):1409–1418.

3. Graus F, Delattre JY, Antoine JC. Recommended diagnostic criteria for paraneoplastic neurological syndromes. *J Neurol Neurosurg Psychiatry* 2004;75:1135–1140.
4. Sadeghian H, Vernino S. Progress in the management of paraneoplastic neurological disorders. *Ther Adv Neurol Disord* 2010;3:43–52.
5. Hasadsri L, Lee J, Wang BH. Anti-yo associated paraneoplastic cerebellar degeneration in a man with large cell cancer of the lung. *Case Rep Neurol Med* 2013;2013:725936.
6. Power DG, McVey GP, Delaney DW. Papillary serous carcinomas of the uterine cervix and paraneoplastic cerebellar degeneration: a report of two cases. *Acta Oncol* 2008;47:1590–1593.
7. Peterson K, Rosenblum MK, Kotanides H, Posner JB. Paraneoplastic cerebellar degeneration.. A clinical analysis of 55 anti-Yo antibody-positive patients. *Neurol* 1992;42:1931–1937.
8. Key RG, Root JC. Anti-Yo mediated paraneoplastic cerebellar degeneration in the context of breast cancer: a case report and literature review. *Psychooncology* 2013;22:2152–2151
9. Furneaux HF, Reich L, Posner JB. Autoantibody synthesis in the central nervous system of patients with paraneoplastic syndromes. *Neurol* 1990;40:1085–1091.
10. Candler PM, Hart PE, Barnett M. A follow up study of patients with paraneoplastic neurological disease in the United Kingdom. *J Neurol Neurosurg Psychiatry* 2004;75:1411–1415.

**How to cite this article:** P JR, Gladson N, Kabeer KA, Shaji CV, Prasanth SR, Anti-Yo antibody associated paraneoplastic cerebellar degeneration in a patient with a metastatic carcinoma -A case report. *J Neurosci* 2019;5(1):38-41