

An Interesting Case of Anti-Yo Antibody Mediated Progressive Cerebellar Ataxia leading to diagnosis of Breast Cancer

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ABSTRACT

Paraneoplastic syndrome are group of disorder, non-metastatic in origin, which are associated with internal malignancy. They may precede manifestation of malignancy by weeks or months and hence diagnosis of malignancy may be delayed, if not properly evaluated thus hampering the prognosis. We herewith present a 54 years old female who presented with subacute onset bilateral cerebellar syndrome without any manifestation of malignancy. Most of her initial investigation were non-contributory. It was only after her anti-neuronal antibodies (Paraneoplastic antibodies) Anti Yo came positive, she was further evaluated and was detected to harbor invasive ductal carcinoma of breast. This report highlights importance of estimation of anti-neuronal antibodies in a case of otherwise unexplained neurological symptoms keeping high index of suspicion of paraneoplastic syndrome.

The report also highlights importance of using combined imaging modalities i.e PET and MRI for early diagnosis of occult breast malignancies like invasive ductal carcinoma.

Key words : Antineuronal antibodies, paraneoplastic syndrome, cerebellar syndrome, Ca-breast, MRI breast.

Introduction :

Sporadic cerebellar ataxia often presents a diagnostic problem and etiology may not be apparent even after extensive investigations. The etiology of subacute cerebellar ataxia is diverse and mainly includes vascular, metabolic, toxic, infective and autoimmune / paraneoplastic causes.

Paraneoplastic syndrome are the group of disorder characterised by non-metastatic manifestation of malignancies. They may precede manifestations of malignancies by weeks or months and hence elude diagnosis of malignancies. We report a case of progressive cerebellar syndrome who did not show any features of malignancy clinically. When all other causes of cerebellar syndrome were ruled out her neuronal antibodies profile (Paraneoplastic antibodies) showed Anti-Yo antibody positive which suggested Ca-breast or Ca-ovary. Her further work up revealed invasive ductal carcinoma of breast. The case highlights importance of Neuronal

antibodies estimation in properly selected group of cases.

Case Report :

A 54 old female, known c/o hypertension presented with progressive difficulty in walking and tendency to fall on one side while walking since 10 days. She had noticed tremors of whole upper limb while approaching an object and also had difficulty in wearing foot wear. The relatives had noticed slurring of speech. These symptoms were progressive over the days. There were no symptoms of raised ICP like headache, vomiting, seizures. There were no symptoms related to cranial nerve involvement, motor weakness, sensory symptoms or bladder / bowel involvement, visual disturbances. There was no h/o similar complaints in past or in family. There was no h/o preceding fever, vaccination or drug intake like anticonvulsants. There was no history h/o cough, dyspnoea. There were no symptoms related to GIT or genito-urinary system. There was no history of any lump in breast, lymph node enlargement. There was no history of anorexia or weight loss which would suggest malignancy.

General examination was largely unremarkable. On CNS examination she had horizontal nystagmus laterelised to left. She had bilateral cerebellar sign in upper and lower limb, cerebellar type of dysarthria,

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cerebellar ataxia on walking. There was no cranial nerve involvement, further examination did not reveal papilledema, motor and sensory system was normal. On other system examination, there was no lymphadenopathy, thyroid swelling, breast lump. Per abdomen and respiratory system examination did not reveal any abnormality. She was diagnosed as a c/o progressive bilateral cerebellar syndrome and was evaluated further.

Investigation : Her routine investigation like CBC, kidney function tests, liver function tests, thyroid profile, Vit-B12 levels, X-Ray chest PA view were within normal limits. MRI brain showed mild bilateral cerebellar atrophy but did not reveal any space occupying, demyelinating or vascular lesion. In view of insignificant findings on these investigations and MRI brain, she was further evaluated.

Her urine for toxin profile was normal. Her genetic testing for spino-cerebellar-Ataxis (SCA panel) was done which ruled out any hereditary spino-cerebellar-ataxia. Since most of the investigation could not reveal the cause of cerebellar syndrome, Anti-neuronal antibodies testing (Paraneoplastic antibodies tests) was done which revealed Anti-Yo (PCA-1) antibodies positive, other antibodies like Anti-Hu (ANNA-1), Anti Ma2, Anti-Ri and Anti-amphiphysin were negative.

Presence of Anti-Yo (PCA-1) antibodies suggested cerebellar degeneration and most commonly associated with this antibodies are carcinoma ovary and breast. So patients USG pelvis was done which did not reveal any ovarian lesion. Serum CA-125 levels were also normal, ruling out ovarian malignancy.

Her mammography was done which also did not reveal breast lump. Since there was strong suspicion of carcinoma breast oncologist opinion was sought. Her PET scan was done which showed right axillary lymph node metastasis, but did not show any breast lesion. So finally MRI of breast region was done. MRI breast revealed right sided nodular breast lesion with enlargement of right axillary lymph node. Findings were suggestive of Right carcinoma breast with axillary lymph node metastasis. FNAC

from axillary lymph node showed features of metastatic adeno-carcinoma. Patient was subjected for Right total radical mastectomy. Histopathology of breast revealed feature of invasive ductal carcinoma of breast with axillary lymph node metastasis. She was further given chemo-radiation by oncologist. Her cerebellar signs have significantly improved after treatment. Final diagnosis arrived was right sided invasive ductal breast carcinoma with right axillary lymph node metastasis leading to paraneoplastic syndrome in the form of bilateral cerebellar syndrome.

Discussion : Paraneoplastic neurologic syndromes are a heterogeneous group of neurologic disorders associated with systemic cancer and caused by mechanisms other than metastases, metabolic and nutritional deficits, infections, coagulopathy, or side effects of cancer treatment.

They can be neurological like cerebellar syndrome, peripheral neuropathy, myaesthesia syndromes, dermatomyositis etc. or can be non-neurological like Cushing's syndrome, SIADH, hypercalcemia, etc. The common malignancy associated with paraneoplastic syndrome are small cell lung cancer, some GIT tumors, breast cancers, lymphoma etc.

The paraneoplastic syndrome may precede symptoms and signs of primary malignancy by weeks to months. Hence there may be a delay in diagnosis and treatment of primary malignancy which may alter outcome of the treatment and survival.⁷

In our case there were no symptoms like breast lump. Even the mammography failed to pick up the lesion. It was only after the anti-neuronal antibody-anti-Yo came positive, patient was advised PET which revealed only axillary lymph node metastasis but did not show breast lesion. Finally MRI breast detected malignant breast lesion and axillary lymph node. Anti-neuronal antibodies (Paraneoplastic antibodies) can play important role in early diagnosis of malignancy in patient presenting with features of paraneoplastic syndrome particularly neurological syndromes¹⁻⁷. The role of MRI diagnosis of small invasive malignant lesion of breast is well documented in literature⁸. These lesion

Neuronal Antibodies and it's Associations with Paraneoplastic antibodies

Antibodies	Neurological syndrome	Associated malignancies
Anti Hu (ANNA-1)	<ul style="list-style-type: none"> ● Sensory neuropathy ● Cerebellar degeneration ● Limbic encephalitis 	Small cell carcinoma of lung
Anti Yo (PCA-1)	<ul style="list-style-type: none"> ● Cerebellar degeneration 	Ca-ovary, Ca-breast
Anti Ma2 (Ma/Ta)	<ul style="list-style-type: none"> ● Limbic encephalitis ● Brain stem encephalitis ● Cerebellar degeneration 	Seminoma Lung cancer
Anti Ri (ANNA-2)	<ul style="list-style-type: none"> ● Brain stem encephalitis 	Small cell Ca of lung, Ca breast
Anti amphiphysin	<ul style="list-style-type: none"> ● Stiff person syndrome 	Small cell Ca of lung, Ca-breast

at times can be missed on mammography and even PET scan⁸ as happened in our case. Hence contrast enhanced MRI of breast has edge over PET scan⁸. In our case also the MRI breast picked up the lesion. Hence literature suggests using combined imaging modalities i.e PET and MRI in picking occult breast malignant lesion like invasive ductal carcinoma if one fails to detect lesion.

Conclusion : It can be concluded that in patient presenting with neurological symptom and signs not explained on routine etiologies, a high index of suspicion should be kept for paraneoplastic syndrome. Neuronal antibodies estimation (Paraneoplastic antibodies) can be of immense help in early diagnosis of occult malignancies in such cases. This case report also highlights importance of MRI breast in diagnosis of small malignant breast lesions like invasive ductal carcinoma, which can be missed on routine screening, mammography and even PET scan. The literature review⁸ shows that MRI breast can detect minimal malignant breast lesion like invasive ductal carcinoma missed even by PET scans. Hence combining these two imaging modalities is always advisable.

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