Case Report

International Journal of Neurology and Neurosurgery
Volume 14 Number 3, July– September 2022
DOI: http://dx.doi.org/10.21088/ijnns.0975.0223.14322.8

Paraneoplastic Neurological Disease: A Case of ZIC-4 Antibody Related Cerebellar Ataxia

Anand[1], Anita Rawat[2], Kishalay Datta[3]

How to cite this article:
Anand, Anita Rawat, Kishalay Datta/ Paraneoplastic Neurological Disease: A Case of ZIC-4 Antibody Related Cerebellar Ataxia/Int J Neurol Neurosurg.2022;14(3): 89-91.

Abstract

Cerebellar Degenration Associated with NNTTR/DNE Antibodies is a Rare Condition that is Seen in Case of Malignancy. However many recent studies have suggested ZIC-4 Antibodies Association with Paraneoplastic Cerebellar Degenration Particularly seen with Small Cell Carcinoma of Lung. However ZIC-4 Antibodt Associated Cases are underestimated beacuse of Prevalence of anti Hu Related Cases.

Keywords: Paraneoplastic Cerebellar degeneration, Zic 4 antibody, anti Hu antibody.

INTRODUCTION

Paraneoplastic Cerebellar Degeneration is a frequent paraneoplastic presentation. The common symptoms include symmetrical limb and truncalataxia nystagmus and dysarthria. There may be other symptoms like low-grade fever, nausea, malaise headache etc. The disease has a progressive course and starts with mild symptoms which progresses to pan-cerebellar dysfunction.

In more than about 50% of the patients symptoms of PCD can antecede Tumour diagnosis. Brain imaging is normal in most of the cases in the initial phase of disease. The cerebral spinal fluid analysis shows elevated protein levels, pleocytosis and intrathecal IgG synthesis

Author's Affiliation: [1]DNB Resident, [2]Consultant, [3]Associate Director, Department of Emergency Medicine, Max Hospital, Shalimar Bagh, New Delhi 110088, India.

Corresponding Author: Anand, DNB Resident, Department of Emergency Medicine, Max Hospital, Shalimar Bagh, New Delhi 110088, India.

E-mail: anandkq22@gmail.com

Received on: 30.05.2022

Accepted on: 02.07.2022

© Red Flower Publication Pvt. Ltd.

Malignancies that are commonly associated with a Neoplastic cerebellar disease are

- Small cell carcinoma of lung 33%
- Ovarian carcinoma bracket open and 25%
- Hodgkin Lymphoma 15%

The pathogenesis of PCD is due to the autoimmune response caused by the underlying malignancy when proteins restricted to immune privileged neurons are presented by the tumour. In around 58% of the cases, anti neural antibodies which target the intercellular proteins are identified. Identification of the associated antibody is important as it helps to establish the diagnosis of PCD and specific association between antibody and cancer type exists.

Anti-Yo, Anti-Hu, Anti TR/DNER are antibodies are the most common antibodies associated with the PCD.

Anti-Yo antibodies also known as the anti purkinje cell antibodies are directed against the purkinje cells and typically associate with ovarian and breast carcinoma.

Anti Hu antibodies also known as the anti-neuronal nuclear antibody type 1/ANNA 1 and

are associated with small cell lung carcinoma and the Patient presents with symptoms of encephalitis

Anti TR/DNER or delta/notch like epidermal growth factor related receptor antibodies are associated with Hodgkin's lymphoma and presents as an isolated cerebellar syndrome.

These are onconeuronal antibodies with zinc finger domain of the intra cellular transcription factor Z I C4 as the target antigen Since Zic4 is Intra cellular, associated autoimmunity is T cell mediated and hence Zic 4 antibodies is used as tumour marker for the syndrome and the tumour.

We are presenting first case of isolated Zic 4 antibodies associated with PCD which led to fatal dysautonomia.

CASE REPORT

Case 1

63 year old male patient presents to the emergency department with complaints of shaking of limbs while doing daily activity associated with generalised weakness since last five days and decreased appetite since last 5 to 7 days.

Patient had no history of fever, cough, cold vomiting diarrhoea giddiness headache trauma chest pain Blurring of Vision Focal Neurological Deficit has been repeated slurring of Speech facial deviation.

Primarysurvey Findings:

Airway Assessment	:	Patent
Breathing Assessment		
Respiration(RR/min)	:	12/min regular
Laboured	:	NO
SpO2	:	100 % on room air
Circulation		
Pulse	:	90/min regular
BP	:	100/60 MMHG
Peripheral Pulses	:	+
Temperature	:	98.3 Degree F
Cardiac Monitor	:	NSR (Normal Sinus Rhythm)
GRBS	:	112 mg/dl
ECG	:	Normal sinus rhythm

Pupils :

Right eye : 3 MM, reactive to light

Left eye: 3 MM, reactivetolight

Secondarysurvey Findings:

Review of Systems

HEENT:

Pallor

Icterus

Cyanosis

Jvp

Tongue/mucousmembranes :moist

Chest	:	B/L clear
CVS	:	S1 S2 normal
Abdomen	:	Soft
Neuro	:	Conscious, Obeying commands

B/L plantarflexor

Powerall 4 limbs 5/5

Past pointing present

Abnormal movements present

nohypotonia

normalsensory examination

cerebellar sign positive

Extremities	:	warm

AMPLE History:

Allergies	:	noknown allergies
Medications	:	notonany medications
Past Medical History	:	No significant past history
Last Meal taken	:	morning tea
Events prior to the incident	:	Non significant

Provisional working diagnosis (After initial assessment)? cerebrovascular accident

Investigations (Labs/Radiological imaging) : planned to bed one

ECG

RBS

Cardiac markers

MR Brain stroke protocol

Treatmentadvised

- IV fluid NS 500 ML

- INJ levepil 1 gmIV stat
- Solumedrol iv therapy
- Ig G therapy

MRI brain reports-no abnormality seen

CSF analysis-pleocytosis

PET scan-normal study

Patient improved on symptoms after pulse therapy of steroid and Ig G administration

DISCUSSION

This is a report of fatal Disautonomy associated with rhombo encephalitis related to Zic 4 Antibodies. There are very few cases of isolated Zic 4 antibodies that have come to clinical attention. And in the majority of the cases early immuno modulatory treatment led to a benign clinical course.

Tests and investigations done showed no other pathology indicating paraneoplastic presentation.

However there is a recent study that shows that there are other antibodies such as Kelch like protein 11 KLHL 1-ab causing a paraneoplastic brainstem and cerebellar syndrome which has a Similarclinical course just like our patient.

REFERENCES

1. Peterson K, Rosenblum MK, Kotanides H, Posner JB. Paraneoplasticcerebellar degeneration. I. a clinical analysis of 55 anti-Yo antibody-positive patients. Neurology. 1992;42(10):1931–7
2. Graus F, Keime-Guibert F, Rene R, Benyahia B, Ribalta T, Ascaso C, Escaramis G, Delattre JY. Anti - Hu-associated paraneoplastic encephalomyelitis: analysis of 200 patients. Brain : a journal of neurology. 2001;124(Pt 6):1138–4
3. Dalmau J, Rosenfeld MR. Paraneoplastic syndromes of the CNS. The Lancet Neurology. 2008;7(4):327–40.
4. Hoftberger R, Rosenfeld MR, Dalmau J. Update on neurological paraneoplastic syndromes. CurrOpinOncol. 2015;27(6):489–95
5. Kerasnoudis A. Isolated ZIC4 antibodies in paraneoplastic cerebellar syndrome with an underlying ovarian tumor. Arch Neurol. 2011;68(8):1073.