INCOORDINATION AND DIFFUSE ASTHENIA IN A YOUNG WOMAN WITH DEPRESSION: STILL A DIAGNOSTIC CHALLENGE.

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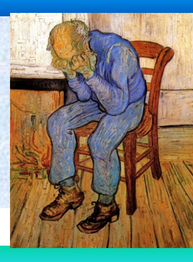
Key Words: major depression, anti-Yo antibody, paraneoplastic cerebellar degeneration, subacute cerebellar ataxia.

BACKGROUND

Generalized signs and symptoms concomitant to a clinically relevant depression are still a challenge in neurology, especially in young patients with a psychiatric history and no known somatic diseases.



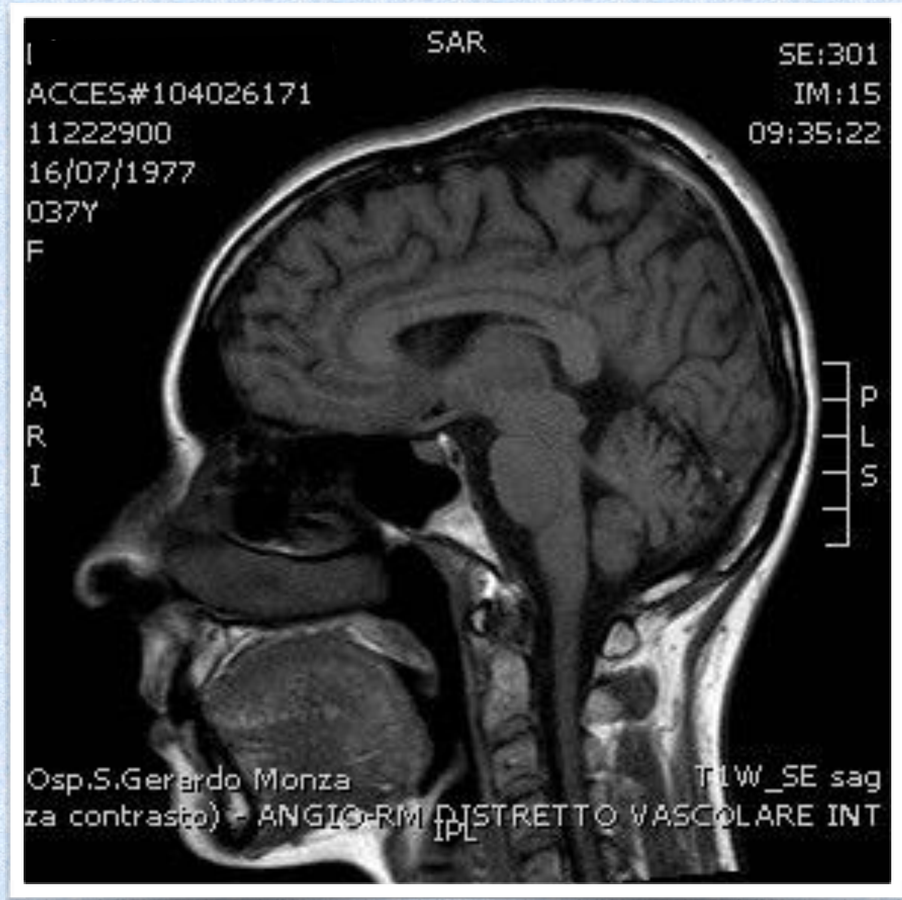
CASE REPORT

We present the case of a 37 y. o. woman with a psychiatric history of post-partum depression, without mention of anything else in her medical history and not taking any drug at home.
She was admitted for a slowly progressive incoordination and a diffuse asthenia which had appeared in the last few months.
At neurological examination patient showed a mild and inconstant gait imbalance.

All performed exams, i.e. EMG, head and spine MRI, cerebral PET, EEG, evoked potential, were negative. On completion of investigation, a lumbar puncture was performed with no cells and normal protein level.
The clinical profile was at this point considered secondary to a possible conversion disorder; a psychiatric consultation reported a major depressive disorder, so the patient was sent home with paroxetine 20 mg once daily.
Two weeks after discharge, the CSF report for oligoclonal bands arrived and came out to be positive (profile 2).
In the meantime worsening of ataxia was described together with a progressive difficulty of speech, demonstrated by slurring of words.
At this time, the physical exam revealed a frankly impaired cerebellar function with a Rankin scale > 3.
Her family history was positive for lung and ovarian cancer, so serology for an onconeural panel was performed and she was found to have positive serum anti-Yo antibodies.

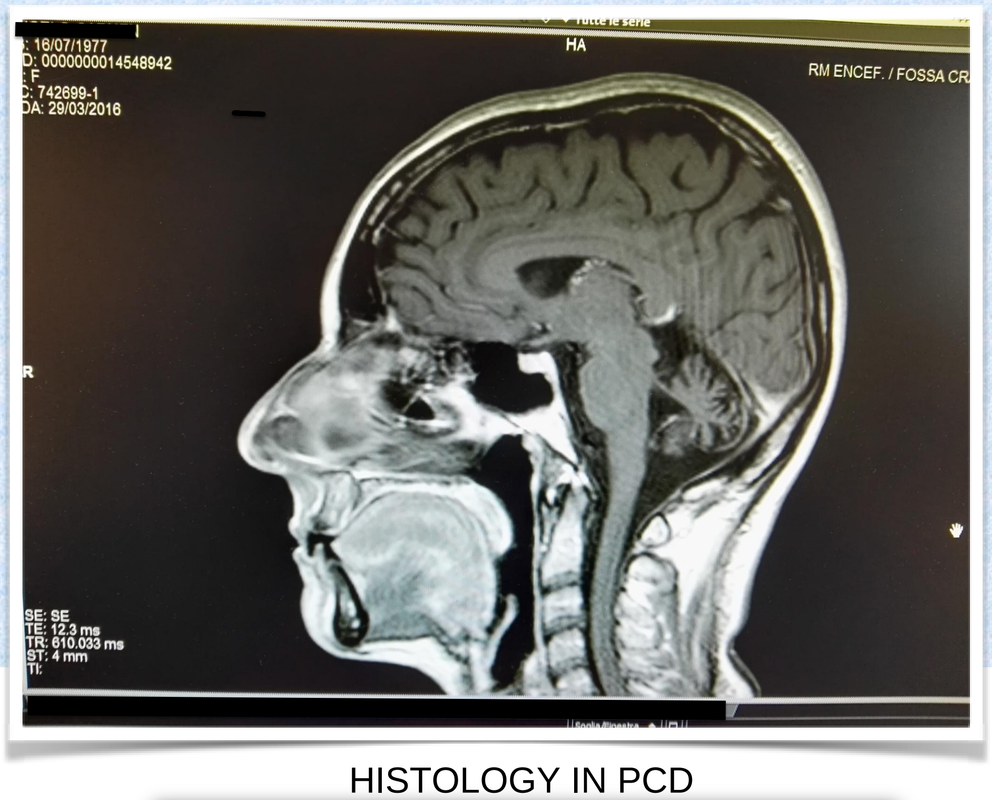
The subsequent work-up for an occult malignancy (comprehensive of breast, ovary, SCLC and Hodgkin's lymphoma) gave no results and it has remained negative after 1 year and half of neuro-oncological follow-up.

Brain MRI March 2015



[a Brain MRI performed after 1 year from the onset of symptoms has showed a significative cortical cerebellar atrophy].

Brain MRI March 2016



DIAGNOSTIC CRITERIA (1)
Definite Paraneoplastic Cerebellar Degeneration (PCD):
1.A classical syndrome and cancer that develops within five years of the diagnosis of the neurological disorder.
2. A neurological syndrome (classical or not) with well characterized onconeural antibodies (anti-Hu, Yo, CV2, Ri, Ma2, or amphiphysin), and no cancer.

To define a cerebellar syndrome as CLASSICAL, the following criteria are required: (2)
- Development in less than 12 weeks of severe pancerebellar syndrome with no MR evidence of cerebellar atrophy other than that expected by the age of the patient.
- The severity of the cerebellar syndrome should cause a Ranking score of at least 3 (symptoms interfere significantly with lifestyle)

Table 1. Differential diagnosis for subacute ataxia in adults.

Demyelinating diseases such as multiple sclerosis
Systemic autoimmune disorders such as sarcoidosis, behcet's, lupus
Alcohol abuse, Wernicke's syndrome, Vitamin E, B12 deficiencies
Medication toxicities e.g., Phenytoin
Miller-Fisher variant of Guillain–Barre syndrome
Steroid-responsive encephalopathy associated with thyroid disease
Anti-GAD antibody-associated ataxia
Gluten ataxia, celiac disease
Atypical infections: progressive multifocal leukoencephalopathy, prion disease, Whipple's disease
Paraneoplastic cerebellar degeneration

Onconeural antibodies PCD related

Paraneoplastic Cerebellar Degeneration	-Breast, ovarian, others	Anti-Yo (PCA-1)
	-SCLC, Neuroblastoma	Anti-Hu (ANNA-1)
	-SCLC,Thymoma	Anti-CV2
	-Hodgkin's lymphoma	Anti-Tr, Anti-mGluR1
	-Breast carcinoma	Anti-Ri (ANNA-2)
	-Seminoma	Anti-Ma

HISTOLOGY IN PCD

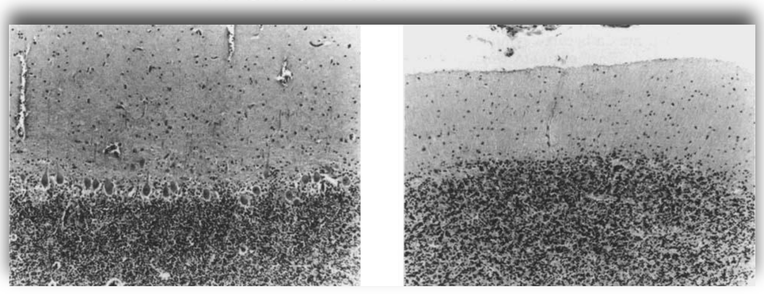


Figure. (A) Photomicrograph of normal cerebellar cortex from a 55-year-oldman who died of disseminated carcinoma without neurologic involvement. Purkinje cells are prominent at thejunction of the molecular and granular layers (hematoxylin-eosin;XlOO before 29% reduction). (B)View of the cerebellar cortex from a patient who died with anti- Yo-positive PCD demonstrating total Purkinje cell loss. Note the absence of inflammatory infiltrates (hematoxylin-eosin; XlOO before 29% reduction).

DISCUSSION AND CONCLUSION

A diagnosis of anti-Yo paraneoplastic cerebellar degeneration can at present be made.
As reported in most Guidelines, clinical examinations and radiological evaluations should be performed at 3-6 months intervals over the first two years and then once a year for the next 5 years. Some cases remain tumor free for all their life.

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