A CASE OF ATYPICAL PML MIMICKING ACUTE ISCHEMIC STROKE

M.T Infante [1], R. Gentile [1], L. Malfatto[1], G. Zocchi [1], G. Novi [2], L. Barletta [3], C. Rolla [3], C. Serrati[1]

1- Department of Neurosciences, Neurology, IRCCS San Martino IST, Genova

2- Department of Neurology, Oftamology, Genetics and Materno-Infantile Sciences, University of Genova

3- Department of Services, Neuroradiology, IRCCS San Martino IST, Genova

BACKGROUND

Progressive multifocal encephalopathy (PML) is a rare but often fatal infectious brain disease caused by the reactivation of Poliomavirus JC (JCV) [1]. This reactivation has been described in immunocompromized individuals with AIDS and leukaemia, on chemotherapy or being treated with immune suppressant drugs such as monoclonal antibodies, described in patient treated with natalizumab, efalizumab and rituximab used for the treatment of haematological malignancies, multiple sclerosis, psoriasis, Crohn's disease and rheumatic disease. [2]

CASE REPORT

A.A.M. is a 75 years old male with previous diagnosis of chronic lymphatic leukemia (CLL) in 2012, treated with clorambucile in 2012, followed by 6 cycles of fludarabine, cyclophosphamide and lenalidomide (in 2013 with complete response); for hemolytic anemia, patient was treated with rituximab and steroids with complete regression in 2014. In the recent history, he had thoracic herpes zoster reactivation in 2015.

On 5th March 2016 he had acute dizziness and balance disturbance, followed after one day by dysarthria and coordination disturbance at left limbs. We was conducted to San Martino Hospital (Neurology Unit) and underwent to **cerebral CT** showing a diffuse ipodensity of the left cerebellum and the middle cerebellar peduncle **(Figure 1-2)**

At neurological examination the patient had dysarthria and dysmetria at left limbs, left-direction nystagmus and balance problems. Suspecting acute ischemic stroke, antiplatelets therapy with aspirin was started, with gradual improvement of symptoms.

After about 7 days the patient presented a worsening of dizziness, with nausea and lack of appetite; we performed **CT scan** (unchanged) and gastroenterological investigations (negative).

The patient was discharged. After 10 days, he had acute onset of involuntary movements at left arm, interpreted as epileptic partial seizures, so antiepileptic therapy with levetiracetam was started with good response. After two days the patient had a rapid worsening of symptoms, with alteration of consciousness; the patient was only responsive at pain stimuli, with hyposthenia at left limbs, gaze deviation to the left. An Angio TC was performed, showing patency of basilar and vertebral arteries, while cerebral CT scan was unchanged. Because of the presence of fever and rigor nucalis, suspecting infective encephalitis, a **lumbar puncture** was performed showing only oligoclonal bands on CSF and serum. PCR for neurotropic viruses (HSV, VZV, CMV, EBV, Adenovirus and Enterovirus) and cultural examination of CSF were negative. A broad spectrum antiviral and antibacterial therapy was started without symptoms improvement . Blood test exams were normal.

A brain MRI revealed an asimmetric T2/FLAIR hyperintensity in bilateral cerebellar white matter from left to right without mass effect, in bilateral middle cerebellar peduncles and similar abnormalities were seen in the upper pons and in a small part of mesenchephalum without contrast enhancement (Figure 3); Diffusion-weighted images (DWI) (Figure 4) showed signal increase without detectable ADC changes.

We performed another lumbar puncture : PCR for JCV virus on CSF was positive (11300 copies/ml), while PCR for JCV on peripheral blood was negative. The patient quickly deteriorated with death after 10 days.

DISCUSSION

Treatment with monoclonal antibodies is a new identified predisposing factor for PML development.

We describe an unusual case of acute brainstem and cerebellar PML following chemotherapy for CCL diagnosed two years before in a 75 years old man without any signs of immune dysregulation at admission. Symptoms onset was very rapid and occurred after more than two years from last rituximab infusion; patient had a **sudden neurological deterioration, with rapid progression to death** in about a month from symptoms onset. Lesions were localized at cerebellum and pons, this pattern has been reported in few cases in literature.

In this case, as shown better by MRI than CT, the absence of a distinctive vascular territory lesion distribution, despite the acute clinical course and the posterior fossa localization, could have been an early clue to a correct diagnosis.

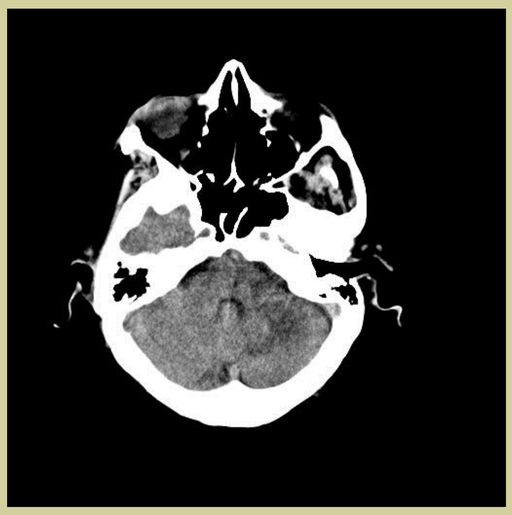

Figure 1: Cerebral CT Scan

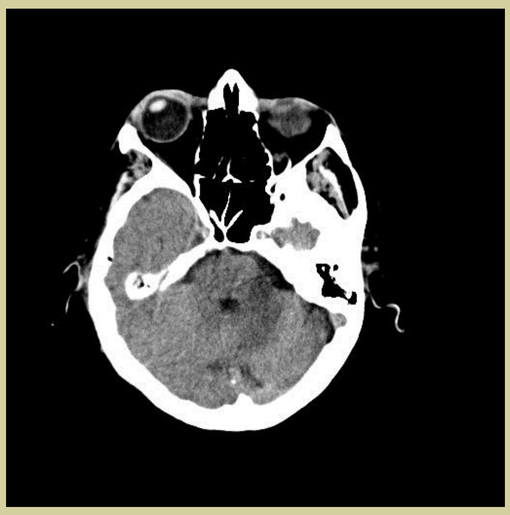

Figure 2: Cerebral CT Scan

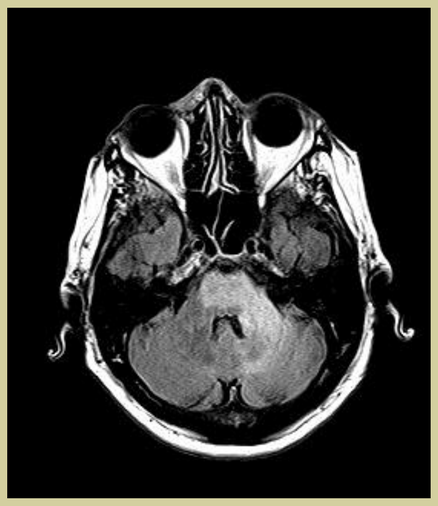

Figure 3: Axial FLAIR MRI

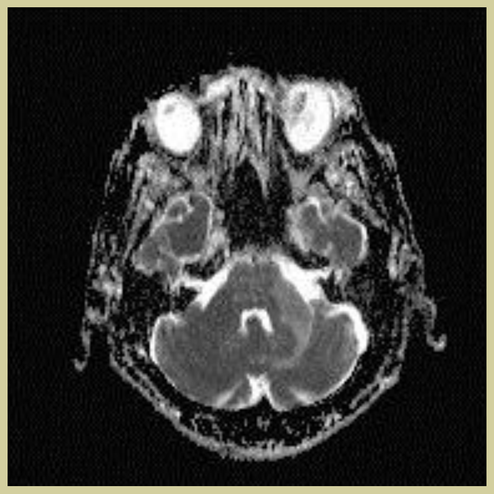

Figure 4: DWI MRI seq

References:

1-M. A. Sahraian, E.-W. Radue, et aò. Progressive multifocal leukoencephalopathy: a review of the neuroimaging features and differential diagnosis. European Journal of Neurology 2012, 19: 1060–1069.

2- V. Felli, A. Di Sibio, et al Progressive Multifocal Leukoencephalopathy Following Treatment with Rituximab in an HIV-Negative Patient with Non-Hodgkin Lymphoma. A Case Report and Literature Review The Neuroradiology Journal 27: 657-664, 2014 - doi: 10.15274/NRJ-2014-10087