Anaplastic lymphoma presenting as paraneoplastic cerebellar degeneration (PCD): A case report and review of literature

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Case Report

Abstract

Paraneoplastic cerebellar degeneration (PCD) is a paraneoplastic neurological syndrome rarely associated with Non-Hodgkin lymphoma. Only 10 cases have been reported in the literature, 6 of them showing poor clinical neurological outcome. We report a case of PCD in a patient with ALK negative anaplastic large cell lymphoma and review of the literature.

Keywords: Anaplastic Lymphoma, Paraneoplastic cerebellar degeneration, Paraneoplastic cerebellar degeneration

Introduction

Paraneoplastic neurological syndromes (PNS) are rare malignancy complications that occur in less than 0.01% of cancer patients. Paraneoplastic cerebellar degeneration (PCD) is generally associated with breast and ovarian cancer, microcytic lung carcinoma and Hodgkin Lymphoma. It is characterized by the presence of acute onset of dizziness and vertigo with progression to ataxia, dysarthria, diplopia and nystagmus.

We report a case of PCD in a patient with ALK negative anaplastic large cell lymphoma. Given that PCD is an atypical manifestation of lymphoma and the low frequency of paraneoplastic neurological syndromes, the presentation of this case is deemed interesting.

Case presentation

A 59-year-old male, with a past medical history of hyperlipidemia and active smoker (40 packs/year), presented to the clinic Emergency Room (ER) with a one-month history of dizziness worsened by postural changes, progressing to ataxia associated with nausea, vomiting, anorexia and weight loss. No headache, fever or sweating.

Physical examination results in slight bradypsychia, dysarthria and extreme thinness. Neither adenopathies nor splenomegaly was present. Neurological examination revealed horizontal-rotary nystagmus with bilateral spontaneous saccadic movements, infraversion and hypometric saccades. Patient had dysmetria, dysdiadochokinesia and dyssnergia in limbs, more evident in both lower limbs; and a wide-based ataxic gait. Tone, motricity and sensitivity were preserved. The remaining examination yielded no relevant findings.

Brain Computed Tomography scan performed in the ER did not detect structural lesions. Urgent analyses performed showed no relevant findings. The patient was admitted to the neurology department with the diagnosis of subacute cerebellar syndrome for evaluation.

A brain magnetic resonance imaging (MRI) performed suggested the presence of stage IV leukoaraiosis and marked signs of cerebral and cerebellar cortical atrophy. Neurophysiological studies did not reveal alterations. The cerebrospinal fluid (CSF) showed discrete hyperproteinorrhachia (56.2 mg/dL normal values [15.0 - 45.0]) and a leukocyte count of 7 cel/μL (NV [0.0 - 5.0]), at the expense of normal lymphocytes; negative microbiological study and absence of malignant cells.

Complete blood cell count was normal, lactate dehydrogenase was 440U/L (NV [208.0 - 378.0]) and Beta-2 microglobulin was 1383 U/L (NV [800.0 - 2400.0]). Liver and renal function tests were normal. The autoimmunity study was negative, as well as the serological studies (Human immunodeficiency virus, Hepatitis C virus, Varicella Zoster virus, Epstein Barr virus, Cytomegalovirus, lues, brucellosis, Listeria, Lyme Disease negative for IgM) and viral PCR’s. All tumor
markers were negative, as were onconeural antigens (Anti-amphiphysin, Anti-CV2, Anti-Ri, Anti-Yo, Anti-Hu, Anti-Ma2, Anti-Recoverin, Anti-TR).

Once structural lesion, meningeal infiltration, autoimmune or infectious disease were discarded, and suspecting a paraneoplastic syndrome, decision was made to carry out an extension study.

Thoracic CT scan allowed observing multiple upper and lower pretraqueal, subcarinal and right hilar adenopathies. The abdominal-pelvic CT scan identified small-size, round and irregular images lacking contrast enhancement in the spleen; prostatic calcifications and no retroperitoneal adenopathies. The Positron Emission Tomography (PET/CT) showed pathological deposits in the left clavicular fossa and in both upper and lower parastrachal regions, infiltrating the hilum; and a large retrosternal mass extending to the left parastrachal region.

The pathology and immunohistochemistry of pretracheal adenopathy, removed by mediastinoscopy, reveals a large cell anaplastic lymphoma CD30 +, CD20 -, ALK -. Bone marrow aspiration and biopsy showed no morphological alterations, nor atypical lymphoid infiltration.

After the pathology results, patient was referred to outpatient hematology consult for staging and treatment. While hospitalized in the neurology department and before the diagnosis was made, the patient was treated with methylprednisolone at a dose of 500 mg for 5 days, and further tapering, with no significant changes observed from the neurological point of view.

With the diagnosis of stage III-A ALK negative anaplastic lymphoma, treatment with Cyclophosphamide, Adriamycin, Vincristine and Prednisone (CHOP) was started. Since there was no evidence of central nervous system (CNS) infiltration, treatment did not include intrathecal chemotherapy or prophylaxis.

Following six CHOP cycles, PET-CT shows complete response, no changes are observed in the MRI and the neurological symptoms persist with no significant changes. Patient is being controlled in outpatient hematology consults, remaining in complete response six months post treatment.

### Table 1: NHL cases associated with PCD

<table>
<thead>
<tr>
<th>Histology</th>
<th>Stage</th>
<th>Onconeural Antibody</th>
<th>Treatment</th>
<th>Clinical neurological outcome</th>
<th>Lymphoma outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>FL</td>
<td>IV</td>
<td>NA</td>
<td>R-CHOP</td>
<td>AlmostResolved</td>
<td>CR</td>
<td>(1)</td>
</tr>
<tr>
<td>DLBCL</td>
<td>NA</td>
<td>-</td>
<td>NA</td>
<td>Worsen</td>
<td>NA</td>
<td>(3)</td>
</tr>
<tr>
<td>ALLC</td>
<td>III</td>
<td>-</td>
<td>CHOP</td>
<td>Worsen</td>
<td>CR</td>
<td>(4)</td>
</tr>
<tr>
<td>HL+B-LPD</td>
<td>II</td>
<td>+ (Anti-TR)</td>
<td>ABVD</td>
<td>Partiallyimproved</td>
<td>CR</td>
<td>(5)</td>
</tr>
<tr>
<td>NHL</td>
<td>I</td>
<td>-</td>
<td>Radiation</td>
<td>Partiallyimproved</td>
<td>CR</td>
<td>(6)</td>
</tr>
<tr>
<td>NHL</td>
<td>II, relapsed</td>
<td>-</td>
<td>COP</td>
<td>Stable</td>
<td>CR</td>
<td>(7)</td>
</tr>
<tr>
<td>T-NHL</td>
<td>IV</td>
<td>-</td>
<td>COP</td>
<td>Worsen</td>
<td>PR</td>
<td>(8)</td>
</tr>
<tr>
<td>T-NHL</td>
<td>III</td>
<td>-</td>
<td>ACOMP-B</td>
<td>Worsen</td>
<td>CR</td>
<td>(9)</td>
</tr>
<tr>
<td>DLBCL</td>
<td>IV</td>
<td>-</td>
<td>R-CHOP</td>
<td>Partiallyimproved</td>
<td>CR</td>
<td>(10)</td>
</tr>
</tbody>
</table>

Discussion

The scarce tumors that cause PNS are often indolent, sometimes hidden and can predate the malignancy diagnosis in up to 80% of patients. PNS constitute a remote effect of the neoplasia in the CNS, not justified by the presence of metastasis, direct infiltration, toxicity or ectopic hormone secretion; being PCD one of the different types of PNS. It is believed they are caused by the activation of onconeural antigens; in fact, antibodies against these antigens have been identified in serum and in the CSF of many patients with PNS. Nowadays their detection constitutes the most useful diagnostic test but they are often negative in lymphoma cases, as were in our patient.

The literature, up to 2014 has only published ten cases of PCD associated with Non-Hodgkin Lymphoma (Table 1), one of them associated with anaplastic lymphoma. Neurological symptoms improved partially in three cases, remaining stable in two as with the case of the patient presented, worsened in four despite chemotherapy, and almost resolved in one of the cases. Two of the latest cases reported presented in gastric diffuse large B-cell lymphomas.

It should be noted that our patient did not respond to high doses of corticosteroids, nor did the neurological symptoms with chemotherapy once complete response was achieved.

Conclusion

PCD is rarely associated with Non-Hodgkin lymphomas. Given the irreversibility of symptoms in most reported cases and aiming to improve prognosis, proper treatment should be started in the early phases of the disease.

Conflict of interest

The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References