Anti-SOX1 antibodies in a patient with neurolymphomatosis: just a coincidence?

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BACKGROUND

Neurolymphomatosis (NL) denotes infiltration of cranial nerves, peripheral nerves, nerve roots or plexus by malignant lymphomatous cells. It is histopathologically characterized by tumor cell infiltration of the endoneurium and perineurium. NL tends to occur with aggressive subtypes of B-cell non-Hodgkin lymphoma (NHL), such as diffuse large B-cell lymphoma, and carry a poor prognosis. On imaging, it is most often demonstrated by nerve root or nerve sheath thickening. It's important to differentiate NL from other causes of peripheral nervous system (PNS) involvement in lymphoma (i.e. paraneoplastic PNS involvement, radiation or chemotherapy induced damage), since their treatment modalities differ. Onconeural anti-SOX1 antibodies target a protein of the Sry-like high mobility group superfamily of developmental transcription factors that are preferentially expressed in the Bergmann glia in the adult cerebellum. They were initially described in patients with small cell lung cancer (SCLC) without neurological disorders and then found to be predictive for a paraneoplastic etiology in Lambert-Eaton myasthenic syndrome associated with SCLC. In 2010 Tschernatsch et al. found anti-SOX1 antibodies in patients with neuropathies of unknown origin in the absence of cancer [1].

CASE REPORT

A 59-years-old woman was referred to us after presenting with a symptomatology characterized by headache, bilateral peripheral facial palsy, masticatory weakness, difficulty swallowing and hypogeusia. These symptoms started insidiously 3 months before and progressively worsened. She had a 3-year history of a diffuse large-B-cell NHL primarily localized in mediastinum, which has been treated with Rituximab, cyclophosphamide, vincristine, adriamycin and prednisone (R-CHOP regimen) with a complete remission for 13 months. Two months before the access to our Unit, she underwent to a brain magnetic resonance imaging (MRI), which was normal.

Appropriate clinical investigations were performed, including:

- Routine blood analysis: unremarkable.
- Cerebrospinal fluid (CSF) examination: normal cell and protein count, no evidence of atypical cells.
- Brain MRI: on T1 weighted and gadolinium-enhanced sequence thickening and contrast enhancement of multiple cranial nerves, possibly related to lymphomatous infiltration [***Figure 1***].
- Total body CT: no signs of relapse of lymphoproliferative disorder on lymph nodes.
- Onconeural antibodies screen: high positivity of anti-SOX1 antibodies.

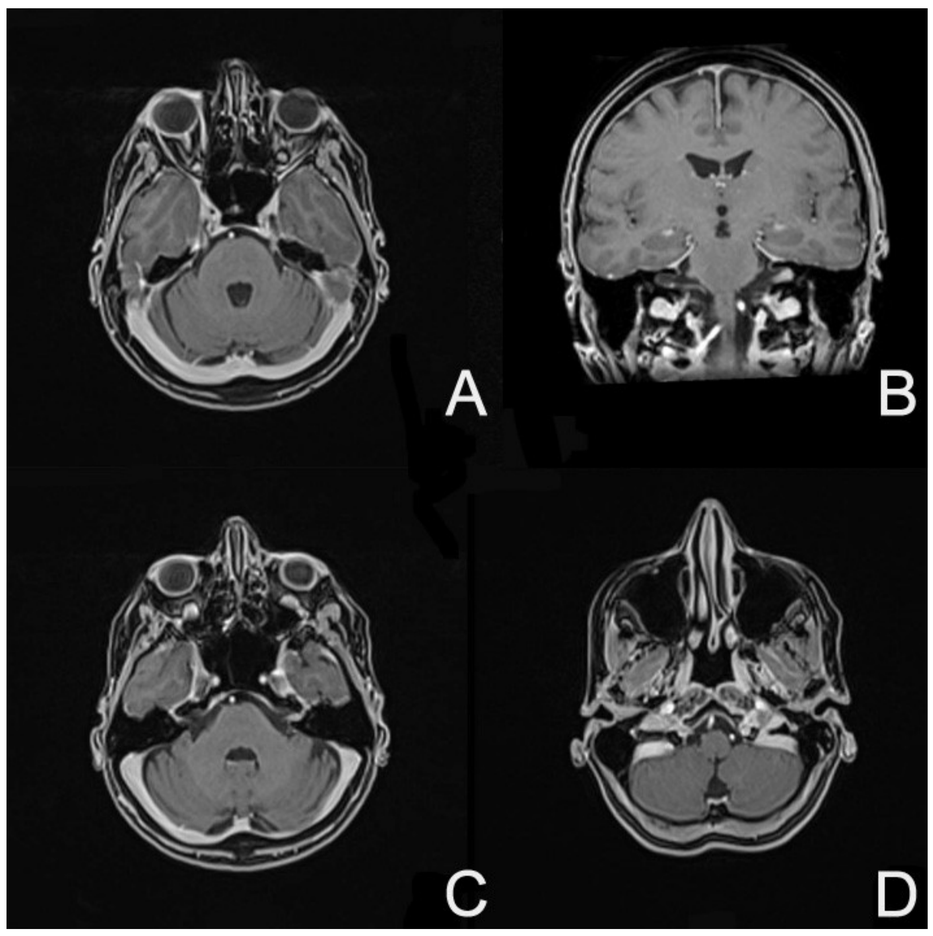

Figure 1. Brain MRI: thickening and contrast enhancement of multiple cranial nerves (bilateral trigeminal [A], bilateral facial [B], bilateral vestibulocochlear [C] and right glossopharyngeal [D] nerve) on T1 weighted sequences.

DISCUSSION

NL is a rare neurologic manifestation of lymphoma and is more common in relapse than in primarily presentation. Here we described a case of a patient with multiple cranial neuropathy, appeared 13 months after remission of a diffuse large-B-cell NHL. In differential diagnosis we considered NL and paraneoplastic neurological syndrome and found a brain MRI suggestive of NL and positivity of onconeural anti-SOX1 antibodies. Anti-SOX1 antibodies have been found in various paraneoplastic and non-paraneoplastic neurological disorder, predominantly polyneuropathy [2]. They have never been reported in NHL and in literature there is only one case report of their positivity in a patient with Hodgkin's lymphoma and paraneoplastic limbic encephalitis [3]. In our case, the presence of anti-SOX1 antibodies could just be an epiphenomenon of the NL or we can speculate to be predictive of a relapse of NHL. One the first brain MRI, performed one month after the onset of the neurological symptoms, there were no signs of disease on cranial nerves. On that time, unfortunately, onconeural anti-SOX1 antibodies were not tested but, being highly positive after two months, we can assume that their production started many weeks before the time we tested.

In conclusion, it is important to further define the potential diagnostic impact of anti-SOX1-positive test result.

REFERENCES

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