Atypical neurologic complications of anticancer target therapy

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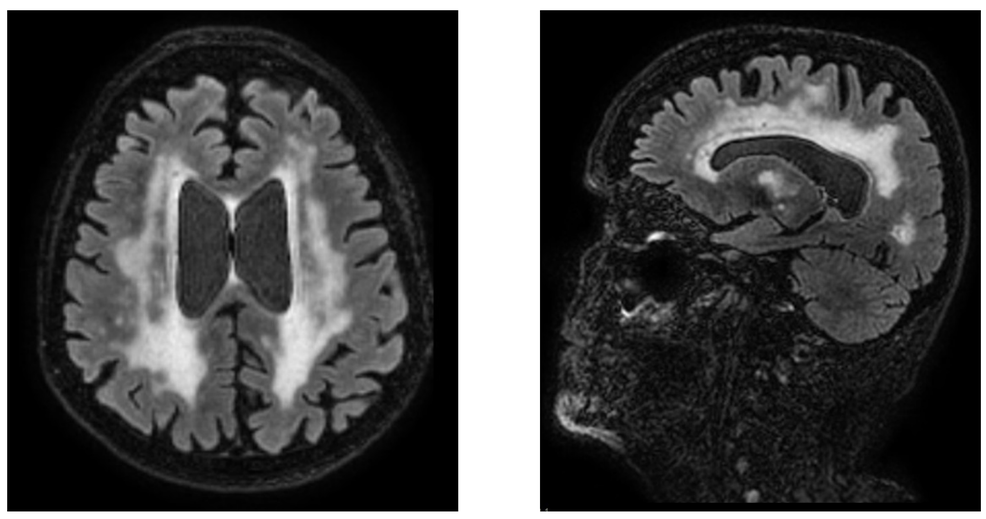
Introduction Monoclonal antibodies (mAbs) are a proven effective therapeutic modality in cancer. Several mAbs are approved to targets critical in oncogenic signaling within tumors cells. Many of the characteristic side effects experienced by patients treated with target therapy are relatively novel compared with cytotoxic chemotherapy previously used to treat cancer. The most common adverse events associated with mAbs target agents are cutaneous, arthralgia, diarrhoea and fatigue. Several neurological adverse effects induced by acute and chronic exposure to these drugs have been reported including inflammatory myopathy, aseptic meningitis, posterior reversible encephalopathy syndrome, Guillain-Barre´ syndrome, and sensorimotor neuropathy. We report 3 cases of atypical neurological complications observed in melanoma patients treated with vemurafenib (BRAF-targeted mAb) in which patients developed peripheral neurotoxicity and a leucoencephalopathy possibly related to ipilimumab (a recombinant human monoclonal antibody that blocks cytotoxic T-lymphocyte antigen-4 and potentiates an immune response) treatment.

Cases 1-2: The first patient was a 61-y old woman that presented neuropathic symptoms from July 2013 with paraparesis, numbness, pricking, cold, sharp and tingling paresthesias in soles of feet. Nerve conductions were suggestive of CIDP. Venurafenib treatment was interrupted and therapy with prednisone was administered with at a dosage as 50 mg/day (1 mg/kg/day) with mild clinical improvement. All autoanticorpal dosage and onconeural antigen were negative. The second patient was a 72-y old female that presented neuropathic symptoms from june 2013 with pain, ataxia and dizziness. Nerve conductions were suggestive of CIDP and she was treated with prednisone therapy 50 mg/day and after with Ig e.v 0,4 mg/kg/die for 5 days. (100 g/die) with mild neurological improvement.

Case 1*: *Electroneurography
Sural nerve: left absent; right ampl= 1.4 μV
Median sensory nerve: right ampl= 2 μV
Tibial nerve: F reflex=55; motor ampl. 0.3 mV
Peroneal nerve:F reflex 53.3; motor ampl 2.6 mV

Case 3
Axial T2 fluid-attenuated inversion recovery (FLAIR) images showing hyperintensity in the periventricular with matter and cortical atrophy.



Results
Case 3: A 52-y old women with metastatic melanoma previously treated with Ipilimumab immunotherapy presented cognitive and gait disturbancies. Brain MRI showed a diffuse leucoencephalopaty. Neurological examination revealed a tetraparesis with extrapyramidal syndrome, ataxia and severe cognitive deficit. The research of neurotropic viral agents and paraneoplastic antibodies were negative in serum and CSF laboratory tests. Patient was treated with steroids without clinical effects and 2 cycles of ev Ig but she presented progressive neurological deterioration.

Conclusions: Recognition of target anticancer related neurological complications is critical to the early institution of appropriate management.

References
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