A case of hypophysitis associated with Nivolumab in a patient with relapsed/refractory Hodgkin's lymphoma

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Introduction*:* Nivolumab is an anti-PD-1 monoclonal antibody (Ab). Its clinical use is approved to treat patients with melanoma and non-small squamous cell lung cancer. Recently, high response rates have been reported in refractory/relapsed Hodgkin lymphoma (HL) (1). Hypophysitis is a side effect of Nivolumab that occurs in 0.5–0.9% of patients (2). We report a case of hypophysitis after Nivolumab treatment in a patient with relapsed/refractory Hodgkin's lymphoma.

Case report: a 43-year-old woman admitted to the Department of Hematology of our hospital for Hodgkin's lymphoma was referred to us complaining of confusion, headache, asthenia and hallucinations. She had a history of relapsed/refractory Hodgkin lymphoma diagnosed in February 2012 and treated with chemotherapy, autologous stem cell transplantation, brentuximab and, in 2014, with allogeneic stem cell transplantation. The patient started Nivolumab in a compassionate use program called "name patient program". Ten days after the first dose of Nivolumab she developed symptoms described above.

Neurological examination showed action and postural tremor in the upper limbs.

Brain MRI with gadolinium showed swelling of the anterior portion of the infundibulum with subtle hyperintensity on FLAIR images (Fig. 2) and marked contrast enhancement in T1 (Fig. 1, 3, 4). The usual hyperintense signal in T1 of the neurohypophysis was not recognizable. The pituitary peduncle appeared thinned. The adenohypophysis was thinned compared with the previous control.

Blood tests showed low levels of serum insulin growth factor-1 (IGF-1), follicle stimulating hormone (FH) and luteinizing hormone (LH) while prolactin level was high; adrenocorticotropic hormone (ACTH) and growth hormone (GH) levels were normal.

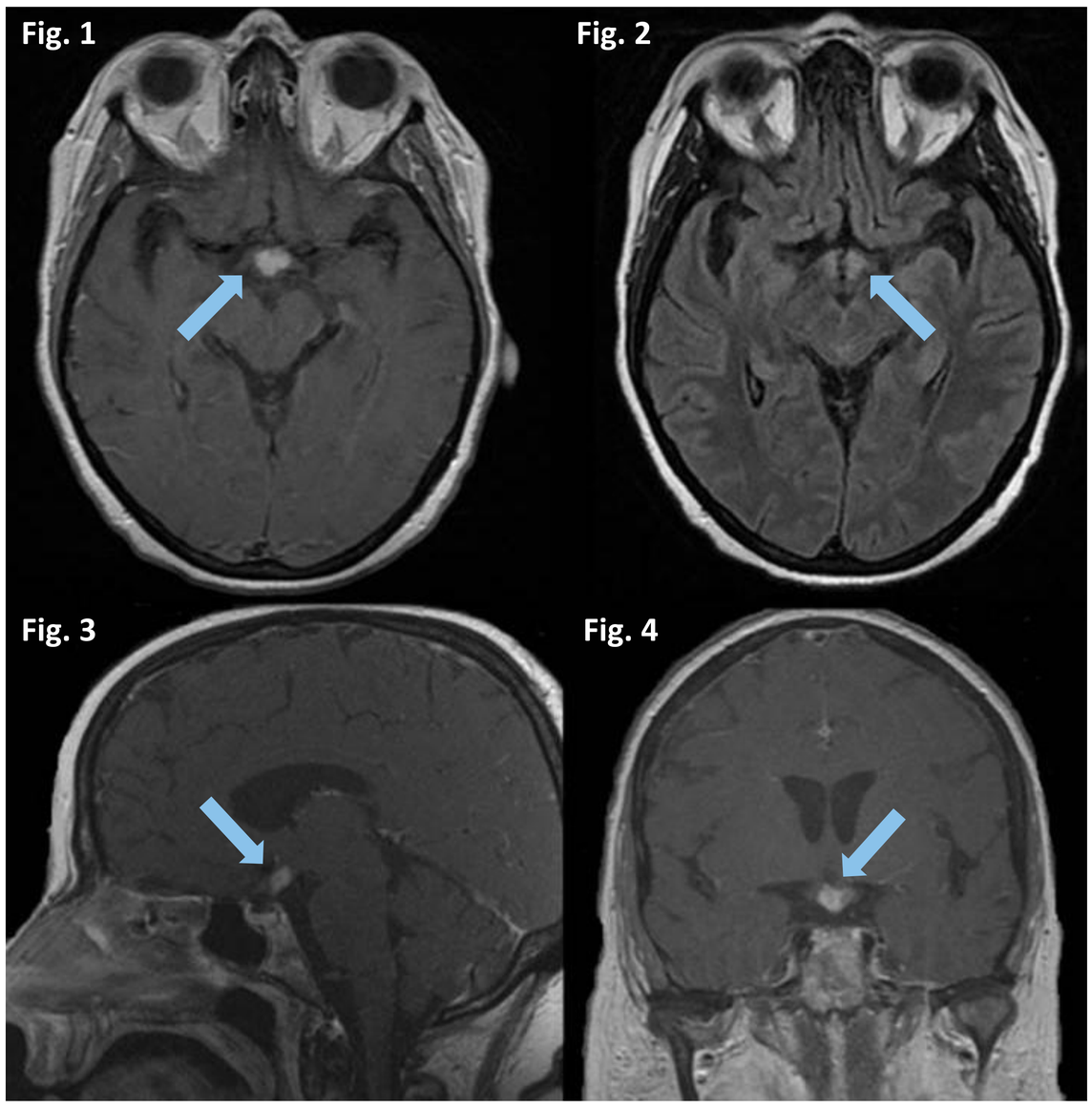

Figure 1, 3, 4: T1-weighted images with gadolinium
Figure 2: FLAIR image

Discussion: immune checkpoint inhibitors (ICI) may trigger autoimmune syndromes involving different organs, including several endocrine glands (pituitary, thyroid, adrenal, and endocrine pancreas). Hypophysitis is frequently associated with Ipilimumab (anti-CTLA4-mAb), whereas thyroid dysfunction is generally secondary to Nivolumab. Anterior pituitary hormone deficiencies are often associated with hypopituitarism secondary to ICI hypophysitis. Prolactin level is usually altered, more frequently low than high. Moreover low serum insulin growth factor IGF-1 levels have been reported in literature.

Conclusion: In patients treated with Nivolumab presenting even non-specific symptoms such as headache, fatigue and confusion, hypophysitis should be suspected. In these cases laboratory exams along with brain and hypophysis MRI are recommended. The treatment strategy consists of high-dose glucocorticoids. The hypophysitis is treatable and does not preclude the therapy with Nivolumab.

•(1) Bone Marrow Transplant. 2016 Feb 1. Major clinical response to nivolumab in relapsed/refractory Hodgkin lymphoma after allogeneic stem cell transplantation. J A Yared, N Hardy, Z Singh, S Hajj, A Z Badros, M Kocoglu, S Yanovich, E A Sausville, C Ujjani, K Ruehle, C Goecke, M Landau and A P Rapoport

•(2) Curr Opin Oncol. 2016 Apr 28. Endocrinological side-effects of immune checkpoint inhibitors. Torino F, Corsello SM, Salvatori R.

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