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# Anti-PD-L1 therapy-associated hypophysitis and limbic encephalitis

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## TITLE PAGE

### Manuscript title:

**Anti-PD-L1 therapy associated hypophysitis and limbic encephalitis**

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## TEXT

A 71-year-old woman with history of neuro-endocrine tumor was admitted to our intensive care unit because of a fluctuating level of consciousness preceded by the subacute onset of a working memory deficit. She had been treated five months before with two cycles of 1500 mg Durvalumab – an anti-PD-L1 (Program Death-Ligand 1) antibody. Initial MRI found bilateral FLAIR hyperintensities of the hypothalamic and limbic regions (Figure 1). Remarkably, ASL exhibited a hyperperfusion suggestive of hypermetabolism, which has been described in encephalitis. CSF analysis showed a lymphocytic pleocytosis (8 cells/ $\mu$ L) with high protein rate (183 mg/dL) and positive oligoclonal bands. Antineuronal antibodies including onconeuronal antibodies were absent in serum and CSF. No evidence of cancer relapse was found. Exploration of the hypothalamic-pituitary-adrenal axis showed central hypothyroidism, hypogonadism, and diabetes insipidus. She was diagnosed with autoimmune hypophysitis and limbic encephalitis associated with immune checkpoint inhibitor treatment. Rapid improvement was observed after high dose IV steroids and therapeutic plasma exchange. One-month control MRI found improvement of limbic lesions with regression of pituitary swelling (Figure 2).

Encephalitis is an increasingly identified complication of immune checkpoint inhibitors. Metabolic consequences of hypophysitis as well as impaired consciousness or status epilepticus frequently lead these patients to intensive care units. Early clinical and radiological diagnostic is important to promptly start immunomodulation treatment.

## FIGURES LEGEND

### Figure 1. Durvalumab-induced limbic encephalitis

Axial (A) and coronal (B) bilateral FLAIR hyperintensities of the hypothalamus, optic radiations, midbrain, and amygdala, hyperperfused in ASL (C), with partial enhancement on coronal T1 post-contrast images (D).

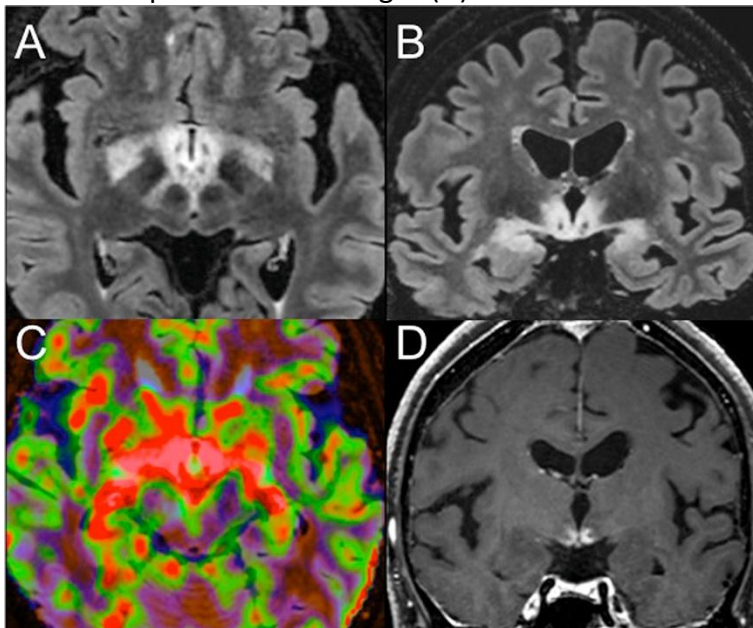


Figure 2. Regressive Durvalumab-induced hypophysitis after treatment

Sagittal T1 post-contrast images: pituitary swelling with homogeneous enhancement (A), regressive on one-month control MRI (B).

