A unique case of IgG4-related pachymeningitis treated with intrathecal rituximab.

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Objective:

Meningeal involvement represents one of the most challenging manifestations of IgG4-related disease (IgG4-RD) in terms of both diagnostic and therapeutic approaches. We report a unique case of IgG4-related pachymeningitis (IgG4-RP) complicated by optic neuritis treated with intrathecal rituximab, and describe clinical, functional, immunological and radiological outcomes.

Methods:

The reported case was investigated with serial neurophthalmological evaluations, serological, microbiological, and flow cytometry studies, cerebro-spinal fluid (CSF) analyses, whole body computed tomography (CT) scan and brain magnetic resonance (MR) imaging.

Results:

A 30 years old Tunisian woman was admitted in August 2015 because of headache with right eye blindness and a hard-palate mass. Blood works showed increased serum IgG4 and plasmablasts levels. A neurophthalmological evaluation confirmed right eye blindness due to inflammatory/compressive neuropathy. Whole body CT scan showed diffused nasal mucosa thickening and multiple osteolytic areas in the skull. MRI showed thickening of the frontal dura mater with diffuse white matter edema and enhancement of both optic nerves. CSF analysis showed an altered blood-brain barrier with intrathecal production of IgG1 and IgG4. Histological examination of the hard palate mass was diagnostic for IgG4-RD. She was treated with 3 intravenous pulses of methylprednisolone (1000 mg in three consecutive days) followed by oral prednisone 50 mg/die. In October 2015 blindness persisted; a brain MR and a neuro-ophtalmological visit showed worsening of the optic neuropathy on the left eye and persistent meningeal thickening. She was therefore treated with rituximab (two 1000 mg infusions 15 days apart). In February 2016, resolution of the hard palate mass and slight improvement of the visual field on the right side were
noted. However, MR and neuro-phtalmological evaluations described worsening white matter edema, persistent dural thickening and bilateral optic neuropathy. In addition the patient experienced generalized seizures. We therefore administered intrathecal rituximab (two 25 mg infusions one month apart) according to protocols already published for central nervous system lymphomas and multiple sclerosis. In April and July 2016 brain MR and neuro-phtalmological evaluations showed progressive improvement of the frontal edema and optic neuropathy with subjective visual improvement of the right eye and colors perception. Interestingly, intrathecal rituximab reduced circulating plasmablasts and CSF IgG subclasses.

Conclusions:

This represents the first case in which rituximab is used intrathecally for an inflammatory pachymeningitis. Our experience suggests that intrathecal rituximab is safe and represents a promising therapeutic strategy in patients with meningeal and central nervous system involvement of IgG4-RD who failed systemic treatments.