Anterior Optic Neuropathy Associated with Adalimumab

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\textbf{Key Words} \\
Adalimumab \cdot Optic neuropathy \cdot Adverse side effects \cdot Eye affection \cdot TNF-\(\alpha\) antagonists

\textbf{Abstract} \\
\textbf{Purpose:} Our purpose was to report a case of anterior optic neuropathy with pupillary edema in a patient treated with the TNF-\(\alpha\)-antagonist adalimumab. \textbf{Methods:} We report the case of a 60-year-old woman with optic neuropathy in 1 eye after 6 months of treatment with adalimumab. \textbf{Results:} The patient developed decreased visual acuity of the left eye. The ocular findings were left optic disc swelling and bleeding at the rim, superior visual field depression in both eyes and left afferent pupillary defect. Adalimumab was discontinued and the visual acuity recovered slowly. \textbf{Conclusions:} Like infliximab, the modern TNF-\(\alpha\) antagonist adalimumab is associated with optic neuropathy. Ophthalmologists should thus be alert when seeing patients treated with adalimumab.

\textbf{Introduction} \\
The FDA approval of the TNF antagonist adalimumab (Humira\textsuperscript{TM}) comprises the treatment of rheumatoid arthritis and Crohn’s disease (FDA License No. 0043). The TNF-\(\alpha\) antagonists infliximab and etanercept were reported to be associated with toxic anterior optic neuropathy, vasculitis, demyelinating events, optic neuritis and multiple sclerosis [1–3]. To our knowledge, adalimumab has been associated with optic neuritis in 2 reports [4, 5].

\textbf{Material and Methods} \\
Herein we report the case of a 60-year-old woman with anterior optic neuropathy who was treated with adalimumab 40 mg subcutaneously every 2 weeks for 2 months because prednisolone and methotrexate had failed to alleviate the severe rheumatic affection of multiple joints. The last dose had been administrated 2 weeks before presentation.

\textbf{Results} \\
The patient presented with blurred vision and reported a black shadow in her left eye for 5 days. The best-corrected visual acuity was 20/25 in the left eye and 25/25 in the unaffected right eye. A left afferent pupillary defect was present. Funduscopic examination revealed optic disc swelling with hyperemic optic nerve, bleeding at the rim of the optic disc and the findings of a mild hypertensive retinopathy (fig. 1). Automated central visual field testing identified a superior visual field scotoma in the left eye and superior altitudinal depression in the right eye (fig. 2). Red color vision was subjectively decreased in the left eye. A review of systems revealed mild hypertension and a treatment for depression. Other medication included prednisolone 4 mg daily, L-thyroxin 50 \(\mu\)g, diclofenac 50 mg, sertraline 50 mg, ramipril 5 mg, atenolol
2.5 mg daily and methotrexate 7.5 g per week. Laboratory workup demonstrated normal levels for complete blood count, comprehensive metabolic panel and erythrocyte sedimentation rate. Serologic testing found no pathological findings of antinuclear antibodies, rheumatoid factor, ACE or treponemal antibody. Ultrasonography of the orbit and gadolinium-enhanced MRI of the brain and the orbit did not reveal any pathology and excluded a reactivation of endocrine orbitopathy for which the patient had been treated with prednisolone 10 years before. In consent with her rheumatologist, adalimumab was discontinued. The patient received ASS 300 daily and pentoxyphylline 600 mg intravenously for 5 days and the prednisolone dose was increased to 1 g daily over 3 days. Six weeks later the visual acuity had recovered completely and visual field testing revealed a decreased superior scotoma.

Fig. 1. Fundus photography of the left eye taken at initial examination showing optic disc edema with bleeding and vasodilata-
tions.

Fig. 2. Automated Octopus 101 central threshold testing (Octopus Interzeag 101, Haag-Streit, Kôniz, Switzerland) of both eyes. Gray scale and pattern deviation show superior visual field depression of the right eye (a) and superior altitudinal scotoma in the left eye (b).
Discussion

TNF inhibitors can offer major benefit to patients with severe rheumatologic diseases that do not respond to standard immunosuppressive therapy. However, at least 10 cases are documented which associate etanercept and infliximab with de novo onset of optic neuritis [1–3, 6]. To our knowledge there are 2 reports of optic neuritis, thereof 1 concerning the onset of multiple sclerosis associated with adalimumab [4, 5]. Our patient displayed anterior optic neuropathy without enhancement in the MRI, which is similar to the published case series of optic neuritis associated with infliximab reported by ten Tusscher et al. [6]. The pattern of the scotoma and the improvement of the patient's condition after treatment disagree with the differential diagnosis of hypertensive ischemic neuropathy.

With regard to a recent study that demonstrated an increased risk of demyelinating events in patients with inflammatory bowel diseases independently of the treatment, the role of rheumatoid arthritis in optic neuritis must be addressed [7]. A review of the literature revealed that, unlike ankylosing spondylitis, rheumatoid arthritis very rarely causes central nervous vasculitis and optic neuritis [8–10]. It has to be mentioned that the immunosuppressant methotrexate, which had been part of the patient’s treatment since years, was associated with demyelinating events in at least 1 report [11]. A link between TNF-α inhibitors and demyelinating diseases is suggested by a number of reports and led to warnings on the prescribing instructions for these substances. In double-blinded trials TNF-α antagonists provoked a decrease in the neurologic condition in patients with multiple sclerosis. With the extended use of adalimumab a growing number of ophthalmological side effects may be expected. The ophthalmologist should be alert in patients who are using adalimumab and other TNF-α inhibitors.

References