



Pseudotumor Cerebri in a Patient with Inflammatory Arthritis Treated with Methotrexate and Etanercept

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Abstract

Pseudotumor cerebri (PTC) is a rare condition marked by elevated intracranial pressure without an identifiable structural lesion. Primary PTC is associated with obesity and female sex, whereas secondary PTC can be triggered by certain medications. We report the case of a 30-year-old woman with inflammatory arthritis who developed PTC while on long-term methotrexate (MTX) and recently added etanercept therapy. Despite having risk factors for primary PTC, her symptoms improved significantly after discontinuing MTX, suggesting a potential medication-related cause. This case underscores the importance of recognizing PTC as a possible adverse effect of MTX, especially in patients with predisposing factors.

Keywords: Pseudotumor Cerebri; Arthritis; Methotrexate; Papilledema; Medication-Related Adverse Effects

Abbreviations

PTC: Pseudotumor Cerebri; IIH: Idiopathic Intracranial Hypertension; MTX: Methotrexate; BMI: Body Mass Index; CSF: Cerebrospinal Fluid; ANA: Antinuclear Antibodies.

Introduction

PTC is a rare neurological disorder characterized by elevated intracranial pressure and papilledema in the absence of hydrocephalus, mass lesions, infection or malignancy. Primary PTC, also known as idiopathic intracranial hypertension (IIH), predominantly affects females of childbearing age with elevated

body mass index (BMI) and no identifiable underlying pathology. Secondary PTC may result from venous sinus thrombosis, medications, and medical conditions such as endocrine disorders, hypercapnia, or anemia [1]. We present a case of PTC in a young woman with inflammatory arthritis treated with MTX and etanercept. Early identification of potential medication-related adverse effects is important for optimizing patient care.

Case Presentation

A 30-year-old woman presented with a 14-days history of intermittent, pressure-like headache without diurnal variation, which had worsened compared to her previous baseline headaches.

She also reported blurred vision, nausea, fever, intermittent vomiting, and pulsatile tinnitus. In addition, she described a 4-week history of cognitive deficits, initially attributed to stress.

Her medical history included reactive arthritis, treated with subcutaneous MTX for three years, and etanercept added two months prior due to persistent joint inflammation. She also had a history of chronic spontaneous urticaria, childhood-onset febrile episodes, and frequent episodic tension-type headaches. On examination, her BMI was 30.1 kg/m², and fundoscopy revealed bilateral grade IV papilledema (Figure 1). Laboratory studies showed a CRP of 18 mg/L, while other tests, including antinuclear antibodies (ANA), were within normal limits. Magnetic resonance imaging demonstrated bilateral posterior globe flattening, tortuosity of the optic nerves, distension of the optic nerve sheaths, and partial empty sella turcica. Lumbar puncture showed an opening pressure of 320 mm cerebrospinal fluid (CSF), with normal CSF composition, confirming a diagnosis of PTC. Treatment with acetazolamide was initiated, and both MTX and etanercept were discontinued. Due to persistent papilledema and the risk of vision loss, the patient underwent optic nerve sheath fenestration of the right eye. Gradual clinical improvement followed, and etanercept was reintroduced after one month without recurrence of symptoms. Acetazolamide was tapered off after five months with no relapse observed. Whole genome sequencing revealed no pathogenic variants associated with autoinflammatory or periodic fever syndromes.

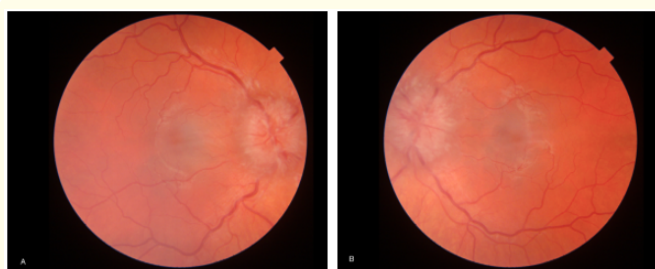


Figure 1: Fundus photos showing grade IV papilledema in right (A) and left (B) eye upon initial presentation.

Discussion

MTX is a cornerstone in the treatment of inflammatory arthritis. While multiple medications, including corticosteroids, have been linked to PTC [2,3], there are only a few case reports describing a possible association between low-dose MTX and PTC [4-6]. Notably, this patient had not received corticosteroids. To date, no published studies have implicated etanercept, alone or in combination with MTX, in the development of PTC. The mechanism by which MTX may contribute to increased intracranial pressure remains unknown. However, the patient's clinical improvement following MTX withdrawal suggests a possible causal relationship. Although etanercept was also discontinued, it was reintroduced after one month without symptom recurrence. Despite the presence of established risk factors for primary PTC, including female sex, obesity, and reproductive age, MTX should be considered a potential contributing factor in this case. Prompt recognition and treatment of PTC are essential to avoid irreversible visual impairment.

Conclusion

This case highlights a potential association between MTX therapy and PTC, consistent with a small number of previously reported cases. Clinicians prescribing MTX, particularly in patients with risk factors for PTC, should remain vigilant for signs of increased intracranial pressure. Early diagnosis and treatment are vital to prevent serious complications such as vision loss.

Conflict of Interest

No potential conflict of interest was reported by the authors.

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