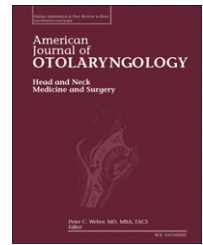


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# Multiple cranial neuropathies following etanercept administration☆☆☆

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## ABSTRACT

There have been recent reports of sarcoid-like granulomatosis development following the administration of tumor necrosis factor (TNF) inhibitors. To date, only four cases of neurosarcoidosis have been reported in association with TNF inhibitors, two of which were attributed to etanercept. We present the first case of etanercept-induced neurosarcoidosis involving multiple cranial neuropathies, including the trigeminal, facial, and vestibulocochlear nerves, while also highlighting the differential diagnoses of multiple cranial neuropathies and the association of TNF inhibitors and neurosarcoidosis.

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## 1. Introduction

There are numerous etiologies for patients presenting with multiple cranial neuropathies. In the largest reported series, Keane described his experience with 1028 patients with multiple cranial neuropathies, noting that 30% were attributed to tumors, most commonly vestibular schwannomas, while vascular and trauma etiologies contributed 12% each, and infections accounted for 10% [1]. However, only three cases within Keane's series were caused by autoimmune diseases: two patients with neurosarcoidosis, and one patient with systemic lupus erythematosus [1]. Regardless, many autoimmune processes, including granulomatosis with polyangiitis, Churg–Strauss syndrome, and Sjogren's syndrome, have been associated with cranial neuropathies. We present the case of a woman, who, shortly after initiating etanercept, developed facial numbness, facial weakness, and hearing loss, all of which resolved following the discontinuation of etanercept and initiation of prednisone. With a negative workup for other disease processes, a temporal relationship between etanercept administration and symptom evolution, and known connection between etanercept and neurosarcoidosis, a diagnosis of possible neurosarcoidosis was

made. This case describes the first report of etanercept-induced neurosarcoidosis involving multiple cranial nerves, including the trigeminal, facial and vestibulocochlear nerves, while also highlighting the rare association between tumor necrosis factor (TNF) inhibitors and neurosarcoidosis.

## 2. Case report

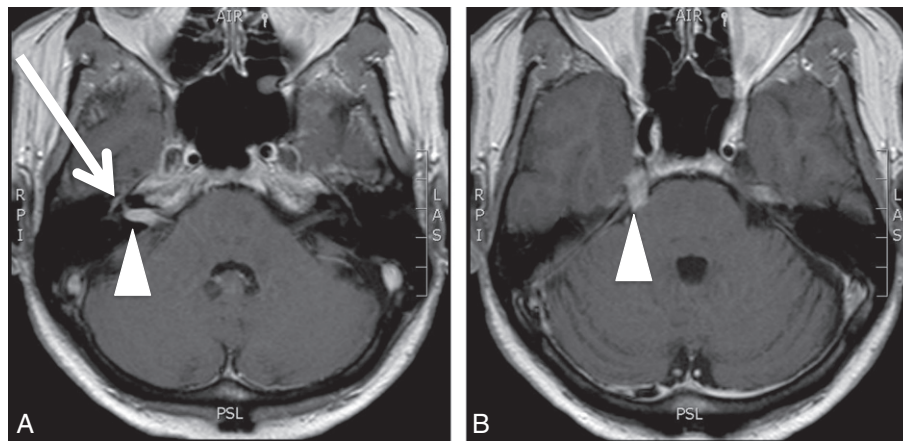
A 61-year-old woman with rheumatoid arthritis (RA), treated with etanercept, presented with a two-month history of right-sided facial pain, otalgia, and hearing loss. The patient complained of disequilibrium, point tenderness and light touch sensitivity to the right side of her face. On physical examination, she demonstrated right facial paresthesias, while her facial nerve function per the House–Brackmann (HB) grading scale was III/VI on the right and I/VI on the left. On pure-tone audiometry, she had a profound sensorineural hearing loss in her right ear, deferring speech discrimination, with normal hearing and 100% speech discrimination in her left ear. Magnetic resonance imaging (MRI) demonstrated two right-sided enhancing lesions on T1-weighted post-contrast

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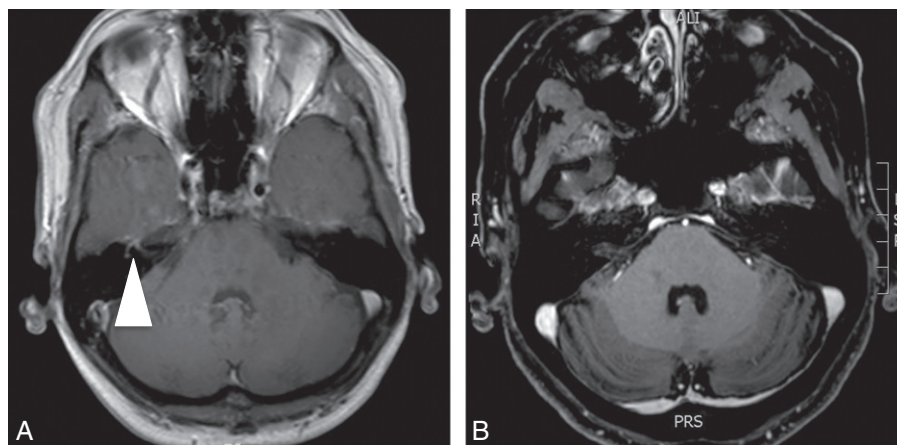
**Fig. 1 – Imaging obtained prior to treatment intervention. (A) Axial MRI with T1-weighted post-contrast demonstrates an enhancing lesion within the right internal auditory canal (arrowhead), with enhancement of the right labyrinthine and tympanic segments of the facial nerve (arrow). (B) Superior axial MRI with T1-weighted post-contrast also shows enhancement and enlargement of the right trigeminal nerve (arrowhead).**

imaging: one located at the internal auditory canal (IAC) and the second one at the trigeminal ganglion (Fig. 1A, B). Etanercept was discontinued, and the patient was started on a 15-day prednisone taper, beginning at 60 mg daily. The differential diagnosis included vestibular and trigeminal schwannomas, metastases, neurosarcoidosis, granulomatosis with polyangiitis, syphilis, tuberculosis, and a fungal infection.

One week later, a lumbar puncture (LP) was non-diagnostic (cerebrospinal fluid (CSF) angiotensin convertor enzyme (ACE) 1.4, nucleated cells 45, red blood cells 0, glucose 74, protein 47, negative for malignancy, gram stain negative) and a chest x-ray was normal. One month later, the patient's facial numbness and weakness had completely resolved, but 10 days later, her right facial numbness returned. Aside from rheumatoid arthritis, a complete rheumatologic workup was negative, but given the persistent symptoms, the patient was

restarted on prednisone 20 mg daily. After another month with persistent facial numbness and hearing loss, the prednisone was increased to 40 mg daily, with a slow taper.

Three months later, repeat pure-tone audiometry demonstrated normal, downsloping to a moderate sensorineural hearing loss in the right ear, with normal hearing in the left ear, and 100% speech discrimination bilaterally. On physical examination, her facial nerve function was I/VI bilaterally on the HB scale. Repeat MRI with contrast showed resolution of the right IAC enhancing mass, though there was persistent enhancement of the right facial nerve labyrinthine segment, along with reduced enhancement of the right trigeminal nerve (Fig. 2A, B). Given the constellation of signs and symptoms, and temporal relationship of etanercept administration, as well as a negative workup for other disease processes, the patient was diagnosed with “possible” neurosarcoidosis.



**Fig. 2 – Images obtained after etanercept was discontinued four months prior to when imaging was obtained. (A) Axial MRI with T1-weighted post-contrast imaging shows persistent enhancement of the labyrinthine and tympanic portion of the right facial nerve, unchanged from prior study (arrowhead). (B) On further axial MRI with T1-weighted post-contrast turbo field echo, there is resolution of the enhancing mass within the right IAC.**

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