Infliximab reverses progressive deafness

Résolution progressive d’une surdité sous infliximab

Loss of hearing is a major concern for ear, nose and throat specialists and its cause often remains unexplained. When deafness is bilateral and occurs in young patients with other systemic manifestations, an autoimmune etiology is often sought. In those cases, after failure of symptomatic treatments, corticosteroids and immunosuppressants are prescribed empirically but their outcomes are unpredictable. Herein, we describe a congenitally blind patient with progressive sensorineural hearing loss and episodic vertigo, for whom the latter two were reversed by infliximab (Remicade®) prescribed after failure of corticosteroids and azathioprine (Imurel®).

Case report

In 2005, a 20-year-old woman with a history of asthma, epilepsy and bilateral blindness, due to exudative vitreoretinopathy linked to a heterozygous mutation of the FZD4 gene, suffered vertigo and acute sensorineural bilateral hearing loss. Physical examination found a vestibular syndrome with a rotatory vertigo, lateralized Romberg but no nystagmus. Videonystagmography was not performed because of bilateral blindness. Speech audiometry has not been done. The patient also complained of mouth and eye dryness. Her blood pressure was normal. Biological and immunological laboratory analyses yielded normal results (protein electrophoresis; muscle enzymes; C3 and C4 levels; and antinuclear [ANA], antineutrophil cytoplasm, anti-DNA, anti-cardiolipin and anti-β2-glycoprotein-1, anti-extractable nuclear antigens [anti-ENA], anti-cochlear antigens [anti-cochlin; anti-heat shock protein 70] autoantibodies were not detected).

Between 2005 and 2007, she was hospitalized monthly for episodes of vertigo and acute sensorineural hearing loss, which occurred despite prednisone (initial dose of 60 mg/day, then progressively tapered to a mean of 40 mg/day), combined with azathioprine (150 mg/day). An attempt to taper prednisone to 13 mg/day failed and relapses occurred. After one 120 mg methylprednisolone pulse for each episode of acute deafness, tinnitus and vertigo disappeared without sequelae. In November 2012, after the frequency of deafness episodes increased to around one per month, plasmaphereses were added to oral prednisone and azathioprine. New diagnostic investigations were performed to identify the underlying disease. Brain magnetic resonance imaging and cerebrospinal fluid analysis were normal. Azathioprine was unsuccessfully switched to mycophenolate mofetil (2 g/day) for 3 months, then to cyclosporine (150 mg/day) for 9 months. The prednisone dose was maintained at 40 mg/day.

In early 2009, azathioprine was reintroduced. Between 2009 and 2012, vestibular crises were frequent, requiring monthly methylprednisolone pulse. In March 2012, an anti-tumor necrosis factor-alpha (TNFα)-blocking agent was chosen for its ability to diminish inflammation and modulate T- and B-cell responses to undetermined antigen(s) implicated in her deafness. Monthly infliximab infusions (5 mg/kg/infusion, i.e. 300 mg) were added to azathioprine (150 mg/day) and corticosteroids (40 mg/day).

The patient improved after 2 months, i.e. two infliximab perfusions. No deafness and vertigo episodes have occurred since May 2012 and her tonal audiogram improved progressively (~90 dB in March 2012 versus ~45 dB in November 2012) (figure 1). Prednisone was stopped in September 2013 and azathioprine was progressively tapered then stopped in January 2015. To simplify anti-TNFα administration, infliximab infusions were switched to subcutaneous golimumab (50 mg) monthly administration. Her remission was considered complete in January 2015, 32 months after starting anti-TNF.

Discussion

We report a case of a young woman suffering from acute bilateral sensorineural hearing loss associated with vertigo episodes and a good response to the anti-TNFα-blocking agent, infliximab. Although the underlying disease remained unidentified, an immune process or an inflammatory disease was considered, justifying the prescription of corticosteroids, cytotoxic drugs and anti-TNFα. A link between deafness and the patient’s congenital ocular disease, familial exudative vitreoretinopathy, was improbable and has never been described to date. This retinopathy represents about 10–15% of childhood retinopathies but without any ear disease [1,2].

Some cases of acute sensorineural bilateral hearing loss have been reported. Among their 823 patients with acute hearing loss without deafness, Fettermann et al. reported only 1.7% with bilateral disease [3]. Patients with a bilateral hearing loss are usually elderly and frequently have concomitant vascular disease (atherosclerosis) and are ANA-positive. Although no direct
A link between a high ANA level (1/160) and atherosclerosis has been confirmed, Pertovaara et al. reported an indirect association represented by reduced carotid elasticity in women [4]. Baek et al. found specific anti-cochlin autoantibodies in patients with bilateral sensorineural hearing loss [5]. Our patient did not have such autoantibodies.

Anti-TNF has been used previously to treat autoimmune deafness and achieved different results. Heywood et al. described a corticosteriodependent patient with hearing loss associated with vertigo and tinnitus that responded to infliximab for 46 weeks but relapsed after its discontinuation. Its reintroduction was effective, highlighting the importance of maintaining this therapy [6]. Infliximab infusion to the inner ear could result in hearing improvement and reduce relapses occurrence [7]. Liu et al. reported on eight patients treated with steroids, methotrexate and cyclophosphamide for autoimmune sensorineural hearing loss who relapsed; only one subsequently improved subjectively on infliximab without improvement of the pure tone audiogram [8].

**Conclusion**

This case emphasizes that an anti-TNFα-blocking agent, like infliximab or golimumab, can effectively reverse bilateral deafness resulting from a suspected inflammatory or autoimmune mechanism. Further investigation and confirmation of anti-TNF efficacy in this context are needed.
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References


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