Clinical and Experimental Rheumatology 2006; 24: 344-346.

Juvenile psoriatic arthritis and acquired sensorineural hearing loss in a teenager: Is there an association?

T. Giani, G. Simonini, C. Lunardi[1], A. Puccetti[2], M. De Martino, F. Falcini

Rheumatology Unit, Department of Paediatrics, University of Florence, Florence; [1]Department of Clinical and Experimental Medicine, University of Verona; [2]Department of Experimental Medicine, University of Genoa, Italy.

Teresa Giani, MD; Gabriele Simonini, MD; Claudio Lunardi, Associate Professor; Antonio Puccetti, Associate Professor; Maurizio de Martino, Professor; Fernanda Falcini, Associate Professor.

Please address correspondence and reprint requests to: Fernanda Falcini, MD, University of Florence, Rheumatology Unit, Department of Paediatrics, Anna Meyer Children's Hospital, Via Pico della Mirandola, 24, 50132 Florence, Italy. E-mail: falcini@unifi.it

Received on August 11, 2005; accepted in revised form on March 20, 2006.

Key words: Sensorineural hearing loss, juvenile psoriatic arthritis, etanercept.

ABSTRACT

Autoimmune inner ear disease is a cause of sensorineural hearing loss, first described in 1979 by McCabe. The occurrence during rheumatic diseases is already documented in adults, but to our knowledge, this evidence is still lacking in children. A 13-yr-old girl affected by juvenile psoriatic arthritis, treated with etanercept, developed a bilateral and asymmetric sensorineural deafness. The patient significantly improved after steroid administration. Once ruled out the principal causes of sensorineural hearing loss, we also considered the hypothesis of an anti-TNF side effect. However, the clinical presentation, the efficacy on steroid treatment and the presence of inner ear auto-antibodies prompt us to consider autoimmune-SNHL as the most plausible diagnosis.

The young age of our patient seems to suggest a genetic susceptibility to autoimmunity and supports the concept of associated autoimmune diseases.

Introduction

McCabe first proposed the clinical entity of autoimmune sensorineural hearing loss (SNHL) in 1979 (1). The occurrence of SNHL during rheumatic diseases has been documented in adults, and a single case report described a 62-year-old man with psoriatic arthritis (2, 3). However, until now it has not been reported in children. We present the first case of immune-mediated-SNHL in a 13-year-old girl with juvenile psoriatic arthritis (JpsA), a subgroup of juvenile idiopathic arthritis (JIA), with onset before 16 years of age, characterized by arthritis and a personal and/or family history of psoriasis (4).

Case presentation

A 12-year-old girl was referred to us for back pain and dactylitis of the first toe on the right foot. Five months later she developed onycholysis and psoriatic lesions over the extensor surface of her elbows. A diagnosis of JPsA was made and treatment with naproxen, sulfasalazine and methotrexate was successfully introduced.

At the age of 13 years, the arthritis flared-up with a swollen and painful right ankle and back pain. The girl experienced nausea and vomiting at each methotrexate administration, and all DMARDs were switched to etarnecept (25 mg/twice/week) with a prompt improvement. One month later, vertigo and a progressive deafness in the right ear occurred. Approximately 15 days later ipoacusia also affected the left ear. Recent medical history was free of any acoustic trauma, infection and exposure to ototoxic drugs. Psoriatic lesions aside, physical and otoscopic examinations were unremarkable.

Laboratory studies were notable only for a serum C-reactive protein level of 41mg/dL (normal < 0.5) and an erythrocyte sedimentation rate of 56 mm/h (normal < 31). Thyroid function studies and serum angiotensin converting enzyme tests resulted in the normal range. Tests for anti-nuclear, anti-phospholipid antibodies, and circulating immune complexes were negative. Serological tests for common infectious diseases were uninformative. Audiological tests suggested a sensorineural hearing deficit: Rinne test revealed a bilateral reduction of both air and bone conduction, Weber test showed a localization of sound towards the left side, tympanogram was type "A" for both ears, and audiometry with pure-tone and speech tests identified a severe loss in the right ear and a mild deafness on the left side. Brain imaging results were normal. The patient underwent three pulses of methylprednisolone (1g/day) followed by oral prednisone (1mg/kg/day), which was gradually tapered off. Symptoms rapidly improved in the left ear, while anacusia persisted in the right side.

One month after corticosteroid treatment was discontinued, deafness relapsed. The patient's medication chart was reviewed and, as a precaution, etarnecept was discontinued, suspected of being involved in the aetiology of SNHL. Three courses of methylprednisolone pulse (1g/day) were repeated and there was complete recovery in the left ear. Oral prednisone (1mg/kg) was then introduced and withdrawn over 3 months. An organospecific autoimmunity was sus-

pected and the patient's serum was tested for antibodies against inner ear antigens: anti-DEP1/CD148 resulted negative, while anti-connexin26, anti-Reovirus III and anti-68 kD protein positive. On the basis of these data etanercept was reintroduced to control the patient's arthritis and no further hearing impairment has occurred.
Our otolaryngology department periodically checks the patient's hearing which remains normal in the left ear, while the right shows persistent damage.

Table I. Aetiology of acquired sensorineural hearing loss.

Ototoxicity	aminoglycosides, salycilates, loop diuretics, antimalarials, chemotherapy agents, bromocriptine, vaccinations, thalidomide
Trauma	loud noise, temporal bone fracture, trauma, barotrauma, perilymph fistulae
Infections	mumps, measles, mononucleosis, Lyme disease, Syphilis, meningitis, encephalitis, *herpes symplex*, varicella/zoster, *Mycoplasma pneumoniae*, influenza B, *Chlamydia trachomatis*
Tumours	vestibular schwannoma, glomus tumor, temporal bone metastases
Autoimmune diseases	Cogan's syndrome, systemic lupus erythematosus, antiphospholipid syndrome, sarcoidosis, Wegener's granulomatosis, Behçet's disease
Vascular diseases	haemorrhage, thrombosis, embolus, hyperviscosity (polycythaemia, hyperlipidemia, sickle cell trait, Waldenstrom macrogloblinemia, leukaemias...), vasospasm, hypertension, arteriosclerosis
Metabolic diseases	diabetes, hypo/hyper thyroidism, uremia
Nervous system diseases	multiple sclerosis, Guillain-Barrè syndrome
Other	Ménière's disease, presbycusis, radiation injury, lumbar puncture

Discussion

At first, once the principal causes of SNHL (Table I) have been excluded, we considered the possibility of an anti-TNF side effect. TNF-α plays a key role in modulating the immune system, particularly in the down-regulation of cytokine production and in the apoptosis of auto-reactive inflammatory cells (5). Clinical trials have not yet revealed a direct risk, but there are worries about the potential evolution of demyelinating and autoimmune diseases triggered by anti-TNF-α agents (6, 7). It would be possible to hypothesize such an event related to etanercept in our patient, otherwise a drug-induction of pathogenetic inner ear antibodies cannot be excluded, even if it has never been described before. However, recent data show etanercept to be an efficacious treatment for autoimmune-SNHL (8).
Besides, the reassessment of the entire case, in particular the patient's clinical presentation, her unresponsiveness to the interruption of etanercept, the efficacy of steroid treatment, and the presence of inner ear auto-antibodies point to autoimmune-SNHL as the most plausible diagnosis.
Autoimmune-SNHL can be a primary, localized disorder, due to site-specific immune mediated damage in the inner ear (9). Alternatively it can be a secondary expression of a systemic autoimmune disease in which the involvement of the inner ear is as a part of a broader spectrum of illness (10). Clinical presentation is characterized by a bilateral, asymmetrical, often asynchronous and fluctuant deafness which progressively worsens over a period of weeks or months (9). Tinnitus, vertigo, and disequilibrium may also be documented. Occurrence is more common in females and onset is normally in middle age. Clinical diagnosis follows the exclusion of other possible causes and can be confirmed by a favorable response to steroid therapy (9).
Sera from patients contain antibodies to a 68 kD protein of bovine inner ear tissue, identified as the inducible heat shock protein70, that plays a role in cell survival (11). These antibodies are neither sensitive or specific but they are considered useful for diagnosis, and appear to be predictive of responsiveness to steroid treatment (12). In our patient antibodies against Reovirus III, connexin26, and 68 kD antigen tested positive, while antibodies against DEP1/CD148, frequently described in Cogan's syndrome, were negative, supporting the hypothesis of an autoimmune-SNHL (13, 14). In this patient the deafness could be interpreted as an independent event, coincidental with the psoriatic arthritis; otherwise a common underlying autoimmune link can be supposed and the SNHL interpreted as the consequence of the same immunological disturbance. Although a clear relationship is still uncertain, a general immune impairment can involve several organs, with an increased susceptibility to a second autoimmune disease (15). The young age of our patient suggests a genetic predisposition to autoimmunity and supports the hypothesis of an associated autoimmune disease, despite this being the first case described in JIA.
Paediatric rheumatologists should be aware of the possibility of an autoimmune-SNHL in a child with JIA who develops deafness. Consultation with a otolaryngologist who may confirm diagnosis and cooperate in the patient's care is recommended.

References

1. MCCABE BF: Autoimmune sensorineural hearing loss. *Ann Otol Rhinol Laryngol* 1979; 88: 585-9.
2. ANDONOPOULOS AP, NAXAKIS S, GOUMAS P, LYGATSIKAS C: Sensorineural hearing disorders in systemic lupus erythematosus. A controlled study. *Clin Exp Rheumatol* 1995; 13: 137-41.
3. SRIKUMAR S, DEEPAK MK, BASU S, KUMAR BN: Sensorineural hearing loss associated with psoriatic arthritis. *J Laryngol Otol* 2004; 118: 909-11.
4. PETTY RE, SOUTHWOOD TR, BAUM J *et al.:* Revision of the proposed classification criteria for juvenile idiopathic arthritis: Durban, 1997. *J Rheumatol* 1998; 25: 1991-4.
5. LOCKSLEY RM, KILLEEN N, LENARDO MJ: The TNF and TNF receptor superfamilies: integrating mammalian biology. *Cell* 2001; 104: 487-501.
6. DEKKER L, ARMBRUST W, RADEMAKER CM, PRAKKEN B, KUIS W, WULFFRAAT NM: Safety of anti-TNFalpha therapy in children with juvenile idiopathic arthritis. *Clin Exp Rheumatol* 2004; 22: 252-8.

7. MOHAN N, EDWARDS ET, CUPPS TR *et al.*: Demyelination occurring during anti-tumor necrosis factor alpha therapy for inflammatory arthritides. *Arthritis Rheum* 2001; 44: 2862-9.
8. RAHMAN MU, POE DS, CHOI HK: Etanercept therapy for immune-mediated cochleovestibular disorders: preliminary results in a pilot study. *Otol Neurotol* 2001; 22: 619-24.
9. BROUGHTON SS, MEYERHOFF WE, COHEN SB: Immune-mediated inner ear disease: 10-year experience. *Semin Arthritis Rheum* 2004; 34: 544-8.
10. TOUBI E, BEN-DAVID J, KESSEL A, HALAS K, SABO E, LUNTZ M: Immune-mediated disorders associated with idiopathic sudden sensorineural hearing loss. *Ann Otol Rhinol Laryngol* 2004; 113: 445-9.
11. LOVEMAN DM, DE COMARMOND C, CEPERO R, BALDWIN DM: Autoimmune sensorineural hearing loss: clinical course and treatment outcome. *Semin Arthritis Rheum* 2004; 34: 538-43.
12. HEFENEIDER SH, MCCOY SL, HAUSMAN FA, TRUNE DR: Autoimmune mouse antibodies recognize multiple antigens proposed in human immune-mediated hearing loss. *Otol Neurotol* 2004; 25: 250-6.
13. MOSCICKI RA, SAN MARTIN JE, QUINTERO CH, RAUCH SD, NADOL JB JR, BLOCH KJ: Serum antibody to inner ear proteins in patients with progressive hearing loss. Correlation with disease activity and response to corticosteroid treatment. *JAMA* 1994; 272: 611-6.
14. LUNARDI C, BASON C, LEANDRI M *et al.*: Autoantibodies to inner ear and endothelial antigens in Cogan's syndrome. *Lancet* 2002; 360: 915-21.
15. STAGI S, GIANI T, SIMONINI G, FALCINI F: Thyroid function, autoimmune thyroiditis and coeliac disease in juvenile idiopathic arthritis. *Rheumatology* 2005; 44: 517-20.