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

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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 etanercept (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 anaacusia 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, etanercept 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.

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 pathogenic 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 steroid treatment (12). In our patient antibodies against Reovirus III, connexin26, and 68 kD antigen tested negative, patients’ serum was tested for antibodies against Reovirus III, Cogan’s syndrome, systemic lupus erythematosus, antiphospholipid syndrome, Wegener’s granulomatosis, Behçet’s disease (13, 14). In this patient auto-reactive inflammato-

Table I. Aetiology of acquired sensorineural hearing loss.

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ototoxicity</td>
<td>aminoglycosides, salicylates, loop diuretics, antimalarials, chemotherapy agents, bromoconnective, vaccine sera, thalidomide</td>
</tr>
<tr>
<td>Trauma</td>
<td>loud noise, temporal bone fracture, trauma, bursitis, penicillin injection</td>
</tr>
<tr>
<td>Infectious</td>
<td>mumps, measles, mononucleosis, Lyme disease, Syphilis, meningitis, encephalitis, herpes simplex, varicella/zoster, Mycoplasma pneumoniae, influenza, Echovirus and Coxsackie virus</td>
</tr>
<tr>
<td>Tumours</td>
<td>vestibular schwannoma, glomus tumor, temporal bone metastases</td>
</tr>
<tr>
<td>Autoimmune diseases</td>
<td>Cogan’s syndrome, systemic lupus erythematosus, antiphospholipid syndrome, sarcoidosis, Wegener’s granulomatosis, Behçet’s disease</td>
</tr>
<tr>
<td>Vascular diseases</td>
<td>haemorrhage, thrombosis, emboli, hyperlipidaemia, hyperlipidaemia, sickle cell trait, Waldenström macroglobulinemia, leukaemias, arthritis, vasospasm, hypertension, arteriosclerosis</td>
</tr>
<tr>
<td>Metabolic diseases</td>
<td>diabetes, hyper/hypothyroidism, uremia</td>
</tr>
<tr>
<td>Nervous system diseases</td>
<td>multiple sclerosis, Guillain-Barré syndrome</td>
</tr>
<tr>
<td>Other</td>
<td>Ménière’s disease, presbycusis, radiation injury, lumbosacral pain</td>
</tr>
</tbody>
</table>

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 autoimmune-SNHL in a child with JIA who supports the hypothesis of an association between autoimmunity and SNHL (8).

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 association between 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 an otolaryngologist who may confirm diagnosis and cooperate in the patient’s care is recommended.

References
Autoimmune deafness in juvenile arthritis / T. Giani et al.


