WB-MRI can perform a non-irradiating whole-body examination in a single session, these results suggest that WB-MRI could be a promising alternative to established multimodal imaging in ECD.

**Rheumatology key message**
- MRI is a promising alternative to established multimodal imaging strategies in Erdheim-Chester disease.

**Disclosure statement:** The authors have declared no conflicts of interest.

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**Tubulointerstitial nephritis, uveitis, hearing loss and vestibular failure: TINU-atypical Cogan’s overlap syndrome**

Sir, TINU syndrome is a rare autoimmune condition with acute tubulointerstitial nephritis and uveitis [1, 2]. Cogan’s syndrome is a rare autoimmune disease with non-syphilitic interstitial keratitis and auditory-vestibular symptoms occurring within 2 years, sometimes associated with large-vessel vasculitis [3, 4]. Atypical Cogan’s syndromes include other forms of inflammatory eye and inner ear disease [4]. We describe a case with initial presenting features of TINU, later progressing to atypical Cogan’s syndrome, illustrating that the phenotype of both these entities may be broader than previously described, and may overlap.

A previously well 12-year-old boy of non-consanguineous Afro-Caribbean origin presented with a 6-week history of bilateral acute anterior uveitis that responded well to CS eye drops. Four weeks later he re-presented with 10 days of fever without infectious cause, transient left lower motor neurone facial nerve palsy (now resolved), weight loss and loin pain. Examination confirmed low-grade pyrexia (38 °C), anterior cervical lymphadenopathy and moderate hypertension: 134–140/85–90 mmHg. Bilateral moderate sensorineural hearing loss was detected using tuning fork tests. Neurological assessment was otherwise normal, with no evidence of residual facial nerve palsy or abnormality of balance or coordination. Investigations revealed normocytic, normochromic anaemia with haemoglobin 9.6 g/dl (11.5–15.5 g/dl), elevated white count of 20.45 × 10⁹/l (80% neutrophils), ESR 170 mm/h (reference range 0–15 mm/h), CRP 21 mg/l (<20 mg/l), creatinine 100 μmol/l (34–67 μmol/l), hypokalaemia of 3.3 mmol/l (3.5–5.5 mmol/l), hypophosphataemia 1.07 mmol/l (1.1–1.75 mmol/l), haemoglobin 35 g/l (37–56 g/l), strongly positive proteinuria on dipstick test but minimally elevated urinary albumin:creatinine ratio of 8.6 mg/mmol (0.1–7.4 mg/mmol), elevated urinary N-acetyl-β-D-glucosaminidase:creatinine ratio of 251 U/mmol (2–12 U/mmol), elevated urinary retinol binding protein:creatinine ratio of 988 μg/mmol (3.9–32 μg/mmol), tubular reabsorption of phosphate 94% (70–100%) and normal plasma calcium 2.26 mmol/l (2.19–2.66 mmol/l). Workup for infections was negative, including negative screening for: HIV, EBV, varicella, CMV, adenovirus, Mycoplasma pneumonia and Mycobacterium tuberculosis. The following tests were also negative or normal: ANA, ANCA, RF, LA and aCL, serum angiotensin-converting enzyme; and glomerular basement membrane antibody. Pure tone audiometry confirmed severe bilateral sensorineural hearing loss (see supplementary Fig. 1A, available as supplementary data at Rheumatology Online). A US scan of the kidneys and chest X-ray were normal. CT and MRI of the brain, brain stem and inner ear were normal. Renal biopsy confirmed acute tubulo-interstitial nephritis (TIN; see supplementary Fig. 1B, available as supplementary data at Rheumatology Online). The combination of TIN plus uveitis led to a diagnosis of TINU, although atypical features included hearing loss and resolved Bell’s palsy. Therapy was started with the aims of reversing the hearing loss and treating the acute TIN, and comprised i.v. methylprednisolone (30 mg/kg, six doses over a 2-week period) followed by tapering oral prednisolone starting at 1 mg/kg/day and AZA 2 mg/kg/day. He initially responded well to steroid treatment with some subjective improvement in hearing loss, confirmed on pure tone audiometry. Renal function and tubular proteinuria normalized, and the uveitis remained in remission. On weaning prednisolone his hearing deteriorated and he complained of dizziness and unsteadiness. Complete vestibular failure was confirmed with formal vestibular function testing. Repeat MRI of the inner ear and brain showed reduced signal from the semicircular canals, raising the possibility of early labyrinthitis ossificans. The clinical features of acute anterior uveitis, deafness and vestibular failure suggested the alternative diagnosis of atypical Cogan’s...
There has only been one previous report describing TINU overlapping features of TINU and atypical Cogan’s syndrome. Hearing loss and subsequent vestibular failure with overt attachments often associated with neurological and cutaneous manifestations (e.g. tinnitus, vertigo and hearing loss have been described)

Mitochondrial cytopathies

Non-inflammatory multisystemic organ failure: syndrome of ‘illegitimate associations’ including neuro-metabolic disease; polyglucanoid endocrinopathy; tubulopathy; enteropathy; ophthalmoplegia; piosis; corneal endothelial pathology mimicking interstitial keratitis described; progressive hearing loss without vestibular failure

NLRP3: NOD-like receptor family, pyrin domain containing 3.

Table 1 Differential diagnosis for non-infectious inflammatory eye disease in association with acquired sensorineural hearing loss

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Typical associated features</th>
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<tr>
<td>Systemic vasculitides and autoimmune diseases</td>
<td></td>
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<tr>
<td>ANCA-associated vasculitides, particularly granulomatosis with</td>
<td>Granulomatous respiratory tract vasculitis; glomerulonephritis; ANCA positivity</td>
</tr>
<tr>
<td>PAN</td>
<td>Systemic necrotizing medium-vessel vasculitis, particularly cutaneous vasculitis</td>
</tr>
<tr>
<td>Kawasaki disease</td>
<td>Mucocutaneous lymph node syndrome; coronary artery aneurysms; most commonly in pre-school children; uveitis and/or hearing loss occasionally described; TIN may develop after IVIG therapy</td>
</tr>
<tr>
<td>Cogan’s syndrome</td>
<td>Typical: interstitial keratitis; hearing and vestibular failure; sometimes aortic root dilatation</td>
</tr>
<tr>
<td>SLE with or without APS</td>
<td>Atypical: other inflammatory eye pathology associated with deafness and vestibular failure described; ototoxicity can occur from HCQ therapy</td>
</tr>
<tr>
<td>SS with or without APS</td>
<td>Protein systemic autoimmune features; hearing loss and vestibular failure occasionally described</td>
</tr>
<tr>
<td>Primary APS</td>
<td>Sensorineural hearing loss and uveitis occasionally described</td>
</tr>
<tr>
<td>Relapsing polychondritis</td>
<td>Ulcerative colitis and Crohn’s disease associated with Cogan’s syndrome</td>
</tr>
<tr>
<td>Autoimmune inflammatory arthritides</td>
<td>RA and AS occasionally associated with audiovestibular failure</td>
</tr>
<tr>
<td>Auto-inflammatory disorders</td>
<td></td>
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<tr>
<td>Sarcoidosis</td>
<td>Multisystemic non-caseating granulomatous process with uveitis, skin involvement, arthritis, chest involvement, parotid gland involvement and occasional hearing loss</td>
</tr>
<tr>
<td>Cryopyrin-associated periodic fever syndromes</td>
<td>Features of familial cold urticarial syndrome; Muckle–Wells syndrome; or chronic infantile neurological cutaneous articular syndrome; associated with mutation in NLRP3; hearing loss usually occurs without vestibular failure</td>
</tr>
<tr>
<td>Behçet’s disease</td>
<td>Multisystemic involvement including oral and genital ulceration; various skin rashes; pathergy; panuveitis; systemic vasculitis; neurological involvement; thrombophlebitis; occasional hearing loss and vestibular failure described</td>
</tr>
<tr>
<td>Miscellaneous causes</td>
<td></td>
</tr>
<tr>
<td>TINU syndrome</td>
<td>Uveitis associated with TIN. One previous report of associated sensorineural hearing loss without vestibular failure</td>
</tr>
<tr>
<td>Vogt–Koyanagi–Harada syndrome</td>
<td>Multisystemic disorder characterized by granulomatous panuveitis with exudative retinal detachments often associated with neurological and cutaneous manifestations (e.g. hair loss, poliosis, vitiligo). Tinitus, vertigo and hearing loss have been described</td>
</tr>
<tr>
<td>Susac’s syndrome (retinocochlear vasculopathy)</td>
<td>Microangiopathy characterized by encephalopathy, branch retinal artery occlusions and sensorineural hearing loss</td>
</tr>
<tr>
<td>Mitochondrial cytopathies</td>
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</table>

syndrome. AZA was changed to MMF (600 mg/m² twice daily), and he received a further three pulses of i.v. methylprednisolone, and a second weaning course of prednisolone. Despite this his hearing and vestibular function failed to improve, although renal function and uveitis remained in remission, and he is currently (10 months after presentation) being assessed for possible cochlear implantation.

The differential diagnosis of inflammatory eye disease associated with acquired sensorineural deafness is broad (Table 1). We present an unusual case of uveitis, TIN, hearing loss and subsequent vestibular failure with overlapping features of TINU and atypical Cogan’s syndrome. There has only been one previous report describing TINU associated with hearing loss [5]. Although renal involvement in typical and atypical Cogan’s syndrome has been reported [6, 7], TIN has never been described as a feature. Our case thus reveals a possible variant of TINU-atypical Cogan’s overlap. Immunosuppression successfully treated the acute TIN and uveitis, but failed to prevent hearing loss or vestibular failure. We failed to identify an underlying systemic disease such as sarcoidosis, ANCA-associated vasculitis or other autoimmune disease (Table 1). Measurement of autoantibodies against inner ear antigens that may be involved in the pathogenesis of Cogan’s syndrome [8] or anti-renal tubular antibodies described in TINU [9] is not routinely available and thus was not performed. Successful therapy with infliximab [10], rituximab [11] or MMF [12] has recently been described in typical and atypical Cogan’s syndromes, but this remains experimental. Rheumatologists should be aware of the broad differential diagnosis in patients
who present with uveitis associated with audiovestibular failure, and for the potential for renal involvement, since immunosuppressive therapy may be required for reversible renal disease even if the prognosis for hearing and balance is guarded.

**Rheumatology Key message**

- The differential diagnosis in patients who present with uveitis associated with audiovestibular failure is broad.

Disclosure statement: The authors have declared no conflicts of interest.

**Supplementary data**

Supplementary data are available at *Rheumatology* Online.

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**Sustained response to tocilizumab, anti-IL-6 antibody, following anti-TNF-α failure in a patient with relapsing polychondritis complicated by aortitis**

Sir, Relapsing polychondritis (RP) is a rare autoimmune disease of unknown aetiology in which the cartilaginous tissues, especially of the ears, nose, joints and tracheobronchial tree, are the target of inflammation and progressive destruction [1]. We previously reported on a 43-year-old Caucasian woman diagnosed with RP successfully treated with adalimumab [2]. Her disease was characterized by collapse of the nasal bridge and recurrent ocular inflammation, bilateral auricular chondritis, a non-erosive polyarthritis, costochondral pain and histologically confirmed aortitis requiring emergency aortic valve replacement in 1998.

Between 1993 and 2002, due to persistent chronic inflammation and recurrent disease relapses, she had both oral and pulsed CSs in combination with a series of immunosuppressant drugs, as previously reported [2]. All were ineffective or caused significant side effects.

Due to poor response to conventional therapy and persistent aortitis confirmed on PET scanning [1], infliximab (5 mg/kg) 8-weekly was commenced in combination with oral MTX 10 mg weekly and oral CS (deflazacort 18 mg/day) in July 2002. After initial complete resolution at 3 months, she developed recurrence of symptoms and an increase in CRP to pre-treatment levels in spite of increasing the dose frequency to 6-weekly and then increasing the dose to 10 mg/kg at 5 months. This lack of response was likely due to the development of anti-chimeric antibodies.

In June 2003, she was switched to adalimumab 40 mg fortnightly in combination with MTX and deflazacort. Treatment resulted in a rapid clinical improvement with normalization of her CRP and stable aortic dimensions on annual MRI assessment. In contrast to infliximab, adalimumab resulted in sustained remission for 6 years.