

# NEURO-OTOLOGICAL SYNDROMES FOR THE NEUROLOGIST

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Neurologists may be tempted to regard deafness as “somebody else’s problem”—generally the cause will lie within the remit of an ear, nose, and throat (ENT) specialist. While such an approach is often reasonable, there are a number of circumstances in which knowledge of deafness and the syndromes with which it can be associated can take on real importance. Neurologists need to structure their thinking about loss of hearing and be aware of the neurological syndromes that may present with deafness as a component. The complaint can thus be used as “part of the puzzle” when constructing a differential diagnosis in the neurology clinic, and acknowledged and referred to an ENT colleague when the problem is non-neurological.

## CAUSES OF HEARING LOSS

Hearing is the result of complex processes involving the structure of the ear, the function of the inner ear and vestibulum, and the function of the auditory nerve. Peripheral hearing loss can be divided into two main categories, which may co-exist in the same patient. Conductive hearing loss is caused by failure of sound conduction from the environment to the inner ear, and is usually due to problems in the external ear, eardrum, tympanic membrane or middle ear. Common causes include malformations, middle ear infections, trauma causing disruption of the eardrum or middle ear, and stiffness of the eardrum or middle ear bones (otosclerosis). Sensorineural hearing loss (SNHL) is the result of disorders of the inner sensory apparatus. It can be caused by problems in the inner ear, cochlea, auditory nerve, or auditory nerve nucleus. Although some “neurological” diseases are associated with conductive hearing loss, generally neurological causes are sensorineural.

Peripheral neurological causes of SNHL are listed in table 1. The text and tables that follow expand on the categories in table 1, highlighting particularly the syndromic diseases and patterns that can include hearing loss. Central hearing loss (or disorders of central auditory processing) are dealt with in the second section of this article.

### GENETIC Syndromic

A number of different causes of genetically inherited deafness are syndromically recognisable.<sup>1</sup> Most present in children, and examples are given below:

- ▶ *Alport syndrome*—renal failure, SNHL, and retinopathy presenting in the first decade.
- ▶ *Treacher-Collins syndrome*—An autosomal dominant disorder of craniofacial development, causing external ear abnormalities, atresia of external auditory canals and malformation of ossicles (and therefore conductive deafness), downward sloping palpebral fissures, eyelid colobomas, mandible hypoplasia and cleft palate.
- ▶ *Pendred syndrome*—An autosomal recessive disorder consisting of SNHL and diffuse thyroid enlargement. Causes about 5% of childhood deafness
- ▶ *Usher syndrome*—A congenital disease causing sensorineural deafness and vestibular disorder. Progressive retinitis pigmentosa and ataxia begin in late childhood or adolescence. Sometimes patients have learning difficulties, cataracts and glaucoma.
- ▶ *Waardenburg’s syndrome*—An auditory-pigmentary syndrome causing congenital SNHL which is observed at all ages. Absence of melanocytes from the skin, hair, and eyes causes pigmentary abnormalities. Dystopia canthorum (lateral displacement of the inner canthus of each eye) and arm abnormalities may be seen.

The major genetic syndromic cause of deafness likely to present to adult neurologists is neurofibromatosis type 2.

### Neurofibromatosis type 2 (NF2)

Neurofibromatosis type 2 (NF2) is an autosomal dominant disorder caused by inactivating mutations of the NF2 gene. It is much less common than neurofibromatosis type 1, accounting for 5–10% of neurofibromatosis cases. Historically the two conditions have been grouped together (“von Recklinghausen disease” or “multiple neurofibromatosis”), chiefly because café-au-lait

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**Table 1** Peripheral neurological sensorineural hearing loss

Acute		Chronic	
Unilateral	Bilateral	Unilateral	Bilateral
<b>Vascular</b> Cochlear ischaemia/infarction AICA infarction Venous (hyperviscosity)	<b>Ototoxic drugs</b> Aminoglycosides NSAIDs Loop diuretics Antimalarials	<b>Other</b> Vestibular schwannoma Meningioma Latent or tertiary syphilis Ménière's disease Paget's disease <b>Miscellaneous*</b> <b>Autoimmune*</b>	<b>Genetic*</b> Syndromic Non-syndromic <b>Mitochondrial*</b> Syndromic Non-syndromic <b>Miscellaneous*</b> <b>Autoimmune*</b> <b>Metabolic*</b>
<b>Infective</b> Bacterial/TB meningitis Ramsay Hunt syndrome Neurosyphilis (secondary) Lyme disease <b>Autoimmune*</b>	<b>Infective</b> Bacterial TB meningitis Neurosyphilis (secondary) Lyme disease <b>Autoimmune*</b>		
<b>Other</b> Peripheral vestibulopathy (or labyrinthitis or vestibular neuronitis) Ménière's disease Trauma Vestibular schwannoma Migraine	<b>Other</b> Ménière's disease		<b>Other</b> Latent or tertiary syphilis Ménière's disease Paget's disease Presbycusis

Causes marked with \* are discussed in detail in the text.

AICA, anterior inferior cerebellar artery; NSAIDs, non-steroidal anti-inflammatory drugs; TB, tuberculosis.

spots and peripheral nerve tumours can occur in either. In the 1980s the greater morbidity and mortality in NF2, the mapping of the NF2 gene to chromosome 22, and the appreciation that acoustic neuromas are absent in NF1, culminated in the consensus opinion that the two conditions were distinct.

Approximately half of diagnosed patients have no family history and are presumed to represent new mutations. Clinically NF2 comprises the development of nervous system tumours, ocular abnormalities, and skin tumours. Various diagnostic criteria have emerged, with the "Manchester" criteria<sup>2</sup> being shown to be the most sensitive.

### MANCHESTER CLINICAL DIAGNOSTIC CRITERIA FOR NF2

Note: "any two" means two individual tumours or cataracts.

- Bilateral vestibular schwannomas
- First degree family relative with NF2 and unilateral vestibular schwannoma or any two of the following: meningioma, schwannoma, glioma, neurofibroma, posterior subcapsular lenticular opacities
- Unilateral vestibular schwannoma and any two of the following: meningioma, schwannoma, glioma, neurofibroma, posterior subcapsular lenticular opacities
- Multiple meningiomas (two or more) and unilateral vestibular schwannoma or any two of the following: schwannoma, glioma, neurofibroma, cataract.

Vestibular schwannomas (usually, but not always, bilateral) occur in ~95% of adult patients with NF2 (fig 1A,B). Mean age at onset is 22 years, and it is rare to present after the age of 50 years. Presentation is usually with tinnitus, alteration in hearing or vestibular symptoms attributable to vestibular schwannoma, but in the 18% of patients that present in childhood, initial symptoms of a meningioma, spinal or cutaneous tumour are more common.

The best predictor of mortality is age at diagnosis. Other important predictors are the presence of intracranial meningiomas, the type of constitutional NF2 mutation, and the type of treatment centre.<sup>3</sup> In general people with constitutional nonsense or frameshift mutations have severe disease, those with missense mutations, in-frame deletions, or large

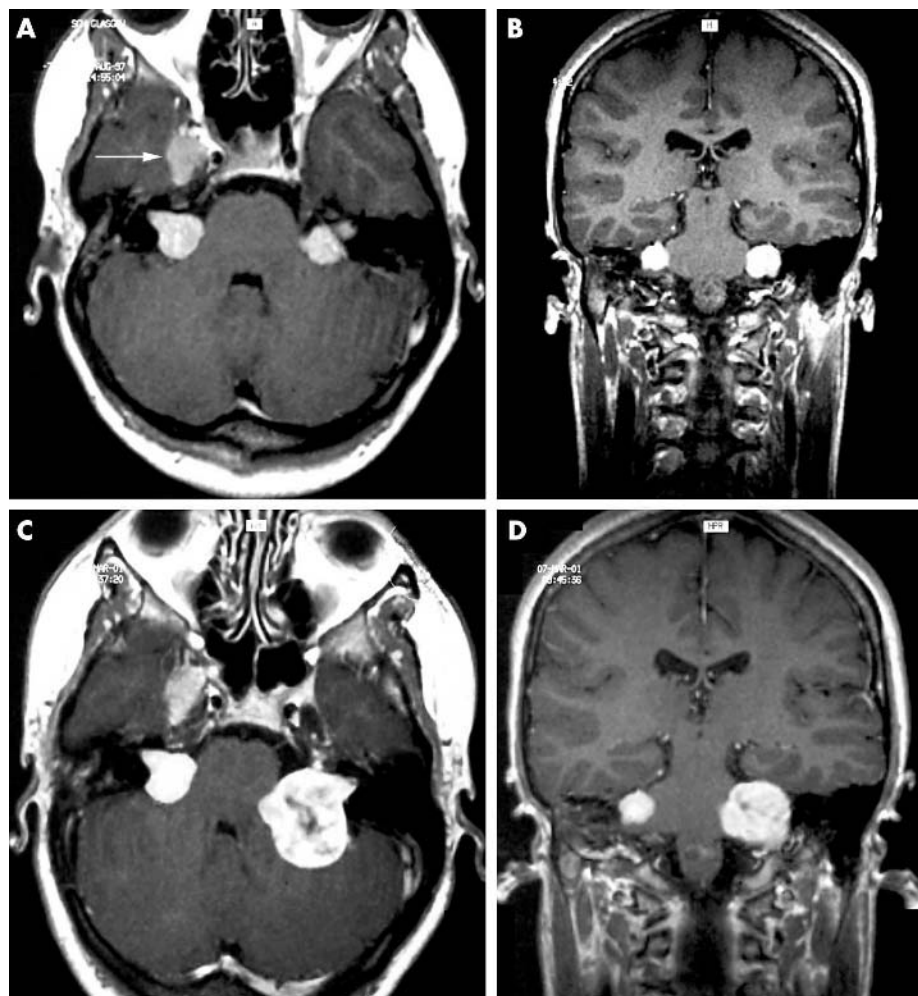
deletions have mild disease, and those with splice site mutations have variable disease severity.<sup>4</sup> Multiple NF2 patients in the same family often have similar disease severity, but specific disease features and disease progression can differ even between monozygotic twins with NF2. In families with early onset neurofibromatosis 2, screening should probably begin in childhood, and if magnetic resonance imaging (MRI) shows no evidence of schwannoma at 30 years, the likelihood of gene inheritance is considered remote.

Vestibular schwannoma growth rates are extremely variable. Opinions about management once they are detected remain controversial and are still evolving. Some NF2 patients with unilateral vestibular schwannomas, and a subgroup with bilateral tumours that progress slowly, may be asymptomatic or have mild or stable symptoms for a long time. Such patients, if MRI shows no change in the size of the tumour, can be clinically and radiologically observed. However, vestibular schwannomas in NF2 are generally more invasive than isolated schwannomas (fig 1C,D). Both microsurgery and radiation treatment have a role in management. Patients with NF2 should be referred to specialty treatment centres to be managed by a multidisciplinary team expert in their disorder.<sup>3,4</sup>

The large majority of patients with NF2 develop substantial or total deafness. Some develop blindness from progression of the subcapsular lens opacities to cataracts, or morbidity from other tumours. Mortality from NF2 is high, the mean age at death being around 40 years, with a mean survival after diagnosis of 15 years.<sup>2</sup> Death usually occurs from progressive growth of vestibular schwannomas causing increased intracranial pressure from brainstem displacement.

### Non-syndromic

The most common forms of genetic deafness are non-syndromic.<sup>5</sup> Inheritance is usually in an autosomal recessive pattern. Both X linked and dominant forms occur, but autosomal recessive inheritance accounts for more than 75% of childhood pre-lingual deafness. The most recent data on



**Figure 1** Bilateral vestibular schwannomas in a patient with neurofibromatosis 2 (NF2). (A, B) Axial and coronal T1 weighted images with gadolinium enhancement are shown. Note the presence of an associated trigeminal schwannoma (arrow). (C, D) Significant enlargement has occurred over four years, with the left sided vestibular schwannoma causing displacement of the brainstem.

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genetic loci can be obtained at the Hearing Loss Homepage ([www.uia.ac.be/dnalab/hhh/](http://www.uia.ac.be/dnalab/hhh/)).

### MITOCHONDRIAL

Mitochondria derive from the ovum and, as a general rule, mitochondrial mutations are passed via the female pedigree. Pathogenic mutations affect a proportion of the mitochondrial genome, and mutant and wild type mitochondria coexist in the same cell, a situation known as heteroplasmy. A minimum number of mutant mitochondria must be present before a tissue exhibits signs of dysfunction, and the threshold for disease is lower in cell types dependent on high degrees of oxidative phosphorylation, such as brain, skeletal muscle, heart and endocrine organs. Heteroplasmy and the threshold effect partly explain the degree of phenotypic heterogeneity seen in this group of conditions, and the relatively poor correlation between genotype and phenotype.

### MITOCHONDRIAL SYNDROMIC

Syndromic hearing impairment secondary to mitochondrial mutations occurs most commonly in MELAS (mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes), MERRF (myoclonic epilepsy with ragged red fibres) and Kearns-Sayre syndrome (KSS). The clinical features of these disorders are summarised in table 2. The mitochondrial mutation found in MELAS (3243A to G) is also found in

maternally inherited diabetes and deafness (MIDD), in which progressive SNHL is associated with young onset diabetes mellitus.

### MITOCHONDRIAL NON-SYNDROMIC

It is uncertain why the mitochondrial mutations resulting in non-syndromic hearing loss preferentially affect hearing. Five such mutations have been described: 1555A to G, 7445A to G, 7472insC, 7510T to C, and 7511T to C.<sup>6</sup> Carriers of the 1555A to G mutation are susceptible to hearing impairment after aminoglycoside antibiotics, even at normal therapeutic levels. The 7472insC mutation results in a phenotypic spectrum ranging from progressive SNHL as the sole manifestation to a severe neurological syndrome associated with ataxia, dysarthria, or rarely myoclonus. Affected members of the same pedigree may have different levels of phenotypic expression, emphasising the importance of an accurate family history.

### DIAGNOSING MITOCHONDRIAL DISEASE

Diagnosis of mitochondrial disease may be a straightforward process of pattern recognition and appropriate investigation. However, heteroplasmy and the threshold effect result in great variation in phenotype within the tissues of individual patients, and within different individuals of the same family.

Most mitochondrial syndromes present before the age of 40 years. A detailed general medical history may reveal the presence of diabetes, hypoparathyroidism, cardiomyopathy,

**Table 2** Clinical features of mitochondrial syndromes associated with deafness

Condition/syndrome	Neuro-otologic syndrome	Main clinical features	Additional features	Epidemiology	Laboratory markers
MELAS	Cochlear origin; symmetric gradual onset SNHL	Encephalopathy (seizures $\pm$ dementia); stroke-like episodes; mitochondrial myopathy	Short stature; normal early psychomotor development; recurrent headache and vomiting	Usually first decade; sometimes 10–40 years	Ragged red fibres on muscle biopsy; increased lactate
MERRF	Symmetric gradual onset SNHL	Myoclonus; epilepsy; cerebellar syndrome; myopathy	Short stature; dementia; optic atrophy; cardiomyopathy; Wolff-Parkinson-White syndrome; peripheral neuropathy	Usually childhood onset, but may be adults	Ragged red fibres on muscle biopsy; increased lactate
KSS	Symmetric gradual onset SNHL	Retinitis pigmentosa; ophthalmoplegia	Cardiac conduction block; cerebellar syndrome; short stature; impaired intellect	Onset <20 years; majority are sporadic	Ragged red fibres on muscle biopsy; increased lactate, raised CSF protein

CSF, cerebrospinal fluid; KSS, Kearns-Sayre syndrome; MELAS, mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes; MERRF, myoclonic epilepsy with ragged red fibres; SNHL, sensorineural hearing loss.

cardiac conduction block, or pancreatic dysfunction. Family history is crucial, concentrating on the maternal pedigree, remembering that carriers may be oligo- or asymptomatic. Diseases secondary to mitochondrial deletions (for example, KSS) usually occur sporadically, and so a negative family history does not exclude the possibility of mitochondrial disease. Examination should note the presence of short stature and any evidence of psychomotor retardation, visual loss (cortical blindness, optic atrophy, retinitis pigmentosa), ptosis, ophthalmoplegia, SNHL, myopathy, neuropathy, or movement disorders such as myoclonus or dystonia.

Blood tests should include a blood count, electrolytes (renal tubular acidosis may occur in KSS and MELAS) and creatine kinase (which may be elevated). Serum lactate and pyruvate are often elevated at rest and increase further on modest exercise. Cerebrospinal fluid (CSF) examination may reveal elevated protein in KSS and MERRF, although this rarely exceeds 1 g/l. An ECG may show the pre-excitation of Wolff-Parkinson-White syndrome in MERRF and cardiac conduction block in KSS. An electroencephalogram (EEG) may demonstrate epileptiform discharges in MERRF and MELAS. MRI of the brain may demonstrate high signal lesions on T2 weighted scans in MELAS, especially posteriorly and characteristically not corresponding to the territory of a single major vessel. Calcification of the basal ganglia may be seen in all mitochondrial syndromes. KSS may be associated with a leucoencephalopathy, whereas atrophy is a more common finding in MERRF. Nerve conduction studies and electromyography (EMG) may demonstrate myopathy and/or a neuropathy, which is usually axonal. Muscle biopsy may demonstrate ragged red fibres when stained with modified Gomori trichrome. Staining with cytochrome c oxidase (COX) is negative in MERRF and KSS, but most ragged red fibres stain positively in MELAS. A further characteristic feature of MELAS on muscle biopsy is the overabundance of mitochondria in smooth muscle and endothelial cells of intramuscular blood vessels.

Molecular genetic testing is available for common mitochondrial mutations. In the case of MERRF and MELAS, the mutation can be detected from blood leucocytes. Heteroplasmy results in varying tissue distribution of mutated mitochondrial DNA, and so in patients presenting with only a few symptoms of MERRF or MELAS, the mutation may be undetectable in leucocytes, and may only be detected in other tissues such as cultured skin fibroblasts, oral mucosa, or (most reliably) skeletal muscle. The deletion associated with KSS is only observed in muscle mitochondria,

and therefore cannot be detected in lymphocytes or fibroblasts.

### DISORDERS WITH INDIRECT MITOCHONDRIAL INVOLVEMENT

Other disorders causing deafness may be associated indirectly with mitochondrial dysfunction, although the precise mechanism remains controversial. Cytosolic proteins are imported into mitochondria by means of mitochondrial tagging signals. One mutation of the mitochondrial protein importation mechanism has been described which results in Mohr-Tranebjaerg syndrome, an X linked recessive disorder causing progressive SNHL, dystonia, and psychiatric symptoms.<sup>7</sup> Friedreich's ataxia, in which deafness is an occasional feature, is caused by an expansion of GAA trinucleotide repeats in the FRDA gene encoding frataxin. Frataxin is targeted to mitochondria and has a role in iron homeostasis. Mitochondrial dysfunction may be a final common pathogenic mechanism in these conditions.

### AUTOIMMUNE

Immune mediated inner ear disease (IMIED) is a well recognised presentation of systemic autoimmune disease, but has an uncertain pathogenesis. Animal experiments have refuted the traditional concept of the inner ear being an "immunologically privileged" site, and in 1979 a series of patients with bilateral progressive SNHL responsive to steroids was described.<sup>8</sup> However, evidence for specific autoimmunity is indirect, being chiefly derived from clinical observations of SNHL in systemic autoimmune disease, and steroid responsiveness in patients with otherwise unexplained hearing loss.<sup>9</sup> Autoimmunity has since been proposed as an aetiological factor in other disorders originally thought to have an alternative pathogenesis—for example, Ménière's disease (see Luxon, p iv45).

IMIED characteristically presents subacutely over weeks to months, though can be either insidious (over years) or sudden. It tends to be progressive, but may fluctuate, and hearing loss tends to involve high frequencies. It is bilateral in most cases, though generally asymmetric and asynchronous, weeks or months separating involvement of the two sides. Other vestibulo-auditory symptoms are common including aural fullness, tinnitus, lightheadedness, and vertigo, and this can lead to confusion with Ménière's disease.

Underlying systemic autoimmune disease is common, but hearing loss may be its presenting feature. Like other autoimmune disorders, prevalence is highest in middle aged

**Table 3** Autoimmune syndromes associated with hearing loss

Condition/syndrome	Neuro-otologic syndrome	Associated findings	Epidemiology	Laboratory markers/diagnostic tests
Cogan's syndrome	"Ménière-like": attacks of vertigo, nausea, tinnitus, and hearing loss	Eye inflammation (keratitis, scleritis, conjunctivitis, uveitis, retinal vasculitis); systemic vasculitis in 10%	Young adults and older children (median 25 years)	Neutrophilia, raised ESR/CRP, MRI enhancement of vestibulocochlear structures
Wegener's granulomatosis	Usually conductive hearing loss; often have otitis media; SNHL reported, but usually as part of mixed picture	Rhinorrhoea and sinusitis; pulmonary, renal, joint manifestations; peripheral nervous system involvement	40 to 50 years; males and females equally affected	Raised ESR/CRP, raised ANCA (proteinase 3), granulomatous infiltration on MRI, biopsy
Polyarteritis nodosa	Rapid SNHL	Systemic vasculitis (kidney, gut); constitutional symptoms; mononeuritis multiplex	Male > female; older age of onset	Leucocytosis, raised ESR, visceral angiography, organ/nerve/muscle biopsy
Systemic lupus erythematosus	Subacute SNHL; may be subclinical (NSAIDs and antimalarials may complicate picture as both may cause SNHL)	Dermatologic, joint, renal, neuropsychiatric; constitutional symptoms	Female > male (5:1); age 15–40 years	Raised ESR, ANA, dsDNA antibodies, antiphospholipid antibodies, complement consumption
Sjogren's syndrome	Often subclinical	Dry eyes, dry mouth; Raynauds and joint symptoms; neuropathies (axonal, sensory ataxic, trigeminal)	Female > male	ANA, Ro, La, Schirmer test, lip biopsy

ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibody; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; MRI, magnetic resonance imaging; NSAIDs, non-steroidal anti-inflammatory drugs; SNHL, sensorineural hearing loss.

females. Table 3 lists the common systemic autoimmune diseases with which IMIED is associated, and provides diagnostic pointers for each.<sup>10</sup> An audiogram is useful to detect high frequency hearing loss that may be asymmetric as well as being useful in monitoring treatment response; exclusion of syphilis is important since it can present in a similar fashion. Routine laboratory tests are often normal—serum testing for antibodies to a non-organ specific 68-kD antigen has proved the most specific diagnostic test, but is not readily available, and the relation of these antibodies to disease pathogenesis and course requires further definition.

IMIED is an important diagnosis to consider because it is reversible. While clinical history and context remain the cornerstones of diagnosis, the other essential feature that separates IMIED from other causes of SNHL is steroid responsiveness—the hearing loss should improve with treatment, and deteriorate on discontinuation of treatment. Steroids are managed in the same way as other autoimmune conditions, and plasmapheresis can be used as an alternative or an adjunct. Many experts add cyclophosphamide or methotrexate if patients deteriorate or demonstrate a partial response.<sup>10</sup> Azathioprine may be useful as a steroid sparing agent.

The anticipated outcome without treatment is sensorineural deafness, but patients who are non-responders should not be subjected to increasingly aggressive immunosuppression. Those who respond to treatment have a course often characterised by fluctuation, with relapses occurring on steroid reduction, and many may require long term immunosuppression. Prognosis for hearing is good in responders.

### Metabolic

There are several inherited disorders of metabolism associated with deafness, many of which have additional neurological features. These conditions are described in an extensive review by Konigsmark,<sup>11</sup> and only a few illustrative examples will be discussed further here.

### Refsum's disease

Refsum's disease is an autosomal recessive disorder characterised by defective peroxisomal  $\alpha$  oxidation of phytanic acid. As a result, patients are unable to metabolise phytanic acid, resulting in an accumulation in tissues. Symptoms

begin in late childhood, adolescence, or early adult life. Hearing loss is a common association, although the cardinal clinical features are retinitis pigmentosa, cerebellar signs, and chronic polyneuropathy. The sensorimotor neuropathy is distal and symmetric, and affects the lower limbs more than the arms. Reflexes are lost and all sensory modalities are affected. Nerves may or may not be palpably enlarged. Neurophysiology shows slowed motor nerve conduction velocities. Cardiomyopathy and ichthyosis (especially on the shins) are common. Anosmia and night blindness may precede the cardinal clinical features by many years.

Investigations demonstrate a raised CSF protein, and all patients have greatly elevated serum concentrations of phytanic acid. Phytanic acid  $\alpha$  oxidase activity can be measured in cultured fibroblasts. Untreated, the disease is steadily progressive, although there may be periods of apparent deterioration or remission. The importance of considering the diagnosis of Refsum's disease is that when dietary phytanic acid is reduced, the progression of the disease is arrested and indeed some clinical improvement may occur. Plasmapheresis at the time of diagnosis may also be useful to accelerate clinical improvement.

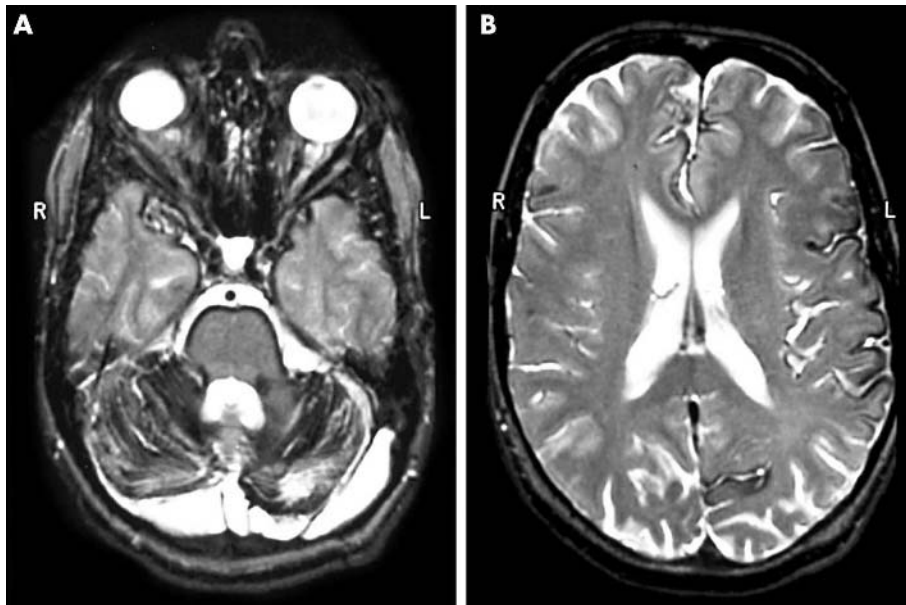
### Mucopolysaccharidoses

Deafness may also be a prominent feature of the mucopolysaccharidoses, disorders in which lysosomal enzyme deficiencies result in the tissue accumulation and increased urinary excretion of mucopolysaccharides. These conditions present in childhood and six syndromes are recognised, of varying severity. Clinical features typically include coarse facies, corneal clouding, organomegaly, bone and joint abnormalities, short stature, and in some cases psychomotor retardation. The diagnosis is suggested by the findings of vacuolated lymphocytes on blood film and the accumulation of glycosaminoglycans in the urine. There is some clinical overlap with the mucolipidoses, lysosomal storage disorders, and glycoprotein storage diseases (for example, mannosidosis). Definitive diagnosis rests on specific enzyme assays in leucocytes or cultured skin fibroblasts.

### Miscellaneous

#### Neurosarcoidosis

In the largest series to date, 72% of patients with neurosarcoidosis presented with cranial nerve palsies, optic



**Figure 2** Superficial siderosis. (A) T2 weighted axial image demonstrating haemosiderin deposition over the surface of the cerebellum. (B) T2 weighted axial image showing a hypointense ring of haemosiderin lying over the surface of the cerebral sulci on the left (Images courtesy of Dr J Bhattacharya).

nerve palsies forming the majority.<sup>12</sup> However, eighth nerve palsy causing auditory or vestibular impairment occurred in 6% of cases, and deafness occurred in 7% of cases in one of the earliest series.<sup>13</sup> Granulomatous vasculitis may lead to ischaemia or granulomatous infiltration may cause nerve compression. Clues include cervical adenopathy, skin lesions, parotid swelling, and abnormal chest *x* ray.

#### Susac syndrome

This is a rare syndrome comprising the clinical triad of encephalopathy, retinopathy, and hearing loss, largely in women. SNHL is often the presenting feature, but may be subclinical, only becoming evident on an audiogram. It may be unilateral or bilateral, and often presents in conjunction with vestibular symptoms or tinnitus. The retinopathy consists of multiple retinal branch occlusions, and the encephalopathy has both cognitive (memory disturbance) and psychiatric components. Pathology of involved structures points to a non-inflammatory vasculopathy. Anti-inflammatory and antiplatelet strategies are sometimes employed, but the disease often fluctuates initially then becomes self limiting.

#### Superficial siderosis

Superficial siderosis is a rare disorder that causes SNHL in association with slowly progressive cerebellar ataxia. Pyramidal signs may also be present, and dementia and bladder disturbance occur in some cases. There has been controversy regarding the aetiology of superficial siderosis, since it was initially hypothesised to be secondary to a metabolic disease analogous to haemochromatosis, but it is now accepted that it is caused by chronic subarachnoid haemorrhage. The diagnosis is often not suspected clinically, but the appearances on T2 weighted MRI are striking, showing a black rim (haemosiderin) around posterior fossa structures and cerebral sulci (fig 2).

#### Disorders of central auditory processing

There are inherent difficulties in the diagnosis and classification of the central auditory processing disorders: separating a specific difficulty with “complex sound processing” from a

peripheral hearing or language disorder, which will often co-exist in the same patient, is fraught with uncertainty. These disorders cause problems with detecting the pattern in sound in one or more of four dimensions (frequency, time, amplitude, and space), at a lower cognitive level than a language disorder, but at a higher level than peripheral hearing loss.<sup>14</sup> Many developmental presentations have been described in children and will not be considered here. In adults, specific syndromes are recognised, but are often masked by variability in clinical presentation. The common causes are stroke, head injury, and brain tumours. Comprehension, reading, and writing are preserved in “pure” syndromes, in which there is no co-existent aphasia.

#### Cortical deafness

This can be defined as the loss of the perception of sound caused by cortical damage. The patient normally presents with deafness. The contribution of attentional deficits is often difficult to assess, and inconsistency in response to sounds is a common feature. Usually there are abnormalities on audiometry, but patients have normal brainstem auditory evoked potentials. Cortical deafness is caused by bilateral lesions affecting the superior temporal gyrus: most reported cases have involved damage to the primary auditory area in Heschl’s gyrus bilaterally. The most common pathology is bilateral temporal lobe stroke, normally occurring in a stepwise fashion.

#### Auditory agnosias

An agnosia is a failure to recognise an environmental stimulus, despite intact sensory function. Patients with auditory agnosias have disordered perception of certain sounds (those with a complex structure) in the presence of preserved hearing. Such sounds include speech (“pure word deafness”), music (“amusia”) and environmental sounds (“environmental sound agnosia”). There is often pronounced overlap between the specific auditory agnosia syndromes—patients with word deafness generally exhibit some non-verbal auditory agnosia as well—supporting the hypothesis that the problem lies in being able to appreciate the pattern of sound in time and space at an intermediate level. Auditory

perception is commonly tested with batteries of words, environmental stimuli and music, and most studies make no attempt to categorise the perception of simple patterned sounds, thus making clear distinction from higher cognitive disorders difficult.

The picture may be further complicated by a degree of peripheral or cortical deafness, but there are several reported cases in which audiometry was normal.<sup>14</sup> Brain stem auditory evoked potentials are normal. Again, pathology is usually vascular, and usually bilateral, with the superior temporal lobes being the site of damage. The left hemisphere appears to have greater participation in processing speech, and the right hemisphere has greater participation in processing non-speech acoustic signals. This observation has been supported recently by functional MRI data, which suggest that the right anterior superior temporal gyrus may respond more strongly to non-speech verbal sounds, while the same area on the left is more specific to speech sounds.<sup>15</sup>

Cortical auditory disorders tend to persist, and treatment is directed at the specific deficit in auditory perception. Patient and carer education is a key factor.

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