CASE REPORT

Sensorineural deafness following routine transurethral resection of the prostate

Benjamin Bowsher

Emergency Department,
Northern NSW Local Health
District, Tweed Heads, New
South Wales, Australia

Correspondence to
Dr Benjamin Bowsher,
benbowsher@gmail.com

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SUMMARY

A man in his 50s presented to a rural Australian emergency department with complete unilateral hearing loss following transurethral resection of the prostate. His hearing impairment progressed from 'muffled hearing' with tinnitus on emergence from anaesthesia, to total sensorineural deafness by day three. His surgery and anaesthesia were uncomplicated and he had remained normotensive throughout. He had no pre-existing auditory disease. He had received 240 mg of intravenous gentamicin intraoperatively for surgical prophylaxis. Renal function was normal. Brain imaging was negative for structural pathology, stroke and circulatory insufficiency. Ear nose and throat advised 7 days of oral corticosteroids, transtympanic dexamethasone and hyperbaric oxygen therapy. A working diagnosis of gentamicin-induced ototoxicity was applied. Intervention has proven unsuccessful and there is no possibility for rehabilitation. The patient is permanently disabled.

BACKGROUND

Patients are not routinely counselled about the risks of gentamicin therapy. Rare, yet severe, side effects include ototoxicity and nephrotoxicity.¹ 'Permission' for drug administration is *inferred* on signing surgical and anaesthetic consent forms, yet explicit reference towards side effects is seldom made. An informed patient may choose a less efficacious, non-ototoxic antibiotic. An informed patient may recognise rare side effects early and present to a doctor.

Gentamicin exhibits greater vestibulotoxicity than cochleotoxicity.² In this case however, symptoms were purely auditory and the vestibular system unaffected. The literature typically describes a bilateral hearing impairment with aminoglycoside-induced ototoxicity.³ Why only one ear has been challenged and the vestibular spared is intriguing.

In operating theatres, a predetermined dose of neat gentamicin is delivered as a series of miniboluses. The practice termed 'staggered bolusing' has evolved for practical reasons and is generally well tolerated, but theoretically could provoke toxic plasma levels and hence requires addressing.

CASE PRESENTATION

A man in his 50s presented to a rural Australian emergency department with complete sensorineural deafness in the left ear and frank haematuria. A suprapubic catheter was in situ, for he was 6 days post transurethral resection of the prostate for benign prostatic hypertrophy. Urinalysis confirmed

an uncomplicated urinary tract infection and he was treated with oral antibiotics. On emergence from anaesthesia, he reported muffled hearing and tinnitus. A doctor performed tuning fork tests and arranged outpatient ENT follow-up. By day 3, the patient was unable hold a telephone conversation using the affected ear. Despite this, he presented late to emergency and had not yet seen ENT.

The patient's surgery and anaesthesia were unremarkable. A 240 mg intravenous dose of gentamicin was administered under general anaesthesia. The patient was normotensive throughout with mean arterial pressures adequate for cerebral perfusion. There was no neuraxial or regional block on board. On removal of the surgical drapes a rash was noted on the chest, yet no features of anaphylaxis were apparent.

Despite various inactive musculoskeletal problems, the patient had no significant medical history. Of note, there were no auditory problems, cardiovascular disease or vascular risk factors predisposing towards circulatory insufficiency. He had no intracranial pathology.

The patient was a non-smoker and consumed only a modest amount of alcohol. He was a non recreational drug user, an active local businessman, and had a supportive wife.

There was no family history to indicate genetic predisposition towards sudden sensorineural hearing loss. His father had minor age-related hearing loss only and functioned well.

INVESTIGATIONS

Bedside otoscopy excluded anatomical and infective causes of acute hearing loss and was normal bilaterally. Rinne's and Weber's tuning fork tests demonstrated profound left-sided sensorineural deficit. These tests differentiate conductive from sensorineural deafness and guide further management.

Bloods were taken to narrow the differential; full blood count, urea and electrolytes, liver function tests, thyroid function tests, CRP, random glucose and plasma gentamicin level were assessed. All results were within normal limits. Of particular note: white cell count was $10.3 \times 10^9/L$, estimated glomerular filtration rate >90 mL/min and random gentamicin was <0.2 mg/L.

CT brain imaging excluded haemorrhage, infarct and structural pathology. This was important given the unilaterality of symptoms, which suggested a possible hemispheric focus of disease. MRI followed, given its greater sensitivity for small acoustic neuroma; this too was unremarkable.

Pure tone audiography demonstrated profound hearing loss for high, mid and low frequencies

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(figure 1). Drug-induced ototoxicity shows predilection for high frequency losses. Gradual progression to mid then lower frequencies may occur according to magnitude of initial injury.⁴ Audiography determines the degree, type and configuration of hearing loss to individualise treatment. Given the extent of damage however, no hearing aid would have been beneficial in this case.

DIFFERENTIAL DIAGNOSIS

The working diagnosis was of gentamicin-induced ototoxicity. This was a diagnosis of exclusion. The temporal sequence suggests an intraoperative event has occurred and immediately there is a suspicious causative agent. A context-specific differential for sudden onset sensorineural hearing loss considers environmental exposures, drugs, inner ear disease, generalised central nervous system (CNS) pathology and localised CNS pathology.

Prolonged exposure to sound >85 dB may cause acoustic trauma. Noises up to 108 dB have been recorded in operating theatres from suction, alarms and monitoring equipment.⁵ Acoustic trauma produces narrow band audiography deficits in contrast to pan-frequency losses observed with aminoglycoside ototoxicity. Furthermore, noise-induced hearing loss shows rehabilitation potential. For these reasons, acoustic trauma is an unlikely aetiology.

The non-steroidal anti-inflammatory drugs (NSAIDs) and loop diuretics are common agents also implicated in sensorineural hearing loss. A single dose of intravenous ketorolac (an NSAID) was given under anaesthesia. NSAID-induced hearing loss however, is reversible on discontinuation of treatment,⁶ and this patient had irreversible damage.

Ménière's disease is characterised by paroxysms of vertigo, tinnitus and hearing loss. In many respects, the patient's symptoms reflect those of Ménière's. However, with no vestibular symptoms or history of previous attacks, the diagnosis is doubtful.

Autoimmune inner ear disease causes progressive hearing loss over weeks to months, immediately differentiating it from the sudden impairment observed in this case. The disease also associates with systemic autoimmune conditions such as ankylosing spondylitis, systemic lupus erythematosus, Sjögren's syndrome and Wegener's granulomatosis, for which there was no history.

Generalised inflammatory CNS conditions include meningitis, encephalitis and neurosyphilis and all can cause sensorineural hearing loss. There was however, no prodrome and no post-operative symptomology commensurate with infective neurological disease. Furthermore, the patient was in a monogamous relationship.

Focal CNS disease was of major concern, as certain pathologies mandate rapid neurosurgical intervention. Brain imaging ruled out cerebrovascular accident, acoustic neuroma, cerebello-pontine angle tumours, aneurysms of the anterior inferior cerebellar artery, arteriosclerosis and multiple sclerosis.

Systematic exclusion of differentials according to history, examination and investigations promotes gentamicin-induced ototoxicity as the preferred diagnosis. Management has been targeted at correcting this pathophysiology alone.

TREATMENT

The on call ENT consultant advised a short course of oral corticosteroids. Efficacy in ototoxicity is variable, however early treatment is associated with better outcome.⁷ Steroids reduce the amplitude of inflammatory response to aminoglycosides in the cochlear, decreasing hair cell swelling, dysfunction and apoptosis.⁸ Prednisolone has a favourable side effect profile. A trial of 40 mg once daily for 7 days was started. Adjuvant trans-tympanic dexamethasone was given as a single dose by ENT.

Three courses of hyperbaric oxygen therapy (HBOT) were subsequently arranged. Each course consisted of five, 1 h sessions where the patient was subjected to 100% oxygen at 2–3 atmospheres. There is evidence to support HBOT in drug-induced ototoxicity, sudden deafness and noise-induced hearing loss.⁹ Treatment is considered safe. Destructive free radicals are produced when hair cells apoptose. HBOT reduces free radical damage by increasing inner ear antioxidants.¹⁰ Furthermore, high pressure increases arterial oxygen content and delivery to the metabolically challenged tissues of the inner ear. Efficacy of both treatment modalities was assessed by serial pure tone audiography.

OUTCOME AND FOLLOW-UP

Neither corticosteroid nor HBOT resulted in tangible hearing improvement. Pure tone audiography was virtually identical pre and post intervention. The patient is plagued by tinnitus and

Figure 1 Pure tone audiogram: profound left-sided sensorineural hearing loss.

there is no possibility of rehabilitation. He has been discharged from ENT. A cochlear implant may restore limited hearing,¹¹ but would only be considered with profound bilateral hearing loss. The socioeconomic impact has been severe and lawyers seek remuneration for personal damages and loss of future earnings. Any payout is expected to be significant.

DISCUSSION

A pivotal issue raised by this case is informed patient consent. Where should we draw the line? When does explicit detailing of risk transcend from good moral practice to onerous fear-mongering? Is it in the patient's best interest to 'shield' them from low risk realities or should we present a statistical analysis of all events which may befall them? Suffice it to say, there is no consistency in how we practice.¹² Common invasive procedures such as chest drains, epidurals and lumbar punctures all mandate formal written consent. Adverse outcomes are discussed, recorded and presented alongside complication rates where available. A competent patient then decides on how to proceed. Why then for the ubiquitous aminoglycosides, where potential to cause *serious* harm is well known, do we not require written consent for administration? Based on the outcome of this case, we unquestionably should.

From a health board's perspective, it makes perfect sense to formalise consenting. This would empower patients, decrease payouts and save on rehabilitation. It would however, represent a significant logistical challenge as gentamicin is so widely prescribed. Furthermore, for those without capacity, meetings with next of kin would need to be arranged and for non-consenting individuals, potentially less efficacious antibiotics would need to be substituted.

Unilateral gentamicin-induced ototoxicity is an unusual occurrence. There is no consensus of opinion to explain this phenomenon. Various otoprotective factors have been championed,^{13 14} but why any of these would forsake any particular ear is unclear. Pre-existing inner ear damage can exaggerate ototoxic response to aminoglycosides, however the patient enjoyed normal preoperative hearing and reported no prior acoustic trauma.

Two key gene mutations have been identified that predict aminoglycoside-induced ototoxicity: A1555G and 961delT+C (n).¹⁵ Prevalence is estimated at 1 in 1161 and 1 in 166, respectively.¹⁶ Routine screening for these sequences would undoubtedly confuse management for the majority, but there may be a role in those with a strong family history of drug-induced hearing loss or for those who have already suffered an ototoxic insult.

Gentamicin administration technique is inconsistent. Infusions prevent peak plasma concentration rising too sharply. Sharp rises are a mechanism by which ototoxicity may occur independent of total dose administered.¹⁷ In operating theatres, gentamicin *may* be given as a 'staggered bolus' of neat drug. Small aliquots of a predetermined dose are injected at non scientific intervals until completion. Never will an entire dose be given as a push. This would be reckless. However, one can imagine how staggered boluses may achieve toxic plasma levels inadvertently. There needs to be a safer method for delivery of gentamicin in operating theatres. A major barrier is the surgical insistence for therapeutic gentamicin levels immediately preceding 'knife-to-skin' (or instrumentation). Perhaps an infusion could be started on the ward and timed to finish just as the patient arrives in theatre. This however, may be asking too much of a pressured health service. Alternatively, an infusion could be started in the anaesthetic room, but delays, overruns and

cancellations would follow. One can sympathise with how and why staggered bolusing has come into practice, however should it be implicated in the outcome of this case, then the technique is indefensible. A randomised trial is required to address this issue with clarity, but for now all we can say is that it remains a cause for concern.

Patient's perspective

Since the operation things have got significantly worse. There's a constant screaming vibrating noise in my head. When riding my motorbike with my helmet on it's magnified like being inside a steel drum. This is quite distracting. I'm constantly walking around trying to equalize my ears. At work I cannot hear my customers and am always having to say 'what'. The girls shout things from behind the counter but I cannot hear them. I feel isolated. When there is lots of noise around it is disorientating and I have to move away. Sleep is difficult and things have become pressured with my wife.

Learning points

- ▶ Practitioners should obtain written consent prior to gentamicin administration.
- ▶ Aminoglycoside-induced ototoxicity can present as unilateral or bilateral sensorineural deafness.
- ▶ Treatment for drug-induced ototoxicity is ineffective when patients present late.
- ▶ Gentamicin administration technique must be standardised.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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