(750 mg) but was then found to have a random blood glucose in the diabetic range (>20 mmol/L). This was initially attributed to the steroid therapy but over the next two weeks the diabetes became increasingly difficult to control, with plasma glucose 10–20 mmol/L despite insulin infusion of over 800 units/24 h. In addition there had been a change in physical appearance with complete loss of subcutaneous fat and hirsutism.

When found to have high titres of antibody to the insulin receptor but no antibodies to insulin she was diagnosed as having the syndrome of type B insulin resistance.² She then received four weekly intravenous doses of rituximab 580 mg. There were no obvious side effects and a month after the start of treatment her peripheral B-cell count had fallen by 94% (T-cell count unchanged). The ESR declined from 116 to 9 mm/h. Reduction of the insulin dosage was then begun. Two months after the treatment, daily insulin was about 300 units and blood glucose was 5–12 mmol/L. At three months her daily insulin requirement had fallen to 120 units and at five months she was able to stop insulin therapy. Over this period the fat atrophy resolved and her facial appearance returned to normal.

COMMENT

In these two patients, the production of well-defined autoantibodies led to severe life-threatening disease that proved resistant to strong immunosuppressive drugs. Originally used in the treatment of B cell lymphomas,³ rituximab has lately found a place in management of autoimmune disorders such as rheumatoid arthritis and systemic lupus erythematosus.^{4,5} The B-cell-depleting effect results from complement and antibody dependent cell mediated cytotoxicity, inhibition of cell proliferation and induction of apoptosis of CD20 expressing cells of the B-cell lineage. Lack of expression of CD20 on progenitor cells means that rituximab can deplete peripheral B cells without robbing the bone marrow of progenitor cells. The agent is well tolerated: neutropenic sepsis has been described,⁶ but major infections seem uncommon after its use in rheumatic disease.⁴ Clinicians should consider rituximab therapy when faced with severe antibody-mediated autoimmune conditions resistant to conventional immunosuppressive drugs.

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Hearing loss treated with pamidronate

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Elderly patients who attend an audiology department for hearing loss are commonly found to have a treatable cause.¹

CASE HISTORY

A retired army quartermaster aged 72 sought advice because of hearing loss and tinnitus reminiscent of Morse code. He also reported an increase in regimental beret size from $6\frac{3}{4}$ inches to $7\frac{1}{2}$ inches. This classic detail of the history prompted measurement of serum alkaline phosphatase, which was high at 562 u/L (corrected calcium 2.35 mmol/L). The diagnosis of Paget's disease was confirmed by isotope bone scan.

MRI of his brain and internal acoustic meati confirmed skull vault thickening and showed no evidence of compression of the 8th cranial nerve on either side. The cochleas appeared normal. His audiogram showed the moderate mixed high-frequency sensorineural and low-frequency conductive hearing loss typical of Paget's disease. Tympanograms were normal, and loudness discomfort levels suggested a non-recruiting loss. He was treated with six intravenous pamidronate infusions at one-week intervals and was provided with a hearing aid. At reassessment six months later the conductive component of his hearing loss had completely resolved and in consequence air conduction thresholds had improved (Figure 1). He no longer required the hearing aid. His tinnitus had greatly improved, and the alkaline phosphatase was now 198 u/L.

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Figure 1 Audiogram before (a) and after (b) treatment. X=left air conduction; O=right air conduction; J=left masked bone; [=right masked bone; $\triangle$ =unmasked bone

COMMENT

In the UK, about 5% of the population over 55 have Paget's disease. A quarter have skull involvement, and in half of these the temporal bones are affected, usually bilaterally. Of those with temporal bone involvement about half have hearing loss, a quarter have tinnitus and a quarter have vertigo. These figures suggest that, in a randomly selected population of a thousand over-55s, three would have hearing loss from temporal bone Paget's disease.

Several case reports and one retrospective study record improvement or slowing of hearing loss in Paget's disease. A recent prospective uncontrolled study did not show improvements in hearing with such agents, but about half the patients who reported tinnitus or vertigo said that these symptoms had improved.⁶

There is no unifying explanation of the mechanism by which Paget's disease causes hearing loss.⁷ Ossicular involvement is by no means universal even in those with

a purely conductive loss. The sensorineural component has been thought to result from compression of the 8th cranial nerve as it passes through the internal auditory canal but, as in the present case, the auditory nerve is intact in a large proportion of patients with Paget's disease and hearing loss.⁷

In view of the evidence of benefit from medical treatment, conductive hearing loss or other audiological symptoms in a patient of mature years should prompt consideration of Paget's disease.

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Topical ciprofloxacin can delay recovery from viral ocular surface infection

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If prescribed for a viral ocular infection, topical ciprofloxacin is more likely to do harm than good.

CASE HISTORY

A previously fit and healthy man of 27 attended with painful red eyes. He also reported general malaise and sore throat. For the past week he had been treating his eyes with ciprofloxacin 0.3% ophthalmic solution every two hours on the advice of his general practitioner, and it was a worsening of his eye symptoms that caused him to come to eye casualty. There was no previous history of eye disorder and he was using no other medications. On examination, visual acuities were 6/60 in the right eye and 6/36 in the left eye. Both conjunctivae showed a severe follicular reaction, and fluffy white precipitates were seen adhering to the surface of both corneas (Figure 1). There was mild pharyngitis but lymphadenopathy was absent. The clinical evidence was suggestive of pharyngo-conjunctival fever. When the infiltrates were scraped under local anaesthesia, subepithelial infiltrates typical of adenoviral keratoconjunctivitis were clearly visible (Figure 2). The patient was asked to stop topical ciprofloxacin and was treated with only tear substitute. Six weeks later visual acuities were 6/6 and ocular examination revealed nothing abnormal. On electro-microscopy the corneal scrapings showed needle-shaped crystals and viral cultures grew adenovirus type 3; the bacterial cultures were negative.

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Figure 1 Slit lamp photograph showing corneal epithelial precipitates (in colour online)

Figure 2 Same patient after corneal scraping. Note subepithelial infiltrates as seen in adenoviral keratoconjunctivitis (in colour online)

COMMENT

The formation of white crystalline precipitates is a well known property of ciprofloxacin when it is used for treatment of bacterial ulcer.^{1–3} These precipitates, though sometimes troublesome, have the advantage of yielding high local concentrations of the drug and their presence is beneficial in bacterial keratitis.⁴ The reason for their appearance is that topical ciprofloxacin is made up at low pH to discourage precipitation, and the pH rises when the solution meets the tear film. This is not true of topical ofloxacin. Sometimes ciprofloxacin crystals develop even in the original container, blocking the nozzle track.⁵ Adenoviral keratoconjunctivitis, as seen in the present patient, resolves spontaneously within 10–14 days.⁶ Topical lubricants, and in some cases topical corticosteroids, may be useful, but antibiotic therapy has no role.⁶ The irregular surface formed by precipitates of ciprofloxacin causes discomfort, reduces visual acuity and delays recovery.

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