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Sudden sensorineural deafness and hormone replacement therapy

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Abstract
Whilst the oral contraceptive pill (OC) has been implicated on a number of occasions as a cause of sensorineural hearing loss, there are no published reports linking hormone replacement therapy (HRT) to otological symptoms. A case of sensorineural loss with tinnitus following commencement of HRT is described, followed by a discussion outlining the fundamental differences between the OC and HRT, thus explaining why a vascular aetiology is unlikely. It is hypothesized that otological symptoms in such cases may be due to the effect of oestrogens on electrolyte balance disturbing inner ear function and also a direct effect on the auditory pathways mediated in part by alterations in neurotransmitter receptor concentrations.

Key words: Hearing loss, sensorineural; Oestrogen replacement therapy

Introduction

The average life expectancy for women in developed countries is now around 75 years and one in every two women will experience about 30 years of postmenopausal life. The use of hormone replacement therapy (HRT) has thus become more popular in order to alleviate symptoms thought to be due to the menopause and in response to the potential preventative properties of such treatment against osteoporosis, coronary artery disease and stroke. Oestrogens (usually oestradiol) with or without the addition of a progesterone are the hormones used in HRT therapy.

Case report

Four months following a hysterectomy for fibroids a 45-year-old lady was commenced on Climaval™ (oestradiol) as hormone replacement therapy. Less than two days later she developed tinnitus in the left ear closely followed by difficulty hearing on that side. She was referred by her general practitioner to the ENT department four days later with persistence of the tinnitus and deafness. She denied any previous vertigo or other otological symptoms and there was no history of migraine.

Both tympanic membranes were normal, Weber localised to the right and both Rinne tests were positive. A tympanogram was normal, however, the pure tone audiogram revealed a sensorineural hearing loss in the left ear, worse at lower frequencies (Figure 1).

Routine blood tests were done, including ESR, VDRL and an auto-immune screen, and proved to be normal.

The HRT was stopped and the patient commenced on steroids (40 mg prednisolone). In view of the length of delay from the onset of the symptoms to presentation and the relatively mild severity of the hearing loss it was felt not appropriate to admit the patient to hospital for intravenous vasodilators but to monitor the situation as an out-patient.

A repeat pure tone audiogram was performed three days later which revealed a return to normal hearing (Figure 2). Further tests undertaken on subsequent weeks confirmed this improvement and the patient felt that her hearing had returned to normal and the tinnitus disappeared.

In view of the fact that the patient's hormonal profile showed evidence of ovarian failure, she was commenced on Premarin™, a conjugated oestrogen preparation, six weeks later. It was felt that the benefits of HRT in her case outweighed the risk of further otological problems. She had no symptoms initially with the new preparation but did, over the course of the subsequent 12 months, present to the ENT department on three occasions with docu-

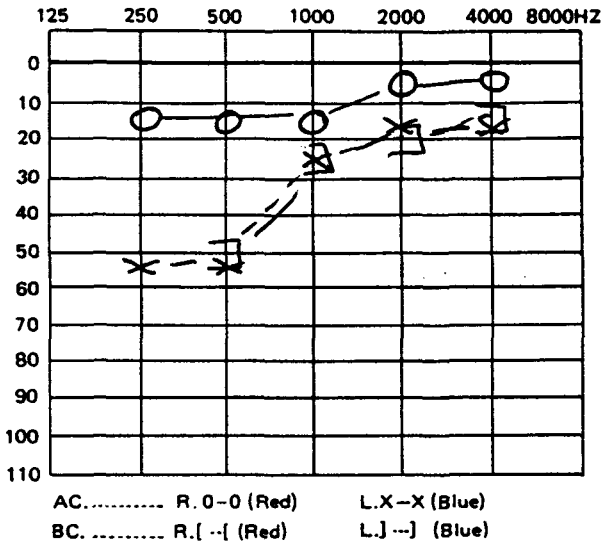

FIG. 1
Audiogram on presentation.

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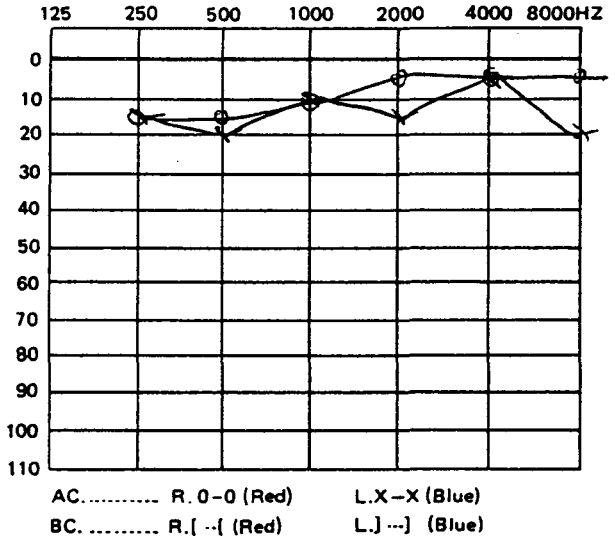

FIG. 2
Audiogram three days after initial presentation.

mented episodes of mild hearing loss similar to the initial episode. She also complained of intermittent tinnitus and vertigo but felt that her symptoms were minor and not interfering with her lifestyle. In view of this and the definite positive advantages of continuing HRT in her situation she has continued taking Premarin™.

Discussion

The Committee on Safety of Medicines has received reports of the following adverse reactions associated with preparations containing oestradiol: deafness, two; ototoxicity, one; tinnitus, 10; vertigo, one (Committee on Safety of Medicines—personal communication), however there are no reported cases in the literature of any preparation of HRT being the cause of a sensorineural hearing loss. This is in stark contrast to the reports implicating the contraceptive pill in sudden sensorineural deafness (Gonzalez *et al.*, 1968; Sellars, 1971; Hanna, 1986). These reports attribute the loss to the known increase in the risk of thromboembolism in those taking the contraceptive pill. Whilst the dose of oestrogen has been reduced in recent years, it would still appear that the overall risk of a cerebrovascular accident is in the order of 1 in 200 000 per year in those using this form of contraception (Kase and Speroff, 1980).

There is a widely held belief that HRT increases the risk of venous thrombotic disease in the same way as the oral contraceptive pill (OC), however there is no evidence to support this (Boston Collaborative Drug Surveillance Programme, 1974). Whilst both preparations involve the use of oestrogens there is a difference between their chemical structure that is fundamental and therefore does not allow one to extrapolate OC data to HRT. The combined oral contraceptive contains a synthetic compound named ethinyl oestradiol with an ethinyl group at the C-17 position which greatly enhances its potency. However this synthetic oestrogen also increases the biological activity of various procoagulant factors such as 2, 7, 10, 12 and fibrinogen. The oestrogens used in HRT are, by contrast, 'natural' oestrogens and appear not to have a thrombotic effect except for a slight reduction in levels of antithrombin-3 when given orally (Ellerington *et al.*, 1992). In fact, when given subcutaneously or transdermally (by patches), this latter effect appears also to be absent (DeLignierres *et al.*, 1986). Thus large scale epidemiological studies have failed to show any significant risk of thrombotic disease amongst post-menopausal 'natural' oestrogen users (Boston Collaborative Drug Surveillance Programme, 1974). The suggestion is, therefore, that a link between HRT and sudden sensorineural deafness can not be attributable to a vascular event caused by thromboembolism. Other factors must be responsible.

There are a number of interesting cases in the literature reporting cyclical sensorineural hearing loss associated with the luteal phase of the menstrual cycle (Miller and Gould, 1967; Andreyko and Jaffe, 1989). Studies by Cox (Cox, 1980) also suggested that fluctuations in hearing do occur in relation to the menstrual cycle in 'normal' subjects with no subjective hearing loss. Although the mechanism by which hormonal changes lead to a increase in auditory thresholds is uncertain, a review of the literature regarding the physiological and biological effects of sex hormones would suggest two possible modes of action.

Firstly, both oestrogen and progesterone have been shown to possess definite electrolyte retaining and excreting properties (Radev, 1973; Kucharczyk, 1984; Hassager *et al.*, 1987) thus partly explaining the marked physiological changes that occur throughout the course of one menstrual cycle. Accordingly the prescribing of supplementary oestrogen in HRT has the potential to alter electrolyte balance to some degree in all body tissues. With inner ear function being dependent upon the maintenance of haemostasis of inner ear fluids and the biochemical integrity of the auditory receptor cells, such alterations in electrolyte balance and subsequent changes in osmolality would explain a change in the auditory thresholds.

Secondly, it is also well established that oestrogens have a direct effect on the excitability of neuronal tissue (Kelly *et al.*, 1976; Silva and Boulant, 1986) and it has been suggested that this is in part due to alterations in neurotransmitter receptor concentrations (Biegon and McEwan, 1982). Thus HRT has the potential to interfere with the neurotransmission of auditory impulses anywhere on the auditory pathway from the cochlea, through the primary auditory centres, to the higher auditory centres in the superior temporal gyrus of the cerebral cortex.

One other symptom worthy of note is that of 'fullness in the ears' commonly experienced by pregnant women and those taking the oral contraceptive pill (Cox, 1980). Whilst Schiff suggested this was related to Eustachian tube dysfunction (Schiff, 1968), in the light of the discussions above it could alternatively be related to alterations within the inner ear or auditory pathway, not severe enough to cause a subjective hearing loss but sufficient to produce a 'fullness'.

This paper draws attention to the potential effect of hormonal treatment on inner ear function. The otologist needs to be aware of this link particularly as many female patients with a hearing loss may not forward the information that they are currently taking HRT.

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