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Human temporal bone findings in acquired hypothyroidism

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Abstract

Histological studies of the auditory organ in patients with acquired hypothyroidism are scarce. Thus the aim of the present study was to examine the temporal bones and the brain in subjects with hypothyroidism. Four temporal bones and two brains from clinically and biochemically hypothyroid subjects were removed and evaluated by light microscopy determine to the morphological changes and deposition of neutral and acid glycosaminoglycans. An audiogram from one of the patients showed a sensorineural hearing loss, which could be ascribed to occupational noise exposure. The study revealed histological changes compatible with age and infectious disease. No accumulation of neutral or acid glycosaminoglycans could be demonstrated in the temporal bones, or in the brains.

Introduction

A causal relationship between acquired hearing loss and hypothyroidism has been claimed since 1888, and since then several studies have demonstrated improvement or normalization in the hearing ability in myxoedematous patients upon substitution therapy with thyroid hormone (Hilger, 1956; Van't Hoff and Stuart, 1979). The hearing loss caused by hypothyroidism has been classified as sensorineural or as mixed conductive/sensorineural. However, controversy concerning the association between hypothyroidism and hearing loss still exists, since others have demonstrated no change in hearing thresholds upon treatment (De Vos, 1963; Bhatia *et al.*, 1977; Parving *et al.*, 1983; 1986). In addition it has been demonstrated that the hearing thresholds in myxoedematous patients do not differ from the hearing thresholds in an age- and sex-matched background population (Parving *et al.*, 1983; 1986; Vanasse *et al.*, 1989).

In experimentally induced hypothyroidism in animals several pathoanatomical changes have been found in the cochlea, predominantly in the morphology of the outer hair cells, pillar cells, strial area, and basilar membrane (De Vos, 1963; Poulsen, 1966; Ritter, 1967; Schätzle and Haubrich, 1967; Kohonen *et al.*, 1971; Withers *et al.*, 1972; Meyerhoff, 1979; Anniko and Rosenkvist, 1982). In addition, deposition of acid glycosaminoglycans has been demonstrated in the cochlea in hypothyroid guinea pigs (Poulsen, 1966; Schätzle and Haubrich, 1967; Meyerhoff, 1979).

Examination of tissues from an 83-year-old woman dying in untreated myxoedema, revealed deposition of acid glycosaminoglycans in all tissues except in the temporal bones and stomach (Parving *et al.*, 1982; 1986). This lack of deposition of glycosaminoglycans and of morphological changes in the human temporal bones further support the lack of causal relationship between hearing loss and myxoedema.

It has been claimed that the hearing loss found in myxoedematous patients may be ascribed to a functional disorder, due to the slow cerebral activity found in these patients (Parving *et al.*, 1986). The presence of a retrocochlear lesion in myxoedematous patients has been supported by psychoacoustic testing procedures (Stephens, 1970), and by electrophysiological investigations (Himmelfarb *et al.*, 1981). A retrocochlear hearing lesion might be due to deposition of acid glycosaminoglycans in the brain tissue, and thus patho-anatomical changes may be the underlying cause of a 'functional' phenomenon.

In order to contribute to the running discussion concerning a causal relationship between hearing loss and hypothyroidism, four temporal bones from four females, and brains from two of them, dying in untreated myxoedema were examined.

Methods

At post-mortem the temporal bones were removed as quickly as possible and fixed in 10 per cent phosphate buffered formalin with 0.5 per cent cetylpyridiniumchloride. By the microslicing technique the bones were cut at 3 mm intervals, using a special, highly refined annular saw, X-rayed, and then slices were examined under a dissecting microscope (Michaels *et al.*, 1983). Selected specimens were then decalcified in 10 per cent formic acid, decalcification taking only five days reducing the possible loss of acid glycosaminoglycans. Following decalcification the slices were embedded in paraffin wax. Sections were cut and stained with haematoxylin and eosin, Alcian blue/PAS at pH 0.2, 1.0, 2.5 and 0.05 per cent toluidine blue in McIlvain buffer

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pH 4.0 in order to investigate the presence of neutral and acid glycosaminoglycans.

The brains from two subjects were removed and fixed in 10 per cent phosphate buffered formalin with 0.5 per cent cetylpyridinium chloride for four weeks. Thereafter the brains were cut in thin slices, and tissue from the auditory cortex was processed for light microscopy. Sections were stained by haematoxylin and eosin and Alcian blue pH 2.5. Furthermore tissue was removed from other relevant organs, fixed in the same fixative and processed by routine laboratory methods.

Case 1

A 67-year-old woman was admitted to hospital due to eight years of increasing fatigue, swollen legs and walking problems. She was clinically and biochemically hypothyroid; T_4<2.5 pmol/l) (normal value: 7.7–28 pmol/l); T_3<0.3 nmol/l (normal value: 1.1–2.5 nmol/l) and TSH>50 uU/l (normal value: 0.4–3.3 uU/l). Antibodies against thyroglobulin were markedly raised 1:1280.

For five years she had suffered from a slowly developing hearing impairment, and she had been exposed to heavy occupational noise for 18 years. The clinical ENT investigation was normal. The cooperation at audiometry was insufficient, but the pure-tone audiogram revealed a bilateral sensorineural hearing loss (Fig. 1). The speech recognition score was more reduced than the pure-tone audiogram would predict, which points towards a retrocochlear involvement. She developed pneumonia and died 20 days after admission in myxoedematous coma. Autopsy revealed an atrophic thyroid gland.

Results

Histological examination of the right temporal bone revealed a few neutrophils and a fibrinous exudate in the cochlea, indicative of a labyrinthitis. No deposition of acid glycosaminoglycans were found. There, was loss of spiral ganglion cells and nerve fibres, and the morphological changes were compatible with and ascribed to age and noise exposure (Fig. 2a,b). No convincing deposition of acid glycosaminoglycans was found in other organs. The brain was not examined.

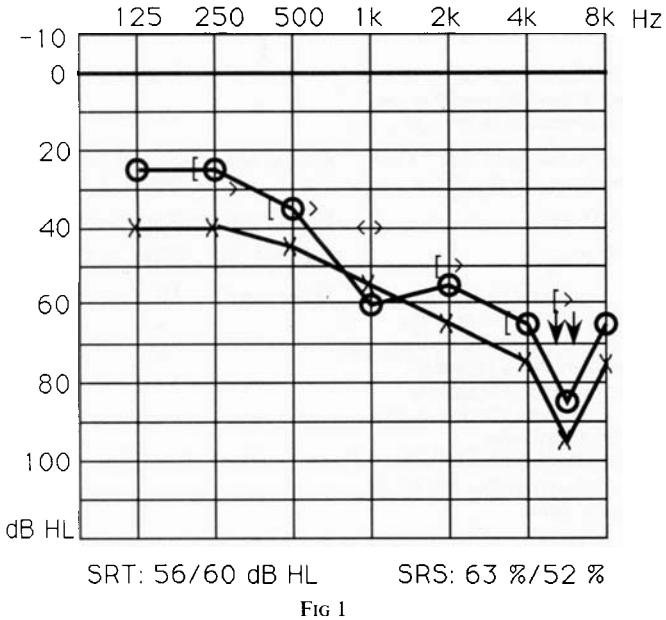

FIG 1

Case 2

A 86-year-old woman was admitted to hospital due to general social incapacity. She was clinically and biochemically hypothyroid (T_4<13 pmol/l (normal values: 60–140 pmol/l); T_3<0.05 mmol/l (normal value: 1.1–2.3 pmol/l) and TSH 90 uU/l (normal value: 0–5 uU/l)). She died seven days after admission due to cardiac failure. No information on the hearing ability was available.

Results

Histological examination of the left temporal bone revealed inflammatory changes, which could be ascribed to chronic otitis media. No accurate assessment of the inner and outer hair cells and inner ear structures was possible due to post-mortem autolysis. However, by specific staining no deposition of acid glycosaminoglycans was demonstrated.

Specimens from the brain including the primary auditory cortex showed no morphological changes and no deposition of acid glycosaminoglycans, but the morphology was compatible with that found in elderly

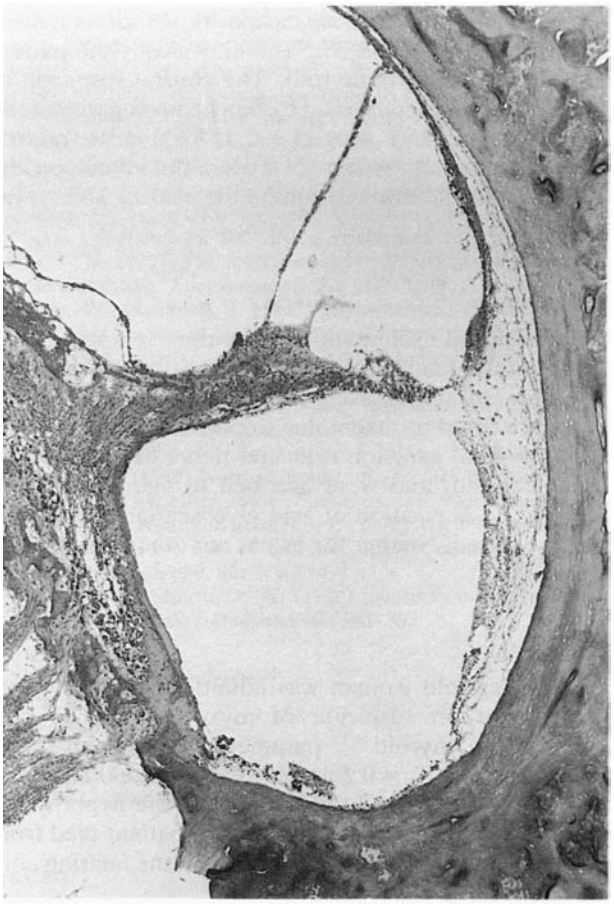

FIG. 2a

Section of cochlea. There is a collection of inflammatory cells and fibrin in the scala tympani. The stria vascularis is atrophic. No deposition of acid glycosaminoglycans was demonstrated. Haematoxylin and eosin ×40.

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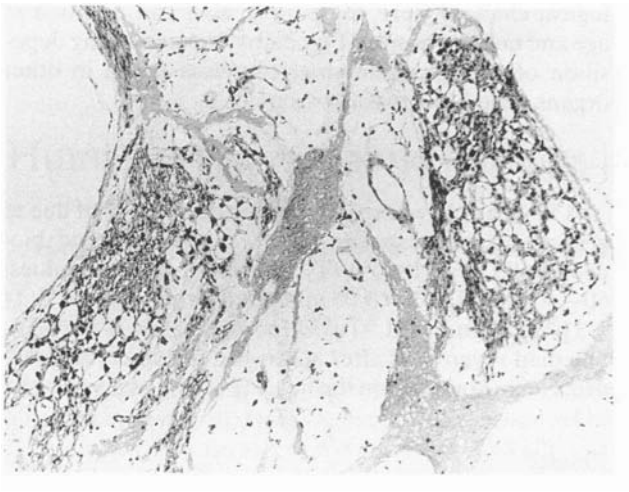

FIG. 2b
Section of modiolus showing loss of ganglion cells and nerve fibres. H + E × 60.

people in general (Klinken, 1991). Tissues from other organs showed deposition of acid glycosaminoglycans in fat tissue, loose connective tissue and within a few peripheral nerves.

Case 3

A 95-year-old woman was admitted to hospital due to dizziness and general social incapacity. At admission her body temperature was 35.5°C and clinically the patient appeared to be hypothyroid. The clinical suspicion of myxoedema was confirmed by biochemical parameters: T_4 = <17 pmol/l; T_3 mmol/l = 0.4; TSH = 39 (normal values as case 2). Within 24 h after the admission the patient died. No information on the hearing ability was available.

Results

Histological examination of the right temporal bone did not reveal any significant morphological abnormality. No accurate assessment of inner or outer hair cell structure could be made, due to post-mortem autolysis. Loss of spiral ganglion cells and nerve fibres could be demonstrated, and were ascribed to age. By specific staining no deposition of acid glycosaminoglycans was demonstrated. Neither the brain, nor other tissues were examined.

Case 4

A 90-year-old woman was admitted to the medical department on suspicion of myxoedema. The biochemical thyroid parameters demonstrated T_4 = 18 nmol/l; T_3 = 0.5 nmol/l; TSH = 62 uU/l (normal values as case 2), and thus confirmed the hypothyroid state. Three days after admission the patient died from pulmonary emboli. No information on the hearing ability was available.

Results

Histological examination of the left temporal bone did not reveal any significant morphological abnormality. No accurate assessment of inner or outer hair cell structure could be made due to post-mortem autolysis. By specific staining no deposition of neutral or acid glycosaminoglycans was demonstrated.

Deposition of acid glycosaminoglycans was found in the fatty tissue and in loose connective tissue, but not in the parenchymal tissues, including the brain. Specifically no accumulation of neutral or acid glycosaminoglycans could be demonstrated in the auditory cortex or pathways. The morphology and histological findings in the brain tissue were unremarkable considering the age of the patient.

Discussion

The present histological examination failed to demonstrate deposition of acid glycosaminoglycans in four temporal bones from patients, dying in untreated myxoedema, and all morphological changes found could be ascribed to the advanced age of the patients. In three cases the autolysis was prominent, allowing only limited conclusions about the cochlear morphology. The temporal bone from one patient (Case 1) showed changes, which could be ascribed to age, supporting previous findings, where no morphological changes were demonstrated in the cochlea from a patient, dying in untreated myxoedema (Parving *et al.*, 1986). In two cases a loss of spiral ganglion cells and nerve fibres was found, compatible with age (Michaels, 1987). No specific pathological alteration of the auditory cortex or pathways was found.

The clinical biochemical parameters confirmed together with the deposition of neutral and acid glycosaminoglycans in other tissues like fat, loose connective tissue, and around nerves in two cases the hypothyroid state. The high frequency sensorineural hearing loss

TABLE I

Morphological alternation	Animal	Reference
Slight degeneration of spiral ganglion cells	Mouse, rat and hamster	De Vos
Hensen and Cladius cells were round and swollen in one animal out of 166	Rat	Ritter
Acid mucopolysaccharides, increased mast cells in peri- and endolymphatic spaces	Guinea-pig	Poulsen
Acid mucopolysaccharides in the scala of cochlea	Guinea-pig	Schätzle and Haubrich
Normal	Guinea-pig	Kohonen *et al.*
Normal	Cat	Withers *et al.*
Ossicular abnormalities, bony obliteration of the round window, cochleae hyperostosis, tectorial membrane irregularity, outer hair cells distorsion, Hensen's cells accumulations, cochlear duct acidophilic precipitate and debris	Guinea-pig	Meyerhoff
Distorsion of the tectorial membrane. Thickening of basement membrane.	Rat	Anniko

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found in Case 1 could be ascribed to long-standing occupational noise exposure, while the insufficient co-operation at audiometry could be due to the myxoedematous state of the patient, resulting in 'slow cerebration'.

It has been argued that the sensorineural hearing loss in myxoedematous subjects reflects lesions in the inner ear (Hilger, 1956; Van't Hoff and Stuart, 1979). Moreover the numerous histological investigations of inner ears performed on experimentally induced hypothyroid animals have failed to find a specific locus (Table I). The morphological changes differ, which may be due to shortcomings and differences in the histological methods used. Thus *in vivo* ear pathology can be changed post-mortem, both due to autolysis and to the histological techniques used for tissue preparation (Kohonen *et al.*, 1971; Meyerhoff, 1979; Anniko, 1981). In addition the observation period in experimental animals with induced hypothyroidism may be too short to result in pathogonmonic hypothyroid changes.

Clinical audiometric tests sensitive for retrocochlear hearing disorders have been found to be abnormal in myxoedematous patients (Marquet, 1956; De Vos, 1963; Stephens, 1970). In addition auditory brain stem responses have been found to be abnormal in hypothyroid patients. Return to normal responses occurs following *l*-thyroxine treatment and restoration of the euthyroid state (Himmelfarb *et al.*, 1981). The lack of morphological changes in the brain found in the present study supports that the retrocochlear involvement, as is indicated by clinical testing, is based on a functional/biological process in the brain (Stephens, 1970; Himmelfarb *et al.*, 1981).

Conclusions

The present investigation fails to demonstrate accumulation of acid and neutral glycosaminoglycans in the temporal bones and brains in patients, dying in untreated myxoedema. In addition no morphological changes could be found in these tissues, however the prominent autolysis in the temporal bones should be taken into account.

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