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Clinical records

Pendred's syndrome

Acoustic, vestibular and radiological findings in 17 unrelated patients

by

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Abstract

Seventeen unrelated Danish patients with Pendred's syndrome, whose case stories have not been published previously, are presented. Acoustic and vestibular functions were examined and endocrinological screening was performed. There was a great variation in hearing ability as well as in thyroid function. Furthermore, in contrast to previous investigations, normal caloric function was demonstrated in the majority. In all patients a Mondini malformation was demonstrated. On the basis of this investigation it is concluded that: (1) the Mondini defect is part of Pendred's syndrome; (2) the inherited Mondini malformation is the underlying cause of the sensorineural hearing impairment; and (3) the hearing sensitivity varies greatly in these patients.

In 1896 Vaughan Pendred described two sisters with goitre and congenital deafness. The definition of Pendred's syndrome (PS) was further delineated in 1958 when, by means of perchlorate, Morgans and Trotter showed that these patients might have an iodine organification defect of the thyroid.

A total of 36 Danish patients with Pendred's syndrome have been reported previously (Johnsen, 1958; Illum *et al.*, 1972; Vesterdal, 1957; Hvidberg-Hansen and Jørgensen, 1968; Agerbæk, 1973; Jensen, 1969; Remvig, 1969). We have identified these patients and discovered that several of them have been described twice and one woman has appeared in three different publications. Consequently, a total of 24 Danish patients with confirmed PS have been described so far. In most reports on PS, the patients suffer from severe hearing impairment (>75 dB. HL.) or have a slight low-frequency hearing remnant.

In order to clarify the degree of hearing impairment in PS, we tested the hearing in 17 unrelated patients who have not previously been described in the literature. As the results of the caloric response in patients with PS are controversial we have tested this, just as we have tried to elucidate the occurrance of the Mondini malformation of the cochlea (Hvidberg-Hansen and Jørgensen, 1968; Mondini, 1891) by means of radiological examination.

Material and methods

The group comprised 17 unrelated patients with PS. It included six men, ranging in age from 14 to 60 years (mean 40 years), and 11 women, ranging in age from 21 to 68 years (mean 42 years). Table I presents data concerning the patients' sex, age, familial deafness and goitre. In four patients the

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TABLE I

SEX, AGE, FAMILIAL DEAFNESS AND GOITRE IN 17 PATIENTS WITH PENDRED'S SYNDROME. THE TERM 'UNKNOWN' IN THE COLUMN FOR FAMILIAL GOITRE INDICATES THAT THE INFORMATION ABOUT FAMILIAL DEAFNESS IS DERIVED FROM THE ROYAL DANISH ARCHIVES OF DEAFMUTES AND NO FURTHER INFORMATION ON THEIR CONDITION WAS AVAILABLE AT THAT TIME

Patient No.		Sex	Age (years)	Familial deafness	Familial goitre
1	KHP	Female	27	+	Unknown
2	AK	Male	54	+	+
3	IK	Female	48	+	+
4	LGR	Female	24	+	Unknown
5	DL	Female	43	+	+
6	JD	Female	51	+	Unknown
7	ABM	Male	60	+	+
8	VF	Female	68	+	Unknown
9	GH	Female	44	−	−
10	BSK	Female	40	+	Unknown
11	MMT	Male	14	−	−
12	ESM	Male	59	−	−
13	LL	Female	21	+	−
14	EP	Female	57	+	+
15	FF	Male	31	−	−
16	LR	Female	34	+	+
17	HM	Male	20	+	Unknown

inheritance could not be proved among the descendants of the probands or among the three preceding generations.

To determine a possible familial occurrence of PS, families were interviewed and a search was made in the Archives of the Royal Danish Institute of Deafmutes.

All patients were examined otologically and hospital records were reviewed with regard to goitre and hearing impairment.

The **audiological** examination was carried out using an OB 822 clinical audiometer (Madsen Electronics). The tests were performed in a soundproof booth and masking was done according to standard procedures (ISO 1964).

The **vestibular** examination included caloric testing ad modum Hallpike and, in most cases, electronystagmography (Vesterhauge *et al.*, 1982).

The **radiological** examination consisted of axial-pyramidal tomography (Poschl, 1943; Jensen, 1967).

The **endocrinological** examination consisted of an iodine perchlorate discharge test (Takeuchi *et al.*, 1970) to verify the diagnosis (normal reference value <10 per cent). T_3, T_4 resin test and TSH were used to evaluate thyroid function. TC-scans were taken to determine thyroid size.

All tests were performed at a time when the patients were free of medicine.

Results

Audiological examination

As shown in Table II, hearing impairment was confirmed in almost all patients before the age of three years. However, in patients Nos. 9 and 10, the hearing impairment was detected at a much later age, probably because of relatively moderate, bilateral, sensorineural losses. Three patients (Nos. 7, 10 and 15) had noticed a slight progression of their hearing loss. In one of these patients (No. 10) the hearing loss had deteriorated by 20 dB. HL. over a period of 20 years. One patient (No. 8) was totally deaf on both ears, and another patient was totally deaf on one side. Fig. 1 shows the average hearing thresholds in the remaining 31 ears. The resultant curve shows a steep slope towards the high frequencies. Threshold values exceeding 100 dB. have not been incorporated in the mean curve. Fig. 2 shows the audiograms from three patients whose thresholds deviated strongly from the mean values. One patient (No. 4) had anacusis on the right side and a flat perceptive hearing loss of about 60 dB. on the left side. The other two patients had symmetrical perceptive hearing losses but in a less severe degree than that indicated by the mean curve in Fig. 1.

Nine of the 17 patients had virtually no verbal communication despite the fact that five of them had hearing aids.

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TABLE II

AUDIOLOGICAL AND VESTIBULAR FINDINGS IN 17 PATIENTS WITH PENDRED'S SYNDROME. 0/0 = NO CALORIC RESPONSE; +/+ = NORMAL CALORIC RESPNSE; −/− = DECREASED CALORIC REPSONSE

Case No.	Age at detection of hearing impairment (years)	Progression of hearing impairment	Age at hearing aid treatment (years)	Speech communication	Vestibular function
1	3	No	4	No	Not exam.
2	1	No	No	No	0/0
3	3	No	No	No	−/+
4	3	No	3	Yes	+/+
5	1	No	10	No	0/−
6	2	No	3–4	No	+/+
7	1	Yes	No	Yes	+/+
8	2	No	No	No	0/0
9	6	No	7	Yes	+/+
10	16	Yes	16	Yes	+/+
11	3	No	3	Yes	+/+
12	2	No	50	Yes	+/+
13	2	No	2	No	+/+
14	1	No	No	No	+/+
15	2	Yes	4	Yes	Not exam.
16	1	No	7	No	Not exam.
17	1	No	1	Yes	+/−

Vestibular examination

The vestibular function was examined in 14 patients. It included ENG in 11 patients and in three patients only caloric testing ad modum Hallpike was performed. Ten patients had normal responses on both sides. Two patients (Nos. 2 and 8) showed no caloric response on either side and an additional two patients (Nos. 3 and 17) showed a unilateral reduction of the response. One patient (No. 5) had no response on one side and a reduced function on the other. Three patients could not be subjected to vestibular examination.

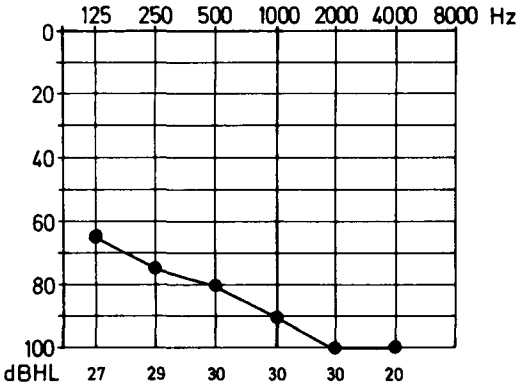


FIG. 1

Mean threshold values in 17 patients with Pendred's syndrome. In the bottom line is indicated the number of ears included in the calculation. Threshold values exceeding 100 dB. have not been incorporated. (Range: 35–100 dB. HL. at 125 Hz; 40–100 dB. HL. at 250 Hz; 45–100 dB. HL. at 500 Hz; 50–100 dB. HL. at 1,000 Hz; 60–100 dB. HL. at 2,000 Hz; 50–100 dB. HL. at 4,000 Hz; 65–100 dB. HL. at 8,000 Hz).

Radiographical examination

Axial-pyramidal tomography demonstrated bilateral Mondini malformation of the cochleae (Mondini, 1891) in all patients except one in whom the tomography was false negative on the right side. At the post-mortem histological examination of the cochleae a Mondini malformation was also demonstrated on the right ear (Johnsen *et al.*, 1986).

Endocrinological examination

Information relating to thyroid function is listed in Table III. All patients either suffered from or had a history of goitre with or without hypothyroidism. Four patients had congenital hypothyroidism and goitre was confirmed before the age of one year; in the remaining 13 patients goitre appeared at a mean age of 14 years (range 2–35 years). Strumectomy had been performed in more than half of the patients; in one patient twice. Fifteen

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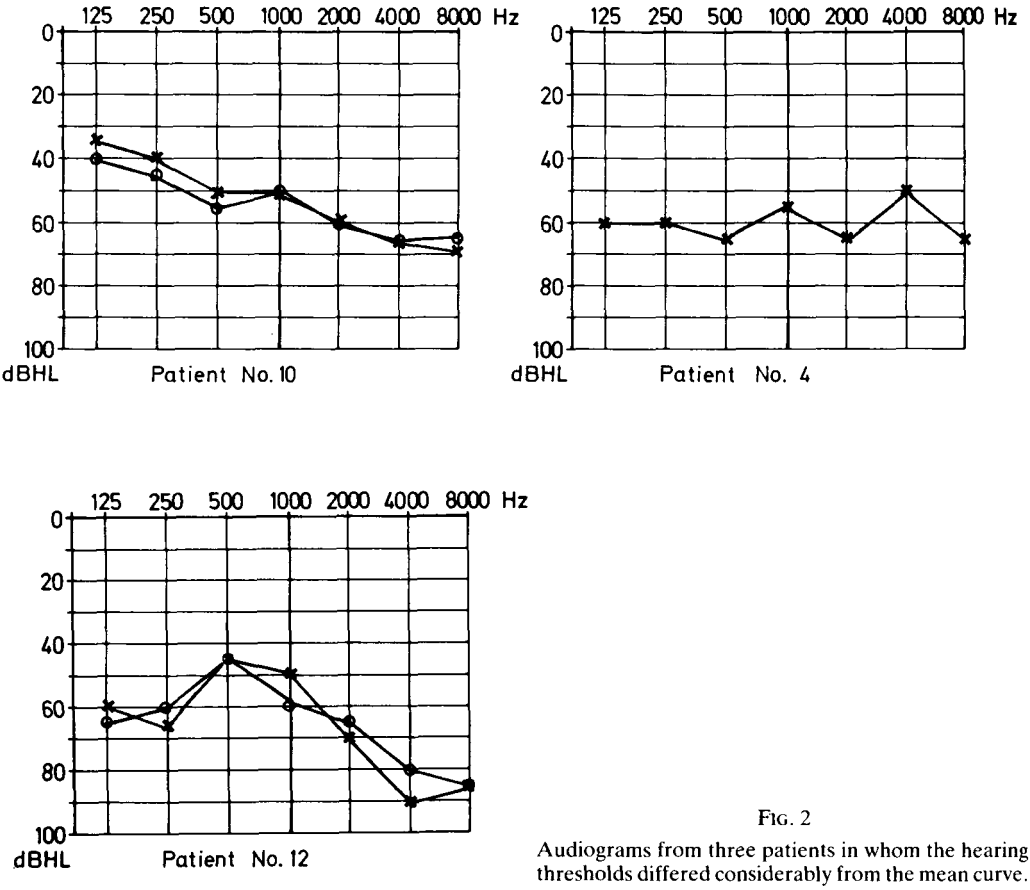


FIG. 2

Audiograms from three patients in whom the hearing thresholds differed considerably from the mean curve.

patients had a pathological iodine perchlorate discharge test concordant with Pendred's syndrome. In two patients with strumectomy, no iodine absorption could be demonstated and the test could not be carried out. One of these patients did show a pathologic discharge prior to strumectomy and we have demonstrated pathological discharge tests in family members of the other patient. The discharge rate varied from 16 per cent to 43 per cent (mean 31 per cent). Without treatment, eight patients were euthyroid, the remainder hypothyroid.

Discussion

The number of patients with PS in Denmark is assumed to range from 150 to 250 (Fraser, 1965). The 17 patients described in this study bring the number of reported cases of PS in Denmark to a total of 41 patients.

The two sisters originally described by Vaughan Pendred were deaf. Later on, some variation of the hearing impairment in this syndrome was described (Nilsson *et al.*, 1964), but according to our studies there is an even greater variation in the hearing than formerly assumed. Thus, one patient (No. 4) had anacusis on the right ear and a flat, sensorineural loss of 60 dB. in the left ear with completely normal speech communication. Another patient (No. 10) managed so well that the hearing impairment remained undetected until the age of 16 years. In patient No. 12 the threshold determinations deviated considerably from the mean threshold curve in that the best thresholds were found at 500 and 1,000 Hz. (Fig. 2).

It has previously been reported that some progression of the hearing loss may take place during early infancy (Konigsmark and Gorlin, 1976), but, audiologically, no study has ever demonstrated a progression similar to that found in patient No. 10, in whom the hearing thresholds deteriorated 20 dB. HL. for all frequencies.

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TABLE III

THYROID FUNCTION IN 17 PATIENTS WITH PENDRED'S SYNDROME

Case No.	Age at diagnosis of goitre (years)	Thyroid function without treatment	Strumectomy
1	10	Euthyroid	+
2	2	Hypothyroid	+
3	Congenital	Hypothyroid	+
4	17	Euthyroid	−
5	12	Euthyroid	+
6	16	Hypothyroid	+
7	15	Hypothyroid	+
8	35	Euthyroid	−
9*	25	Euthyroid	−
10†	Congenital	Euthyroid	−
11	12	Euthyroid	−
12	Congenital	Hypothyroid	−
13‡	3	Hypothyroid	−
14	10	Euthyroid	+
15	7	Hypothyroid	+
16	Congenital	Hypothyroid	+
17	16	Hypothyroid	−

* Goitre disappeared spontaneously at the age of 30 years.
† Hospitalized in the neonatal period because of respiratory obstruction and a swollen thyroid gland.
‡ Tracheostomized three years' old because of respiratory obstruction.

The vestibular function has only been studied sporadically in patients with PS (Johnsen, 1958; Fraser, 1965), but it is generally reported to be either reduced or abolished. Deramaeker (1965), however, found normal reactions in a few patients. We found normal vestibular function in the majority of patients (in 20 out of 26 ears).

Half of the patients were hypothyroid and the other half euthyroid. The onset of goitre varied considerably in our study (0–35 years). There has been no previous report of an onset of goitre as late as the age of 35 years and no report of spontaneous remission of goitre (patient No. 9) in PS.

In 1967, Jensen was the first to describe radiologically the Mondini malformation in PS. In contrast to Illum *et al.* (1972), we found that the Mondini defect appeared consistently in all 34 ears studied.

Thus, great variations may be found among patients with PS with regard to the degree of hearing impairment, onset of goitre and thyroid function. However, the following common features were demonstrated in all patients with PS in this study: bilateral Mondini cochlear malformation, sensorineural hearing impairment and a pathological perchlorate discharge test.

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