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How common is hearing impairment in osteogenesis imperfecta?

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Abstract

Hearing impairment has long been recognized as a common feature in osteogenesis imperfecta. The figures in some publications could be taken to imply that, with increasing age, the proportion of osteogenesis imperfecta patients with hearing impairment approaches 100 per cent.

The incidence of hearing loss in a large survey of 1394 patients with osteogenesis imperfecta was examined. It was found that the most common age of onset was in the second, third and fourth decades of life. At the age of 50 approximately 50 per cent of the patients had symptoms of hearing impairment; over the next 20 years there was little further increase.

Differences were shown between patients with different clinical types of osteogenesis imperfecta as delineated in the Sillence classification; hearing loss was significantly less common in the type IV disease than in the type I disorder. Among the 29 families with osteogenesis imperfecta type IA there were distinct differences in the likelihood of hearing loss. These findings provide insights which will be valuable in giving patients advice on the likelihood of developing hearing loss in the future.

Key words: Deafness; Genetic Counseling; Hearing Impaired Persons; Osteogenesis Imperfecta

Introduction

One real concern among patients with osteogenesis imperfecta is the likelihood of deafness. That hearing loss is an associated feature of osteogenesis imperfecta was recognized by Adair-Dighton in 1912[1] in one member of a family of patients with what would now be called osteogenesis imperfecta type I. Subsequently Bronson[2] and van der Hoeve and de Kleyn[3] independently reported the same association. Bronson suggested that calcium deposition in the middle ear was the cause of hearing loss while van der Hoeve and de Kleyn regarded the condition as a form of otosclerosis.

Many subsequent studies have confirmed that conductive defects, particularly due to abnormalities in the stapes, are common causes of hearing loss in osteogenesis imperfecta but many patients also have a sensorineural component; a substantial minority have a pure sensorineural loss.[4–6] Histological evidence has indicated that the defects in the stapes are distinct from those in otosclerosis.[7,8] Several studies have indicated that the incidence of hearing loss of both types rises with age as does the proportion of patients with mixed types.[4–6,9]

Some studies have implied that, with increasing age, the proportion of patients with hearing loss approaches 100 per cent. In one study, 11 out of 12 patients aged 40–49 were affected as were all seven aged between 50 and 55.[4] In another study, normal audiograms were recorded in only two of 36 osteogenesis imperfecta patients aged over 30.[5] In a third, 17 out of 18 patients aged 40 to 49, nine out of 10 patients aged 50 to 59 and all eight aged 60 to 69 had hearing loss.[9]

The accuracy of this information was assessed in a very large group of patients of all surviving types. Since 1980 we have held a register of patients, mainly from the United Kingdom and Republic of Ireland, for whom detailed questionnaires relating to clinical aspects of osteogenesis imperfecta were completed.[10–12] This paper reports our findings in relation to the presence or absence of symptomatic hearing loss and the age of onset.

Patients and methods

Our survey currently comprises 1431 patients with osteogenesis imperfecta. In each case the patient was classified according to the Sillence scheme where possible.[13,14] Table I shows the number of patients of each type together with those patients in whom the diagnosis of osteogenesis imperfecta was certain but the Sillence type could not be assigned with

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TABLE I

NUMBER OF PATIENTS INCLUDED IN THE SURVEY ON WHICH THE STUDY WAS BASED

Sillence type	Total number of patients	Number of patients used*
IA	746	712
IB	146	143
II	6	0
III	217	207
IVA	142	139
IVB	136	136
Type uncertain	58	57
Total	1431	1394

*After the elimination of patients with osteogenesis imperfecta type II, patients on whom information on hearing impairment was not recorded and patients for whom the age at which hearing loss was first noticed was not recorded.

confidence. In each case a questionnaire ascertaining clinical features of the disorder was completed by the patient or a close relative but in 833 cases (58.2 per cent of the whole group) the patient was interviewed and examined personally by CRP and SJM. The details sought included numbers of fractures, family history, clinical features together with questions relating to the presence of deafness and the age at which symptoms of impaired hearing were first noted. The replies to this question were usually very precise.

The findings were entered into a database (Microsoft Access). For the present study the six patients with osteogenesis imperfecta type II were excluded, as were the 23 patients for whom no information on hearing loss was available, and the eight patients in whom hearing loss was present but the date of onset was not known. After these exclusions the records of 1394 patients with osteogenesis imperfecta were available for study of whom 317 had impairment of hearing.

Results

In the whole group of 1394 patients, 317 were aware of impaired hearing at the time of the most recent evaluation. The age at which this symptom was first noted is recorded in Figure 1. It is clear that most osteogenesis imperfecta patients who develop hearing loss have their first symptoms in the first four decades of life.

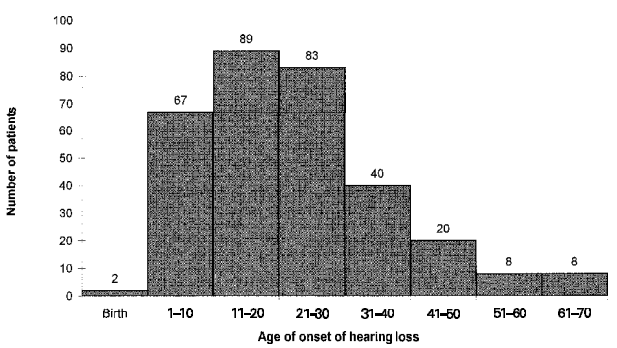

FIG. 1

Age of onset of symptomatic hearing loss in 317 patients with osteogenesis imperfecta.

TABLE II

PROPORTION OF OSTEOGENESIS IMPERFECTA PATIENTS WHO HAD SYMPTOMS OF HEARING IMPAIRMENT AT EACH DECADE

Age	Total number of patients	Total with hearing impairment	Percentage affected
10	925	19	2
20	651	92	14
30	470	148	31
40	271	113	42
50	154	77	50
60	71	38	54
70	22	12	55

The incidence of hearing loss at each age and in each type of osteogenesis imperfecta was examined. At ages 10, 20, 30, 40, 50, 60 and 70 we calculated what proportion of the patients at each age group had symptomatic impairment of hearing. The findings for the whole group are shown in Table II. The study included 466 patients aged less than 10; of these, 20 had symptoms of hearing loss.

Table III shows for each type of osteogenesis imperfecta in the Sillence classification the proportion of the patients who had hearing loss at the age of 30. It is clear that there are substantial differences in the likelihood of hearing impairment between the different types of osteogenesis imperfecta as delineated by this classification.

One question asked by patients with osteogenesis imperfecta is whether deafness in other family members means that an affected individual is more likely to develop hearing loss with the passage of time. To explore this issue we examined the records of all families with three or more individuals with osteogenesis imperfecta aged 30 or over. There were 29 such families with type IA, two families with type IB, four families with type IVA and three families with type IVB. In all, these 38 families included 150 patients aged over 30.

The 29 families with osteogenesis imperfecta type IA were examined in greater detail. Sixteen families had 31 individuals (out of 71) with symptomatic hearing loss at the age of 30. Thirteen families with 43 individuals had no-one with hearing loss at the age of 30. Five (all in different families) subsequently developed hearing loss (at ages 38, 44, 46, 56 and 59). The remaining 38 individuals had no symptomatic

TABLE III

PROPORTION OF OSTEOGENESIS IMPERFECTA PATIENTS OF EACH TYPE WHO HAD SYMPTOMS OF HEARING IMPAIRMENT AT AGE 30

Sillence type	Number of patients aged 30 or more	Number of patients with hearing impairment at age 30	Percentage affected at age 30
IA	276	90	33
IB	60	18	30
III	23	12	52
IVA	32	3	9
IVB	52	15	29
Type uncertain	18	7	39

Type IVA versus type IA: Chi squared = 7.34, $p = 0.0067$
Type III versus type IA: Chi squared = 3.62, $p = 0.057$

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hearing problems at an average age of 51.0 years at the most recent update. This group included two patients in their 90s and four patients in their 70s.

Discussion

We were stimulated to explore this field by concern that patients with osteogenesis imperfecta might be misled by over-pessimistic accounts of the future likelihood of hearing impairment in some publications.[4,5,9] As in other studies it was found that hearing impairment is first noted most commonly in the second, third and fourth decades of life. However, our large numbers of patients, including large numbers of patients aged over 50, make it possible to say with confidence that after the fifth decade there is little further increase in the incidence of hearing loss. At the age of 70 some 55 per cent of the patients had impaired hearing. The implication is that a patient whose hearing is normal by the age of 50 has no undue likelihood of hearing loss thereafter.

Recent research has made it clear that, at a molecular level, osteogenesis imperfecta is enormously heterogeneous.[15] Within each of the clinical types, as delineated in the Sillence classification, many distinct mutations have been identified in the genes coding for type I collagen. Despite this, our findings in the patients classified according to the Sillence scheme have shown that the mutations that underlie osteogenesis imperfecta type IV less commonly lead to hearing loss that those of osteogenesis imperfecta type I. Similarly, within the group of patients with the type IA disorder, it was possible to show distinct differences between families in which hearing impairment was common and families in which it seldom occurred. These differences presumably relate to differences in the underlying mutations.

We recognize that our survey could not include evaluations of each patient for the exact type of hearing loss and could not exclude those whose hearing impairment might have had causes other than osteogenesis imperfecta. However, the very large numbers of patients available provided insights that will be valuable in counselling individual patients about the likelihood of developing hearing loss.

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