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Goitre and Deaf-Mutism

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ABSTRACT

The occurrence of congenital deafness, mutism and goitre unassociated with cretinism or mental retardation in euthyroid patients is known as Pendred's Syndrome. It has been estimated that 4-10 % of children with congenital deafness suffer from this condition. The perceptive hearing loss is considered to be present at birth although it is frequently not recognized for several years. The cause of the hearing defect is a congenital bilateral malformation of the cochlea of the Mondini type. The goitre is not recognized clinically at birth or in early childhood. It becomes apparent in the pre-pubertal years when it presents as a colloid enlargement progressing to a nodular goitre. The thyroid defect has been shown to be a partial defect in iodine organification leading to the underproduction of thyroxine and subsequent thyroid hyperplasia. The syndrome is caused by a single mutant recessive gene responsible for both the deafness and goitre. Its autosomal mechanism gives an equal incidence in both sexes, unusual in thyroid disease. This article reviews the current aspects of pathogenesis and treatment of this syndrome and reports its occurrence in two Sudanese siblings.

INTRODUCTION

The association of congenital deafness and goitre was first described by Wood in 1824 [1]. However, In 1965 Fraser [2] in a detailed monograph reviewed from the literature 233 cases of goitre and congenital deafness and suggested the eponym of Pendred's syndrome after the British general practitioner Vaughan Pendred who in 1896 described two deaf-mute sisters with pronounced nodular goitre [3]. In 1927 Brain reported cases of five families in which 12 members had congenital deafness and developed goitre during childhood [4]. After making extensive studies on his patients he came to the conclusion that the syndrome is a genetic disorder caused by

a single mutant recessive gene responsible for both the deafness and goitre. The gene frequency varies between 1 in 500 to 1 in 1500 and its autosomal mechanism gives an equal incidence in both sexes, unusual in thyroid diseases which is far more common in girls than boys. The responsible gene has high penetrance, but the intenseness of expressivity may vary within the same family and usually only one generation is affected [5]. It has been estimated that 4-10 % of children with congenital deafness suffer from Pendred's Syndrome [6,7].

PATHOGENESIS

The perceptive hearing loss is considered to be present at birth although it is usually not recognized for several years. The nature of the hearing loss is debatable. Earlier workers relate the hearing defect to intra-uterine thyroid hormone deficiency. According to Hodges and his associates [8], the fetal thyroid begins to function at the 12th week of fetal life. If the contribution of the fetus thyroid hormone is inadequate because of an inherited defect the normal development of the nervous system will be incomplete with resultant acoustic nerve damage. Thould and Scowen attributed the nerve deafness associated with goitre to intra-gestational hypothyroidism [9]. The increasing prevalence of goitre and deaf-mutism in regions of endemic goitre support the association between the two conditions [10]. However, most of the published literature regarded the syndrome as a separate entity not directly related to endemic cretinism which is characterized by profound mental retardation and nerve deafness [11]. Individuals with deaf-mutism and goitre are usually euthyroid and have normal intelligence. The deafness in Pendred's syndrome is believed to be due to a congenital bilateral malformation of the cochlea of the Mondini type [12-15]. The increased occurrence of deaf-mutism in places with endemic iodine deficiency is explained by the high frequency of consanguinity and intermarriages in these areas [16].

The goitre is not recognized clinically at birth or in early childhood. It becomes apparent in the pre-pubertal years when it presents as a colloid enlargement progressing to a nodular goitre in the majority of patients. Morgans and Trotter in 1958 demonstrated a presumed specific enzymatic defect as the cause of goitre in this condition [17]. The thyroid defect has been shown to be a partial defect in iodine organification leading to the under production of thyroxine [18]. This triggers the secretion of thyroid stimulating hormone (TSH) which stimulates thyroid gland hyperplasia to compensate for the defect by maintaining the minimal level of thyroid hormones production to keep the patient euthyroid. The organification defect is best demonstrated by the perchlorate discharge test which is considered diagnostic in children with goitrous deafness. However, some authors reported considerable variations in this test [19].

TREATMENT

In the past, thyroidectomy was the standard treatment because of the size of the goitre and the pressure symptoms it was causing and because of the extreme hyperplasia seen on thyroid tissue which was confused with malignancy. Such experience was reported by Elman [20], who found, in two of his patients, changes in the thyroid tissue sufficient for the diagnosis of adenocarcinoma. Smith [21] reviewed the pathology of the thyroid tissue removed at operation from several patients with this syndrome. One of the 14 cases of his series was considered to have malignant changes. Recently, it has been accepted that surgery may not be needed particularly in children. Life long thyroid medication is recommended with the implication that the goitre will be greatly reduced in size or may actually disappear. Unfortunately, once the deafness is recognized no treatment at present will reverse it. However, in 1973, Deol [22] reported a series of fascinating experiments in mice that could be of clinical importance to man. Female mice fed propylthiouracil during pregnancy produced deaf offsprings, but when they fed thyroxine together with propylthiouracil from day one of gestation, no hearing defect occurred in the offsprings. Furthermore, when the offsprings of a female mouse who received antithyroid drugs during gestation, were fed thyroxine started immediately after birth, no hearing defect occurred. Any practical application of these findings can only be evaluated when a group of newborn babies, who have a sibling with Pendred's syndrome, given thyroxine on day one of life and followed prospectively for development of deafness. Because of the high penetrance of this syndrome, it might be advisable to give thyroxine to all newborn siblings of patients with Pendred's syndrome as early as possible.

CASE REPORTS

Two brothers, Ahmed S., 13-year-old, and Osman S., 7-year-old, were referred to the paediatrics clinic of the university hospital in Khartoum, Sudan because of thyroid swelling. Both boys were known to be deaf and mute since the first year of life. The swelling over the neck appeared at the age of 10 years in the elder brother and 8 months before presentation in the younger brother and was increasing in size. The parents were first degree relatives and they have another 4 normal children, 2 boys and 2 girls. There was no history of deafness in other relatives, but a cousin has had an endemic goitre with no hearing problem. They live in a village on the west bank of river White Nile 160 km south of Khartoum, an area with a large number of endemic goitre cases. Examination revealed nice cooperative mute children with apparently normal intelligence. They did not attend any school because the only school for deaf children is in

Khartoum, far away from their village. The thyroid swelling was enormous and nodular in the elder boy and diffuse and relatively small in the younger brother. It were not attached to the skin or underlying structures and no bruit could be heard over them. There was no clinical symptom or sign of hypo or hyperthyroidism and the rest of the physical examination was non contributory. Height was below the 25th centile of NCHS standards [23] and X-ray examination revealed slight retardation in bone age. Thyroid function tests showed thyroxine and T3 levels in the low normal range and an elevated TSH level in both brothers. Thyroid scan showed diffuse hyperplasia of the gland with no hot or cold areas in the younger child and a solitary cold nodule on top of diffuse hyperplasia in the other. Potassium perchlorate discharge test was positive in both patients. The audiogram showed bilateral high tone deafness in both patients. A diagnosis of Pendred's syndrome was made on the basis of the presence of its classical triad namely, goitre, nerve deafness and positive perchlorate discharge test. Although the two patients did not show any clinical symptoms of hypothyroidism, the reduction in height and bone age and the results of thyroid function indicated a slightly decompensated gland. Both children were started on L-thyroxine immediately after confirmation of diagnosis.

Conclusion

Pendred's syndrome accounts for 4-10% of cases of congenital deafness in childhood. It is increasing recognized in places where iodine deficiency is prevalent, although the association is still unclear. The hearing defect appears early in life and is not reversible once established. The goitre usually appears in the prepubertal years and progresses in size thereafter. Surgery is not indicated, but thyroxine should be given as soon as the diagnosis is made and continued for life to reduce the size of goitre and to prevent recurrence. Because of the high penetrance of this condition and because of possible benefits siblings of known cases should be given thyroxine from the first day of life. Genetic counseling should be available to parents who have a child with Pendred's syndrome and to young adults with this condition.

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