

Pandred Syndrome: A Case Report

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Abstract: Pendred syndrome is listed as a "rare disease" by the Office of Rare Diseases (ORD) of the National Institutes of Health (NIH) in the United States of America. Pendred syndrome is characterized by the association of congenital bilateral neurosensory deafness, thyroid goiter, cochleovestibular malformation and potential vestibular dysfunction. Incidence ranges between 1/100,000 and 10/100,000 births, according to geographic location. It is an autosomal recessive inherited condition and the incriminated gene, PDS or SLC26A4, is located on 7q31 and encodes an iodide and chloride transporter.

Keywords: Pendred syndrome, neurosensory deafness, goiter, vestibular dysfunction, congenital deafness.

I. Introduction

Thyroid dysmorphogenesis (or dysmorphogenetic goiter) is a rare condition due to genetic defects in the synthesis of thyroid hormones. One particular familial form is associated with sensorineural deafness (Pendred's syndrome). It was first recognized by Vaughan Pendred, British physician. It is an autosomal recessive inherited condition and the incriminated gene, PDS or SLC26A4, is located on 7q31 and encodes an iodide and chloride transporter. It is characterized by the association of congenital bilateral neurosensory deafness, thyroid goiter, cochleovestibular malformation (Mondini defect) and potential vestibular dysfunction.

Pendred syndrome accounts for at least 5% of cases of congenital deafness. Sensorineural hearing impairment is leading manifestation and mostly present as prelingual deafness. The severity of symptoms and age of onset are extremely variable from one family to another and between members of the same family. Deafness occurs early, starting at birth or during the first years of life. It is bilateral, sometimes asymmetrical, fluctuant and often progressive and become apparent only later in childhood⁴. The hearing impairment of Pendred syndrome involves all frequencies, but higher frequencies are more severely affected and in severe case magnitude can be of at least 60 decibels (dB). The thyroid impairment in Pendred syndrome develops only in 80% of affected individuals in form of a euthyroid or hypothyroid goitre, which is rarely present at birth, when it can be diagnosed by the neonatal screening for congenital hypothyroidism. Thyroid abnormality is of highly variable severity both between families and within the same family, approximately 75% of affected persons will eventually develop a multinodular or diffuse goiter⁵.

II. The Case Report

17 years old male presented with the chief complaint of neck swelling which was gradually increasing since childhood, patient also had bilateral deafness since early childhood. Physical examination revealed a large, firm, multinodular swelling with lobular smooth surface on anterior and lateral compartments of the neck. The goiter was non tender, no infiltration, no retrosternal extension. Thyroid function test showed euthyroid state. Other blood investigations were normal. Ultrasound examination confirmed multinodular colloid goiter. Indirect laryngoscopy confirmed mobile vocal cords. ENT examination suggestive of bilateral sensory neuronal hearing loss Right > Left. FNAC from swelling suggestive of goiter with secondary changes (cystic and hemorrhagic) Colloid background with scant cellularity. Operation was performed under general anesthesia. Subtotal thyroidectomy was performed and the patient had smooth postoperative period.



Pathology

Responsible gene for Pendred syndrome is found on chromosome 7, the PDS gene, or SLC26A4 . This gene is expressed in the thyroid gland, the inner ear, and the kidney. The gene product (pendrin), functions as an iodide transporter from within thyroid cells into the colloid, in which thyroid hormone is synthesized. In the absence of the transporter(pendrin), apical iodide transport is defective and thus organification of iodide is defective, the hallmark of Pendred Syndrome. Mutations in both alleles of this gene cause Pendred syndrome ⁽⁵⁻⁹⁾. In vitro studies have shown that goiter in Pendred syndrome is caused by the lackof pendrin protein function. It has been demonstrated that a number of SLC26A4mutations result in the synthesis of altered pendrin proteins that are abnormallydistributed within the thyroid cells. Rather than being incorporated into the cellmembrane, where pendrin normally carries out its function, these mutated pendrinmolecules remain in the endoplasmic reticulum ¹⁰. This leads to a diminished amount of iodide transport into the thyrocolloid and thus to diminished T3 and T4 synthesis, hypothyroidism, and goiter. However, organification is only partially deficient, even in the complete absence of pendrin, suggesting that other, as yet undefined, mechanisms exist that can partially compensate for lack of the protein.The pathophysiology of the hearing loss associated with Pendred syndrome is less well understood.

Diagnostic Evaluation

Pendred syndrome is diagnosed on clinical grounds alone, because no simple laboratorytest for the disease is available. The diagnosis of Pendred syndrome should be consideredin all patients suffering from a bilateral sensorineural deafness in combination with goiter hypothyroidism, and/or a congenital anomaly of the inner ear. Nearly all patients with Pendred syndrome have a congenital inner ear anomaly ¹¹. An enlarged vestibular aqueduct (EVA) in 85% to 100% of cases. Approximately 20% of all patients also have an anomalously formed, hypoplastic cochlea, the so-called Mondini deformity. EVAis the most common neuroradiological finding in children with sensorineural hearing impairment and is not specific for Pendred syndrome.

The most important thyroid parameters are the serum concentrations of thyroid-stimulating hormone (TSH) and free thyroxine (fT4) ¹². The hypothyroidism associated with Pendred syndrome is of the primary type, Thus, the fT4 concentration is low and the TSH concentration is elevated thyroid ultrasonography

facilitates the diagnostic distinction between Pendred syndrome and inflammatory or malignant diseases of the thyroid gland.

The perchlorate discharge test (PDT) was long considered to be the most important criterion for the diagnosis of Pendred syndrome¹⁵. It is used to demonstrate the presence of an iodide organification defect in the thyroid gland. Until a few years ago, the triad of congenital bilateral sensorineural hearing impairment, goiter, and positive PDT was thought to constitute proof of the diagnosis of Pendred syndrome. Molecular diagnosis of Pendred syndrome has been available since 1997 and is based on sequence analysis of the Pendred syndrome gene (PDS/SLC26A4), there are rare, usually sporadic cases of Pendred syndrome in which no mutations are found. This implies that other genetic causes of Pendred syndrome may exist beyond the single Pendred syndrome gene that has been identified to date. The effective diagnosis and optimal treatment of patients with Pendred syndrome requires the interdisciplinary collaboration of pediatricians, endocrinologists, geneticists, phoniatrists/pediatric audiologists, ENT specialists, and neuroradiologists

III. Discussion

Pendred's syndrome, also known as the goiter-deafness syndrome. It is inherited as an autosomal recessive trait. Pendred syndrome is characteristically segregated as an autosomal recessive disorder. Many patients with this disease may benefit from early diagnosis and treatment. Interestingly, two major clinical manifestations of Pendred syndrome, congenital hypothyroidism (frequency 1:4000) and congenital hearing impairment (frequency approximately 1 to 2:2 000) can now be diagnosed in the neonatal period. Goiter does not appear to be an essential prerequisite for the diagnosis of Pendred syndrome, because it is absent in 50% of reported cases. If present, it varies from a slight enlargement to a large multinodular goiter, probably in relation to different degrees of iodine deficiency. Most patients are euthyroid, independently of the presence of goiter, but some show hypothyroidism. However, the incidence of the syndrome was evaluated on the basis of clinical studies that were frequently incomplete and underscored the fact that the phenotype of patients with Pendred syndrome differs greatly among families and even within the same family, leading to pitfalls in the diagnosis¹⁴. In this case the diagnosis of Pendred syndrome was made clinically. The tests for mutation were not available. In the study of William, et al¹⁵ goiter was present in 43 (83%) of the cohort, generally developed after the age of 10 years, 56% remained euthyroid (age range 9-37 years), and 19 patients (44%) had objective evidence of hypothyroidism, all of them had goiter. In the study of Napiontek U et al, led to the conclusion that other environmental and/or genetic factors have an impact on the PS phenotype¹⁶. Although the therapeutic approach to dysmorphogenetic goitres is still controversial. Banghova K, et al suggested total thyroidectomy as the most advantageous method to prevent the development of malignancies that may arise more frequently from dysmorphogenetic goitres than from goitres of other aetiologies.^(17,18)

IV. Conclusion

As the clinical course of pendred's syndrome is highly variable and molecular diagnosis is not easily available high suspicion of disease is important so early management can be started. The effective diagnosis and optimal treatment of patients with Pendred syndrome requires the interdisciplinary collaboration of pediatricians, endocrinologists, geneticists, phoniatrists/pediatric audiologists, ENT specialists, and neuroradiologists.

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