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Pendred's syndrome diagnosed in adulthood at the high resolution thyroid clinic

Síndrome de Pendred diagnosticado en la edad adulta en la consulta de alta resolución de patología tiroidea

Congenital deafness affects 1–3/1000 live births. Over 50% of cases can be attributed to genetic causes, among which 30% correspond to syndromic causes.[1] Of these, Pendred syndrome (PS) is one of the most common, accounting for up to 4–10% of cases.[2]

We present the case of a 20-year-old woman referred to our Department's high-definition thyroid disease clinic after an ultrasound thyroid scan had been performed on her at another centre for goitre detected in an occupational health check-up. The patient reported having had a non-compressive goitre with no symptoms of thyroid dysfunction for 2 years. As history of interest, she was suffering from moderate-to-severe sensorineural deafness diagnosed 2 years earlier. An ear CT at the age of 8 showed a vestibular aqueduct dilation associated with mild cochlear dysplasia and a deficiency in the modiolus. She had a history of thyroid carcinoma in a maternal aunt and primary autoimmune hypothyroidism in a paternal grandparent, without being able to obtain further data owing to lack of contact with them. She was taking no medication, nor was she consuming any goitrogens.

Upon physical examination, she presented an irregular class III goitre. The ultrasound showed an enlarged thyroid, with 3 nodules on the left thyroid lobe (N1: 1.67 × 3.13 × 2.48 cm; N2: 1.2 × 1.34 × 1.84 cm and N3: 1.34 × 1.34 × 1.96 cm) and 2 on the right lobe (N4: 0.7 × 1.64 × 2.06 cm and N5: 0.92 × 1.96 × 1.82 cm). All of them were well delimited, with hypoechogenic halo, spongiform aspect, except for N2 which was solid and isoechogenic, and with peripheral vascularisation in N2 and mixed vascularisation in the remaining nodules (Fig. 1).

The blood chemistry showed a TSH of 3.94 μIU/mL (NV: 0.35–4.95 μIU/mL), free thyroxine of 0.75 ng/dl (NV: 0.70–1.48 ng/dl), serum thyroglobulin 1,926.00 ng/mL (NV: 3.50–77.00 ng/ml), 24 -h urinary iodine h of 208.1 μg/l (NV: 100.00–199.00 μg/l) and negative anti-thyroid peroxidase and anti-thyroglubulin antibodies.

In light of the suspicion of PS owing to the coexistence of sensorineural hearing loss and goitre, a genetic study was requested, which was positive, with 2 variants being found (c.1198delT and c.1226 G > A) in biallelic expression (compound heterozygosity) in the SLC26A4 gene.

PS is an autosomal recessive disorder characterised by sensorineural hearing loss, goitre, and a partial iodide organification defect. The mutation arises in the SLC26A4 gene at the 7q22.3 locus, responsible for codifying pendrine, a glycoprotein located in the apical membrane of the thyrocytes, where it acts as an iodide transporter, which gives rise to a disruption in thyroid hormone synthesis. Pendrine is also expressed in the kidney and inner ear.[2] The molecular analysis of the SLC26A4 gene is currently considered the gold standard for establishing the diagnosis of PS, owing to the lack of standardisation, and on occasion availability, for performing the perchlorate discharge test

Sensorineural Deafness is a consistent finding in PS, while goitre may be absent in certain cases.[3–5] The predominant thyroidal involvement in PS is goitre, which is present in 50–83% of cases, starting in late infancy and adolescence, diffuse, increasing in size until the appearance of nodules in adulthood. The size of the goitre is variable, depending on iodine intake, reaching large goitres with endothoracic extension. The treatment of rapid-growth compressive goitre with suspicious or malignant nodules is surgery. Up to 30–50% of cases require surgery, which must be a total thyroidectomy, since if a sub-total thyroidectomy is performed, growth over time in the remainder is observed owing to the persistence of pathogenic factors.[5,6]

Thyroid function is variable, depending on iodine intake. Thyroid dysfunction does not usually appear if there is sufficient iodine intake in the diet. 50% of cases present normal thyroidal function, and 30–50% subclinical or clin-

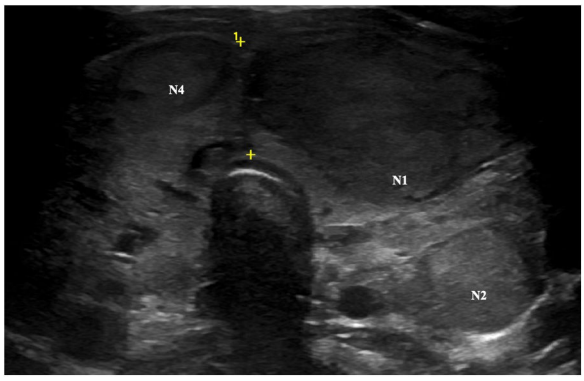

Figure 1 The patient's thyroid ultrasound scan. In this cross section, N1, N2 and N4 can be seen.

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ical hypothyroidism. In their study, Ladsous et al. describe an area with moderate iodine deficiency, hypothyroidism of 79%, some congenital, and 2 cases were transitory.[4] In areas with iodine-rich intakes, normal thyroid function is prevalent, and hyperthyroidism in large goitres has even been described.[7,8] Thyroglobulin levels are elevated in proportion to goitre size. Some cases of PS may coexist with autoimmune thyroiditis, although this is rare.[2] In patients with clinical and sub-clinical hypothyroidism, early treatment with levothyroxinede is indicated. Our patient presented with adequate iodine intake, normal thyroidal function and a multi-nodular goitre with nodules of benign characteristics, asymptomatic, owing to which no treatment is required at the present moment in time.

In patients with dyshormonogenetic goitre, an incidence of thyroid cancer of up to 17% has been described. In patients with PS, cases of thyroid carcinoma, predominantly follicular, have also been described, possibly associated with iodine deficiency, with inadequate levothyroxinede treatment, prolonged high TSH levels and the consequent development of large goitres. Some of them with aggressive behaviour, with bone and lung metastasis.[9] Sakuri et al. describe a case of papillary carcinoma of the thyroid and postulate that organification defects and increased oxidative stress could, in part, explain the development of the carcinoma.[10]

Patients with PS should be subject to periodic clinical monitoring to detect changes in blood chemistry and increase in thyroid size. Those who present a multinodular goitre, such as our patient, must perform this follow-up in high-resolution thyroid disease clinics with ultrasound scans to detect alterations in the size and characteristics of the nodules and/or goitre in order to provide the most suitable treatment at an early stage.

It is important to take the existence of PS into account in clinics when we see a patient with sensorineural deafness and functional thyroid disorder, or a change in the imaging, owing to the clinical implications that an erroneous diagnosis can entail. It is also important to offer genetic advice to family members of patients with PS and early screening for their offspring.

Conflicts of interest

None.

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