OPEN ACCESS

Saudi Journal of Medicine
Abbreviated Key Title: Saudi J Med
ISSN 2518-3389 (Print) | ISSN 2518-3397 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Clinical Case

Pendrid Syndrome; Congenital Hypothyroidism, Sensorineural Deafness, and Bronchiectasis, When the Whole Body Talks about it

Malad Mohamed[1]*, Tadlaoui Abderrahman[1], Riznat Malak[1], Er-rahali Yassine[1], Issouani Jade[1], Guerboub Ahmed Anas[1]

[1]Mohamed -V- Military Training Hospital-Rabat

DOI: https://doi.org/10.36348/sjm.2026.v11i01.002 | **Received:** 04.11.2025 | **Accepted:** 27.12.2025 | **Published:** 06.01.2026

***Corresponding Author:** Malad Mohamed
Mohamed -V- Military Training Hospital-Rabat

Abstract

Congenital hypothyroidism is the first endocrinopathy found in newborns. it is a pathology subject to systematic screening in most countries around the world. Pendrid syndrome is a genetic cause of HC with thyroid gland in situ. It is a genetic condition in "*SLC26A4* gene" (OMIM 605646) encoding Pendrin protein, and resulting in neurosensory deafness with congenital hypothyroidism and goiter. The presence of the 2 major symptoms; deafness and CH, consolidates the diagnosis while genetic sequencing is an element of confirmation. We report the observation of an infant who is a candidate for cochlear implant surgery and who was referred to us for hypothyroidism, in whom there is a history of severe pneumonia on bronchiectasis, which is a manifestation directly related to pendrid syndrome. An adequate thyroid biological and morphological evaluation, as well as screening for other malformations that may be associated with pendrid syndrome are extremely important in a holistic management of this genetic disease. To also recall the vital role that systematic screening for HC can play in preventing neurological disability among children, a procedure that is still not systematic in our country and that we fight to implement it.

Keywords: Congenital hypothyroidism- congenital deafness – Pendrid -Screening.

INTRODUCTION

Congenital hypothyroidism (CH) is the most common neonatal endocrine disorder [1], and, historically, thyroid dysgenesis was thought to account for approximately 80% of cases [2]. Moreover, recent studies have reported a change in the epidemiology of CH, with an increasing in incidence to around 1 in 1500 live newborns, driven by a doubling in incidence of CH with eutopic gland- in-situ (GIS) [3]. As a hands-on approach in front of an established CH, a high level of thyroglobulin allows to guide the etiological reasoning towards dyshormonogenesis, while absent levels suggest athyreosis [4]. Furthermore, assays for thyroid autoimmunity (anti-peroxidase, anti-thyroglobulin antibodies, and in some cases anti-TSH receptor) once positive, allow CH to be linked to trans-placental passage of maternal antibodies [5]. Otherwise, serum and/or urinary iodide measurements may help to determine iodide deficiency or excess, and consequently hypothesize a transient form of CH [6]. Not forgetting imagery, that remains an undeniable tool for etiological evaluation of CH, using thyroid ultrasound and/or scintigraphy [7]. Finally, sequencing will be more easily guided by a possible syndromic presentation, associating with the CH other clinical signs or malformations. In the same perspective, Pendred syndrome (PDS, OMIM 274600) is one of these syndromic causes leading to a CH with GIS. It's an autosomal recessive genetic disease, mainly characterized by sensorineural hearing loss and goiter [8]. The disease is mainly caused by mutations in the *SLC26A4* gene (OMIM 605646) encoding Pendrin protein [9]. Up to now, nearly 500 pathogenic mutations of this gene have been reported, of which 290 are associated with PDS and the rest are associated with Non-Syndromic Enlarged Vestibular Aqueduct (NSEVA) [10]. The difference between PDS and NSEVA is only the presence or absence of a thyroid phenotype, and there has been controversy about whether PDS and NSEVA are two stages of the same disease [10].

CLINICAL CASE

This is an 18-month-old male infant, addressed by the ENT specialist for adjustment of his treatment of hypothyroidism, as a pre-anesthesia consulting (PAC) prior to a cochlear implant surgery for congenital deafness. Third of a sibling of 3, all in good health, notably without hearing problems or dysthyroidism. He

was born at term after a fairly well-monitored pregnancy, without notable incidents, moreover the mother declares not to be under potentially ototoxic treatment during pregnancy. It was There is a personal history of recurrent pneumonia, including a severe episode requiring a short hospitalization for one week. The second medical antecedent, which is more relevant in this context, is a sensorineural hearing loss diagnosed at the age of 14 months. For which the infant is followed and he is a candidate for a cochlear implant. The diagnosis of congenital hypothyroidism was made during the said hospitalization, then 6 months old. The diagnosis was guided by suggestive signs including hypotonia. The initial TSH was 17.9 m IU/L, that of control has still returned high at 21.2 m UI/L with a moderately low FT4 = 10 pmol/L. At this stage we did not note any abnormalities in the complete blood count, ferretin, CRP, renal and hepatic function all normal. the dosage of thyroglobulin before initiating the treatment has not been done. This finding indicated a partial primary congenital hypothyroidism, and levothyroxine treatment was initiated with poor adherence. The main functional sign found in this infant is the delay in psychomotor acquisitions; including a delay in maintaining the head, a delay in standing that is still impossible only with support. The dental eruption is also significantly delayed. The current TSH is 7.8 m IU/L at 25ug per day of Levothyroxin taken orally after cracking tablets and dissolution in water or milk. What makes a dosage of 1.7 ug/kg/day which is very low compared to the recommended dosage for young children. An increase in the dose to 50 ug/day was initiated. And a screening assessment for other malformations was requested, particularly cardiological and renal, whose examinations reveal no malformations on these two sites. The ultrasound finds an eutopic normal thyroid gland, with normal echogenicity and vascularization, measuring 1.8 mL for the right lobe and 1.4 mL for the left lobe. The scintigraphy Tc99 has been requested, whose result is in progress. The etiological assessment was oriented towards a Pendrid syndrome in front of the syndromic presentation, associating congenital hypothyroidism and congenital sensorineural deafness. Genetic sequencing was proposed to the family, but not realized due to economic constraints.

DISCUSSION

Before the start of newborn screening for CH in 1974, the incidence of the disease was estimated at 1/7000; subsequently, it progressively doubled to meet 1/3500 live births [11]. In the last two decades, the incidence of CH has doubled again. A possible explanation for the increase in CH incidence is the change in the screening strategy, notably with the revision of TSH values used as a cut-off, which has significantly increased the sensitivity of the screening test [12]. The main goal of CH screening is the eradication of intellectual disability considered as an ultimate result of CH, and in this regard, the costs of screening seem to be lower than those of treatment in case of missed CH diagnosis during newborn. in our country, there is not yet a national screening program for CH, which complicates the estimation of the real incidence of the disease. The diagnosis of CH is therefore considered in all newborns with abnormal screening results. They should undergo serum FT4, FT3 and TSH measurements to confirm the findings: newborns with hypothyroidism typically have low FT4 and high TSH concentrations [4].

The antecedent of severe pneumonia and CH, what is the link?

The case subject to this discussion had a history of severe pneumonia that led to hospitalization when he was then 6 months old, requiring oxygen, antibiotics, and physiotherapy sessions. It seems that Pendrid syndrome may be associated with bronchiectasis, which represents a chronic pulmonary disorder characterized by chronic cough and recurrent pulmonary exacerbations [13]. The *SLC26A4* gene encodes pendrin, which is a membrane protein expressed in the inner ear, in thyroid, kidney and airways [14]. Pendrin is responsible for transporting many ions across cell membranes, including chloride (Cl^-), bicarbonate ($HCO3^-$), hydroxyl ion (OH^-), moreover iodide (I^-) or thiocyanate (SCN^-) [14]. Dysfunction of pendrin is closely related to Pendred syndrome, which is characterized by sensorineural deafness, inner ear malformation and goiter [15]. In airway epithelium, it was found that pendrin is expressed mainly in secretory non-ciliated cells, in which is involved in transport of Cl^- against $HCO3^-$ or SCN^- [16]. What's more, some researchers have observed a functional coupling between pendrin and cystic fibrosis transmembrane conductance regulator (CFTR), a significant membrane transporter of Cl^- located in airway epithelium [17]. based on this pathophysiological link, the history of severe pneumonia found in this infant could itself be a superinfection from a non-cystic fibrosis bronchiectasis, as mediated by the same etiopathogenic mechanism as the entire referred syndrome.

The sensorineural deafness and Pendrid

According to a significant metanalysis about a total of 110 PDS cases with biallelic genotype and thyroid phenotype in 98 families from 13 countries, there are some cases of missed diagnosis of PDS in clinical practice. Some cases only showed NSEVA in childhood, and PDS was diagnosed with a thyroid phenotype over time [8]. The median age of hearing phenotype onset in PDS cases reported in multiple databases was 1.0 years, while the median age of thyroid phenotype onset was about 14.5 years [8]. this finding suggests that this infant is considered to be diagnosed at a relatively good time, especially considering the lack of systematic screening in the country. However, in last years, it was found that thyroid phenotype appeared in long-term follow-up of NSEVA cases [18,19].

The thyroid function evaluation and treatment

From a volumetric point of view, thyroid volume in newborns ranges from 0.84 ± 0.38 to 1.62 ± 0.41 mL, and remains stable during the first 3 weeks of life; whereas after the 1st year of life the size of a thyroid lobe is generally around an average of 0,95 mL [20][21]. This would therefore allow to conclude at a slightly above-normal volume in the child subject to this discussion, which is in favor of pendrid syndrome. Scintigraphy that we insist to perform in this child is a key examination in the etiological evaluation, because it allows to eliminate an ectopic gland, a diagnosis easily reached by ultrasound, but it especially allows to eliminate captation abnormalities due to a mutation of the NIS. Scintigraphy can be performed using 99m-Technetium (Tc-^{99}) or Iodine-123 (I-^{123}), both captured by NIS on the basal membrane of thyroid follicular cells [22]. Note that the I123 scintigraphy remains less irradiative, but in contrast more expensive [23]. In infants underwent a CH screening, treatment with L-thyroxine should be started as soon as possible and no later than 2 weeks after birth [24]. The aim of substitutive therapy is to normalize FT4 levels within 2 weeks and TSH values within 1 month [25]. As it has been demonstrated in several trials, an initial dosage of 10-15 mg/kg/day is the recommended dose interval to normalize TSH rapidly [4][26]. Despite the difficulties in the galenic in the infant population L-thyroxine should be administered orally, once daily, if possible, at the same time each day. These prescription rules seem to complicate proper treatment adherence in young children and therefore continue to raise challenge for clinicians and families. Finally, some authors recommend the use of branded formulation in levothyroxine rather than the generic one [27].

CONCLUSION

The issue of HC lies in tragic neurological comorbidities that affect the well-being of the child. In underdeveloped countries where screening is not yet systematic, we continue to see syndromic forms and invalidating psycho-motor delays. In our country some authors have proposed novel screening methods with inexpensive and reliable assay kits [28]. Efforts made in this noble cause are to be encouraged especially when it comes to single-centre initiatives for mass screening, often very fruitful allowing the diagnosis of several unknown cases of CH, such as in the region of Fez [29]. At the same moment national societies of endocrinology and pediatrics continue their fierce battle to make screening a legitimate right for every Moroccan newborn.

Abbreviation:

CH: congenital hypothyroidism
CFTR: cystic fibrosis transmembrane conductance regulator
NSEVA: Non-Syndromic Enlarged Vestibular Aqueduct
OMIM: Online Mendelian Inheritance in Man
PDS: Pendrid syndrome
Tc99 : Technétium-99m
TSH: Thyroid stimulating hormone

REFERENCES

1. Paolo Cavarzere, Valentina Mancioppi, Riccardo Battiston, Valentina Lupieri, Anita Morandi and Claudio Maffeis. Primary congenital hypothyroidism: a clinical review. Frontiers in endocrinoloy. 05 August 2025. - DOI 10.3389/fendo.2025.1592655
2. Adeline K. Nicholas, Eva G. Serra, Hakan Cangul, Saif Alyaarubi, Irfan Ullah, Erik Schoenmakers, Asma Deeb, Abdelhadi M. Habeb, Mohammad Almaghamsi, Catherine Peters, Nisha Nathwani, Zehra Aycan, Halil Saglam, Ece Bober,nMehul Dattani, Savitha Shenoy, Philip G. Murray, Amir Babiker, Ruben Willemsen, Ajay Thankamony, Greta Lyons, Rachael Irwin, Raja Padidela, Kavitha Tharian, Justin H. Davies, Vijith Puthi, Soo-Mi Park, Ahmed F. Massoud, John W. Gregory, Assunta Albanese, Evelien Pease-Gevers, Howard Martin, Kim Brugger, Eamonn R. Maher, V. Krishna K. Chatterjee, Carl A. Anderson, and Nadia Schoenmakers. Comprehensive Screening of Eight Known Causative Genes in Congenital Hypothyroidism with Gland-in-Situ. J Clin Endocrinol Metab, December 2016, 101(12):4521–4531. doi: 10.1210/jc.2016-1879
3. Corbetta C, Weber G, Cortinovis F, *et al.,* A 7-year experience with low blood TSH cutoff levels for neonatal screening reveals an un- suspected frequency of congenital hypothyroidism (CH). Clin En- docrinol (Oxf). 2009; 71:739 –745.
4. American Academy of Pediatrics, Rose SR, Section on Endocrinology and Committee on Genetics, American Thyroid Association, Brown RS, and Public Health Committee, Lawson Wilkins Pediatric Endocrine Society, Foley T, *et al.,* Update of newborn screening and therapy for congenital hypothyroidism. Pediatrics. (2006) 117:2290–303. doi: 10.1542/peds.2006-0915
5. van Trotsenburg ASP. Management of neonates born to mothers with thyroid dysfunction, and points for attention during pregnancy. Best Pract Res Clin Endocrinol Metab. (2020) 34:101437. doi: 10.1016/j.beem.2020.101437
6. Delange F, Heidemann P, Bourdoux P, Larsson A, Vigneri R, Klett M, *et al.,* Regional variations of iodine nutrition and thyroid function during the neonatal period in Europe. Biol Neonate. (1986) 49:322–30. doi: 10.1159/000242547
7. Stoupa A, Kariyawasam D, Nguyen Quoc A, Polak M, CarréA. Approach to the patient with congenital hypothyroidism. J Clin Endocrinol Metab. (2022) 107:3418–27. doi: 10.1210/clinem/dgac534
8. Y.-L. LI1,2, F.-Y. GONG1,2, Z.-Y. DANG2, W. XIONG2, M.-D. ZHANG2, Y.-X. WANG3, C.-C. WANG2, Z.-G. JIN2. Analysis of clinical characteristics of thyroid phenotype in Pendred syndrome based on multiple databases. European

Review for Medical and Pharmacological Sciences . 2023; 27: 5390-5396
9. Everett LA, Glaser B, Beck JC, Idol JR, Buchs A, Heyman M, Adawi F, Hazani E, Nassir E, Baxevanis AD, Sheffield VC, Green ED. Pendred syndrome is caused by mutations in a putative sul- phate transporter gene (PDS). Nat Genet 1997; 17: 411-422.
10. Azaiez H, Yang T, Prasad S, Sorensen JL, Nishimura CJ, Kimberling WJ, Smith RJ. Genotype-phenotype correlations for SLC26A4-related deafness. Hum Genet 2007; 122: 451-457.
11. Barry Y, Bonaldi C, Goulet V, Coutant R, Léger J, Paty AC, *et al.,* Increased incidence of congenital hypothyroidism in France from 1982 to 2012: a nationwide multicenter analysis. Ann Epidemiol. (2016) 26:100– 5. doi: 10.1016/ j.annepidem.2015.11.005
12. Lain S, Trumpff C, Grosse SD, Olivieri A, Van Vliet G. Are lower TSH cut-offs in neonatal screening for congenital hypothyroidism warranted? Eur J Endocrinol. (2017) 177:D1–D12. doi: 10.1530/EJE-17-0107
13. Zhu K and Jin Y (2023) Case report: A case of SLC26A4 mutations causing pendred syndrome and non-cystic fibrosis bronchiectasis. Front. Pediatr. 10:1077878. doi: 10.3389/fped.2022.1077878
14. Mount DB, Romero MF. The SLC26 gene family of multifunctional anion exchangers. Pflugers Arch. (2004) 447:710–21. doi: 10.1007/s00424- 003-1090-3
15. Wemeau JL, Kopp P. Pendred syndrome. Best Pract Res Clin Endocrinol Metab. (2017) 31:213–24. doi: 10.1016/j.beem.2017.04.011
16. Tamma G, Dossena S. Functional interplay between CFTR and pendrin: physiological and pathophysiological relevance. Front Biosci. (2022) 27:75. doi: 10.31083/j.fbl2702075
17. Bajko J, Duguid M, Altmann S, Hurlbut GD, Kaczmarek JS. Pendrin stimulates a chloride absorption pathway to increase CFTR-mediated chloride secretion from cystic fibrosis airway epithelia. -FASEB Bioadv-. (2020). doi: 10.1096/fba.2020-00012:
18. Li XC, Everett LA, Lalwani AK, Desmukh D, Friedman TB, Green ED, Wilcox ER. A mutation in PDS causes non syndromic recessive deafness. Nat-Genet 1998; 18: 215-217.
19. Baldwin CT, Weiss S, Farrer LA, De Stefano AL, Adair R, Franklyn B, Kidd KK, Korostishevsky M, Bonné-Tamir B. Linkage of congenital, recessive deafness (DFNB4) to chromosome 7q31 and evidence for genetic heterogeneity in the Middle Eastern Druze-population. Hum Mol Genet 1995; 4: 1637-1642.
20. Perry RJ, Hollman AS, Wood AM, Donaldson MD. Ultrasound of the thyroid gland in the newborn: normative data. Arch-Dis-Child Fetal Neonatal Ed.-(2002) 87: F209–11. doi: 10.1136/fn.87.3.F209
21. Chanoine JP, Toppet V, Lagasse R, Spehl M, Delange F. Determination of thyroid volume by ultrasound from the neonatal period to late adolescence. Eur J Pediatr. (1991) 150:395–9. doi: 10.1007/BF02093716
22. Stoupa A, Kariyawasam D, Nguyen Quoc A, Polak M, CarréA. Approach to the patient with congenital hypothyroidism. J Clin Endocrinol Metab. (2022) 107:3418–27. doi: 10.1210/clinem/dgac534
23. Meller J, Becker W. The continuing importance of thyroid scintigraphy in the era of high resolution ultrasound. Eur J Nucl Med Mol Imaging. (2002) 29:425–38. doi: 10.1007/s00259-002-0811-8
24. Bongers-Schokking JJ, Koot HM, Wiersma D, Verkerk PH, de Muinck Keizer- Schrama SM. Influence of timing and dose of thyroid hormone replacement on development in infants with congenital hypothyroidism. J Pediatr. (2000) 136:292–327. doi: 10.1067/mpd.2000.103351
25. Germak JA, Foley TP Jr. Longitudinal assessment of L-thyroxine therapy for congenital hypothyroidism. J Pediatr. (1990) 117:211–9. doi: 10.1016/S0022-3476(05) 80532-3
26. Esposito A, Vigone MC, Polizzi M, Wasniewska MG, Cassio A, Mussa A, *et al.,*Effect of initial levothyroxine dose on neurodevelopmental and growth outcomes in children with congenital hypothyroidism. Front Endocrinol (Lausanne). (2022) 13:923448. doi: 10.3389/fendo.2022.923448
27. Van Trotsenburg P, Stoupa A, Leǵer J, Rohrer T, Peters C, Fugazzola L, *et al.,*Congenital hypothyroidism: A 2020–2021 consensus guidelines update-an ENDO-European reference network initiative endorsed by the European society for pediatric endocrinology and the European society for endocrinology. Thyroid. (2021) 31:387–419. doi: 10.1089/thy.2020.0333
28. Abdelghani Iddar1, khadija erregragui1, younes sbihi1. congenital hypothyroidism: development, optimization and validation of a radioimmunometric assay applied to the diagnosis. revue marocaine de santé publique 2023, vol 10, n° 16
29. Saâd Maniar 1 , Chadia Amor 2 et Abbas Bijjou 3. Dépistage de l'hypothyroïdie congénitale au Maroc : étude pilote. EMHJ – Vol. 24 No. 11 – 2018.