case report

Diagnosed congenital hypothyroidism with missing follow-up: Is it time for a national registry?

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A treatable and preventable disorder, congenital hypothyroidism (CH) is still a common cause of mental retardation. A 17-year-old Saudi boy with CH due to an ectopic thyroid gland was diagnosed by the neonatal screening program. Thyroxine replacement therapy was started for one month when the family chose to discontinue medication and follow-up. He was not then seen until 11 years of age. Thyroxine was restarted with a close follow-up, although thyroid function tests gradually improved back to normal levels, but his final height was short (159 cm) and IQ was negatively affected. Despite the diagnosis having been made at an appropriate time, patient was lost to follow up. This indicates an obvious flaw in the system for follow-up care. We recommend a registry of patients with CH to monitor their care. The aim of such a registry would be to monitor the efficiency and efficacy of neonatal screening.

Congenital hypothyroidism (CH) is one of the most common treatable and preventable causes of mental retardation.[1,2] Its incidence worldwide is approximately 1 in 3000 to 4000 live births.[3,4] In the Saudi population, the incidence of permanent CH diagnosed by routine neonatal screening in the Najran health region (Southern Province) has been reported to be 1 in 1400 newborn infants,[5] a figure far higher than that reported in other regions of Saudi Arabia and worldwide. The incidence in Riyadh is 1 in 2666.[6] Reports from other regions of Saudi Arabia suggest that the incidence of CH is 1 in 2500 to 3500.[7-9] These figures are comparable with the worldwide incidence of CH. The high incidence of CH in the Saudi population supports the need for a neonatal screening program.

Newborn screening in Saudi Arabia started as an individual program, initially in ARAMCO in 1987-1988, and 2 years later in National Guard hospitals. In 1985, it was started in a military hospital[9,10] followed by the Ministry of Health in 1989, and in King Saud University and private hospitals in 1992.[6,11] The screening in these programs was not mandatory, and no monitoring happened at the national level.

Since the development of pilot screening programs for CH in Quebec, Canada, and Pittsburgh, United States in 1974, newborn screening for CH has become a routine in almost all developed countries.[12] These newborn screening programs are excellent, function efficiently, and achieve their objective of diagnosing a common cause of preventable mental retardation. Certainly, the main objective of screening is the eradication of mental retardation after CH has been diagnosed. In addition to the profound clinical benefit of screening, it has been estimated that the cost of screening for CH in newborns, 12 Saudi Riyals per each test, is much lower than the cost of treating CH diagnosed at an older age.[2,13] Any newborn screening program should include screening, follow-up, diagnosis, management, system evaluation, and education. Without proper follow-up and education, newborn screening programs will fail.[2,14] The aim of such a registry is to monitor the efficiency and efficacy of neonatal screening, provide disease surveillance, and allow identification of possible etiological risk factors for the disease.[13]

CASE

A 17-year-old Saudi boy with CH due to an ectopic thyroid gland was diagnosed by the neonatal screening program. His cord thyroid stimulating hormone (TSH)

was 373 mIU/L, and his free thyroxine (FT4) was 10.4 pmol/L. A repeat serum thyroid function test revealed a TSH of >196 mIU/L, FT4 of 9.1 pmol/L, and FT3 of 4.4 pmol/L. Thyroid microsomal and thyroglobulin antibodies were both negative. His thyroglobulin level was 223 ng/mL (<60), and his thyroxine binding globulin was 27 μg/ml (12-28). A thyroid scan and uptake showed the presence of ectopic, sublingual thyroid tissue with an uptake of 1.8%. The patient was immediately started on the thyroxine replacement therapy after confirming the diagnosis, but unfortunately the parents discontinued L-thyroxine after the first neonatal visit at 1 month of age. This lasted for 11 years. At that time, he presented to the pediatric endocrine clinic in a tertiary hospital with complaints of short stature and poor school performance.

At presentation, he had coarse facial features and dry yellow skin with normal sclera. His growth parameters were both below the 5th percentile (**Figure 1**). His height was 107 cm (24 cm below the 5th percentile), and his weight was 23 kg. His father's and mother's heights were 162.8 cm and 146 cm, respectively, giving a mid-parental height of 160.9 cm. His TSH value was 585 mIU/L (0.4-5.5) and his FT4 was low at 3.7 pmol/L (11.5-23.2). His fasting lipid profile demonstrated a cholesterol level of 10.5 mmol/L (3.1-5.2), triglycerides of 1.9 mmol/L (0.15-1.4), low density lipoprotein of 7.3 mmol/L (1.3-4.0), and very low density lipoprotein of 0.9 mmol/L. Renal and liver function tests were both normal, apart from an elevated aspartate amino transferase level of 54 U/L (15-37). His cortisol level was normal, and his prolactin level was high at 57.4 μg/L (2.1-17.7).

His bone age was delayed by 4 years, with a standard deviation of 6.6 months, and a pituitary gland MRI showed a pituitary macroadenoma (**Figure 2**). An initial IQ assessment using the Stanford Binet Intelligence Scale was 81. The patient was restarted on thyroxine, and the dose was adjusted accordingly. He was followed up closely in the endocrine clinic, and his thyroid function tests and fasting lipid profile gradually improved back to normal. Six months later, a repeat pituitary MRI showed a resolved macroadenoma, and a repeat IQ assessment gave a score of 83. On follow-up, the patient remained euthyroid. His growth velocity was normal, and his puberty assessment at the age of 16 years showed Tanner stage 5 and the final height at 17 years was 159 cm.

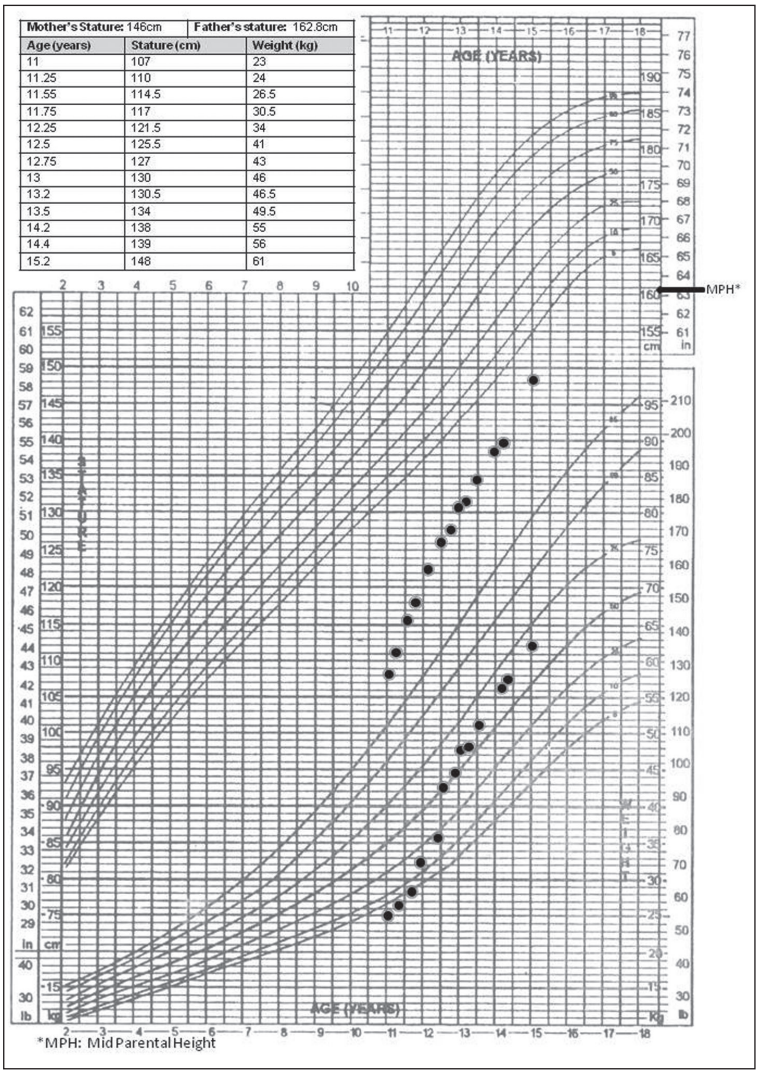

Figure 1. Growth Chart

DISCUSSION

The transmission of this patient's abnormal test results, with notification of a pediatric endocrinologist, was performed properly, and the follow-up confirmatory testing of serum samples for TSH and FT4 levels was performed to verify the diagnosis. An ectopic, sublingual gland was demonstrated on thyroid radionuclide imaging; thus, a permanent form of CH that requires a lifelong full thyroid hormone replacement therapy with regular medical monitoring and follow-up was diagnosed. The treatment was initiated as soon as the confirmatory blood samples were drawn.

As an infant diagnosed with CH, the patient should be followed in a pediatric endocrinology outpatient clinic at regular intervals and should be monitored clinically for linear growth, weight gain, developmental progression, and overall well-being, with biochemical measurements of his TSH and FT4 levels. His levothyroxine dose should be adjusted according to the patient clinical response and serum TSH and FT4

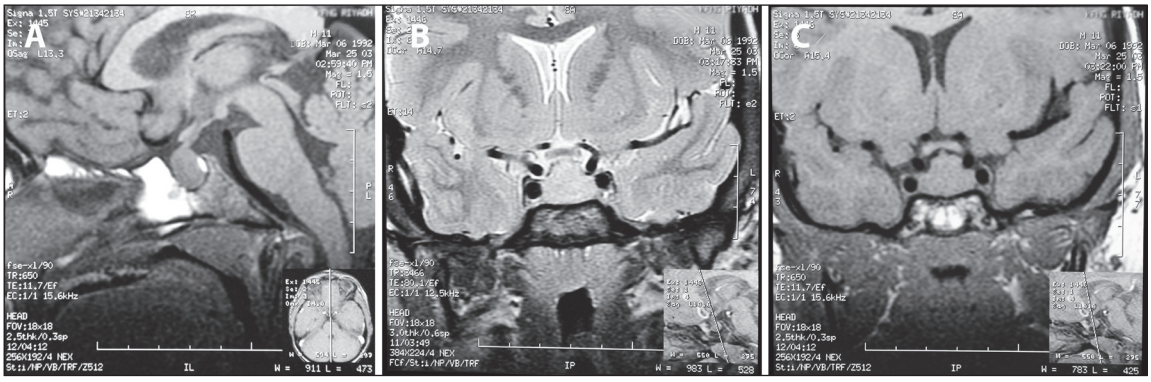

Figure 2. MRI of pituitary gland A) saggital view, B) coronal view, and C) with contrast (coronal view).

levels. Unfortunately, his parents chose to discontinue the therapy and follow-up during early infancy, without consulting the treating physician, until the patient was 11 years of age, when they presented to another tertiary hospital. At that time, the patient had clinical and biochemical evidence of CH as demonstrated by coarse facial features, short stature, learning difficulties, and a low IQ. He had a high TSH level, low FT4, dyslipidemia, and markedly delayed bone age. A pituitary MRI showed a macroadenoma. The patient was started on levothyroxine with a close follow-up at frequent intervals in the clinic. His parents underwent ongoing counseling regarding the importance of adherence to and compliance with medical therapy. On follow-up, he had a normal growth velocity and had entered puberty. His thyroid function tests and fasting lipids normalized, and a repeat pituitary MRI was normal.

The clinical evaluation of an infant with CH should be conducted at frequent intervals during the first 3 years of life, a critical time for brain development when thyroid hormone is crucial. It is essential that follow-up laboratory assessments be obtained in a timely manner and that there be no loss to follow-up if poor compliance is suspected or if abnormal results are obtained.[2] The education of parents by trained personnel with booklets or visual aids is highly desirable. This education should focus on (a) their child's disorder, (b) the etiology of CH, (c) the benefits of early diagnosis in preventing mental retardation, and (d) the potential problems associated with a lack of treatment or inadequate treatment and the benefits of early treatment. Instructions on the appropriate manner in which thyroid hormone is administered and the substances that can interfere with its absorption (e.g., soy, iron, calcium, and fiber) should be included, in addition to guidance regarding adherence to the treatment plan. Lastly, the importance of periodic follow-up care should be emphasized.[2,13]

Because learning problems are possible, even with early diagnosis and treatment, parents should be advised when to seek psychomotor and educational evaluations and interventions. Early childhood intervention programs, if available, should be encouraged.[15-17] In Italy, a National Register of Infants with Congenital Hypothyroidism (INRICH) was established in 1987 that was 10 years after the nationwide newborn screening program started. The study group for CH published their experience for more than 20 years. These studies explain the importance of a registry in providing continuous surveillance of CH. INRICH helps a great deal to characterize the Italian population of babies with CH. It also allows to them to perform a standardization of screening procedures and improvements at the time at starting treatment and in the determining the dose of therapy. Furthermore, the program provides a unique opportunity for research. In general the registry is considered a potent tool of surveillance, epidemiological research, and knowledge on CH.[13] In our patient, although the newborn screening program diagnosed CH and treatment was initiated as early as possible, there was an obvious and clear defect in the system and follow-up care of the patient. We recommend a registry for each patient with CH to recall when a follow-up appointment is missed.

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