European Journal of
Nuclear
Medicine

Original article

Thyroid scintigraphy and perchlorate discharge test in the diagnosis of congenital hypothyroidism

Mahmoud El-Desouki[1], Nasir Al-Jurayyan[2], Abdulrahman Al-Nuaim[3], Abdullah Al-Herbish[2], Abdullah Abo-Bakr[2], Yaqoub Al-Mazrou[4], Abdulrahman Al-Swailem[4]

[1] Division of Nuclear Medicine, Department of Medicine, College of Medicine, King Saud University, Riyadh, Saudi Arabia
[2] Division of Endocrinology, Department of Paediatrics, College of Medicine, King Saud University, Riyadh, Saudi Arabia
[3] Division of Endocrinology, Department of Medicine, College of Medicine, King Saud University, Rigadh, Saudi Arabia
[4] Ministry of Health, Riyadh, Saudi Arabia

Received 19 December 1994 and in revised form 26 February 1995

Abstract. Quantitative thyroid scanning using low doses of technetium-99m sodium pertechnetate was performed on 147 infants (55 males and 92 females) with congenital hypothyroidism detected through the national neonatal screening programme. Thirty-two (21.8%) were athyrotic, while 62 (42.2%) had an ectopic thyroid and 53 (36%) had a eutopic gland with increased ^{99m}Tc uptake (mean 17%; range, 5%–38%). The perchlorate discharge test (PDT) was performed in nine of the infants with ectopic glands and 15 with eutopic glands; the findings were consistent with an organification defect in 22 cases (seven ectopic and 15 eutopic). Thyroid scintigraphy and PDT can add useful aetiological, genetic and prognostic information in the clinical evaluation of infants with congenital hypothyroidism detected by neonatal screening.

Key words: Congenital hypothyroidism – Thyroid scintigraphy – Perchlorate discharge test

Eur J Nucl Med (1995) 22:1005–1008

Introduction

Neonatal screening programmes for congenital hypothyroidism (CH) reveal an incidence of approximately 1 in 2500–4500 [1, 2]. Primary CH may be due to an absent or hypoplastic gland, an ectopic gland or an inborn error of thyroid hormone metabolism [3]. Determination of the cause of CH is of genetic, epidemiological and prognostic importance [4, 5].

Thyroid scintigraphy was recommended by Fisher et al. [6] as part of a screening programme, and this was emphasized by Connolly et al., who concluded that scanning was useful in permitting treatment to be started with confidence [7].

In this report, we describe the scintigraphic pattern in 147 infants referred to King Khalid University Hospital (KKUH) for further evaluation of CH. The role of thyroid scintigraphy and the perchlorate discharge test (PDT) in determining the cause of CH is also discussed.

Correspondence to: M. El-Desouki, College of Medicine and King Khalid University Hospital, King Saud University, P.O. Box 7805 (46), Riyadh 11472, Saudi Arabia

Materials and methods

Between February 1989 and March 1994, 147 infants were sequentially referred to the Nuclear Medicine Department at KKUH, Riyadh, for thyroid imaging studies, having been diagnosed as having CH on the basis of the neonatal screening programme which utilizes cord thyroid stimulating hormone (TSH) supplemented with L-thyroxine (T_4) when necessary [2]. There were 55 males and 92 females. Their mean age at the time of recall was 22 days (range: 6–64). Serum TSH and T_4 were measured using the Delfia immunofluorescent method (Pharmacia Diagnostic, Wallacory, Finland), and antithyroid antibodies were measured by the haemagglutination method. No patient received thyroid replacement therapy prior to the radionuclide study.

Technetium-99m pertechnetate was performed on all children using a gamma camera equipped with a low-energy general-purpose collimator. ^{99m}Tc pertechnetate was used in a dose of 500 μCi given intravenously. An initial zoomed image of the thyroid gland was obtained 15 min post injection and the uptake was measured between 20 and 30 min post injection. An additional unzoomed image including the salivary glands and stomach was obtained. Radioactivity in the syringe was measured both before and after injection to give the corrected administered dose.

The PDT was performed 24–48 h after the ^{99m}Tc thyroid scan using iodine-123 (King Faisal Specialist Hospital and Research Centre, Riyadh) in a dose of 50 μCi instilled directly into the mouth followed by water or milk to wash the mouth. Using a scintillation probe and scaler, 1- and 2 h thyroid uptake was determined, followed by a 400 mg oral dose of potassium perchlorate. Thyroid uptake was subsequently measured every 15 min for 1 h and every 30 min for an additional 1 h. A discharge of greater than 50% indicates a virtually complete organification defect.

Table 1. Sex distribution, thyroid function and ^{99m}Tc pertechnetate thyroid scan findings in 147 infants

Scan pattern	No.	Sex		Cord blood (screening) mean (range)		Venous blood (recall) mean (range)	
		M	F	TSH (mU/l) normal: <60	T_4 (nmol/l) normal: 80–200	TSH (mU/l) normal: <10	T_4 (nmol/l) normal: 80–180
Athyrosis	32	12	20	399 (269–572)	60.3 (53–71)	589 (411–900)	15 (13–20)
Ectopic	62	19	43	410 (150–602)	61.4 (37–84)	442.5 (188–560)	47 (13–94)
Eutopic with increased uptake	53	24	29	398.7 (129–483)	67.3 (32–85.4)	489 (83–715)	48.9 (13–112)

while a discharge of 20%–50% indicates a partial organification defect [2].

For thyroid scan and PDT, all infants were sedated using chloral hydrate at a dose of 50 mg/kg given orally. The ^{99m}Tc scans were reviewed by one of the authors (M.D.) without knowledge of the confirmatory laboratory tests. Imaging patterns were assigned to three categories: (1) no detectable thyroid activity, (2) ectopic location, with variable size and uptake, (3) normal location with normal or increased size and uptake. The findings were then correlated with the laboratory values and eventual clinical diagnosis.

Results

Sex distribution, thyroid function tests (screening and recall), and results of radionuclide studies are summarized in Table 1. Thirty-two infants (21.8%) were athyrotic, while 62 (42.2%) had an ectopic thyroid and 53 (36%) were eutopic with increased uptake. None of the patients were found to have anti-thyroglobulin or antimicrosomal antibodies. The mothers did not receive any medication containing iodine or an anti-thyroid medication, nor did they have goitre or signs or symptoms of hypo- or hyperthyroidism. They received dietary iodine at the recommended daily allowance during pregnancy.

In all patients with thyroid aplasia, activity was visualized in the salivary glands and stomach (Fig. 1), which ruled out the possibility of congenital malfunction of the iodine-concentrating (trapping) mechanism. In patients with ectopic thyroid, the gland was in either the lingual or the sublingual position. No case was detected in the mediastinal region. In three patients there were two areas of uptake in the lingual and sublingual regions (Fig. 2). The ectopic glands were either small or large, and the uptake was either decreased or increased for the size of the gland, ranging from 0.2% to 2.6% (normal: 1%–4%) [8]. In those with high uptake the gland appeared enlarged (Fig. 3a). Therefore, organification defects or iodine deficiency was suspected. The PDT was performed in nine of these cases and was consistent with an organification defect in seven (Fig. 3b) (perchlorate discharge

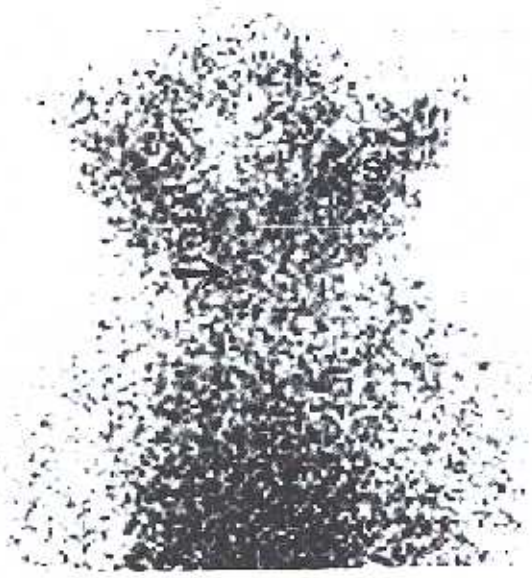


Fig. 1. ^{99m}Tc pertechnetate thyroid scintigraphy in a newborn with thyroid aplasia. No thyroid tissue is seen in the neck (*arrow*). Activity is seen in the salivary gland (*S*)

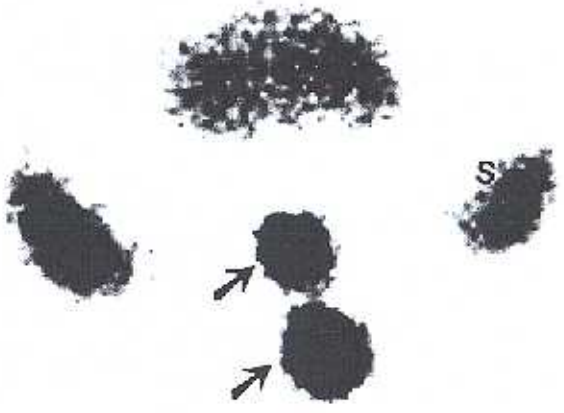
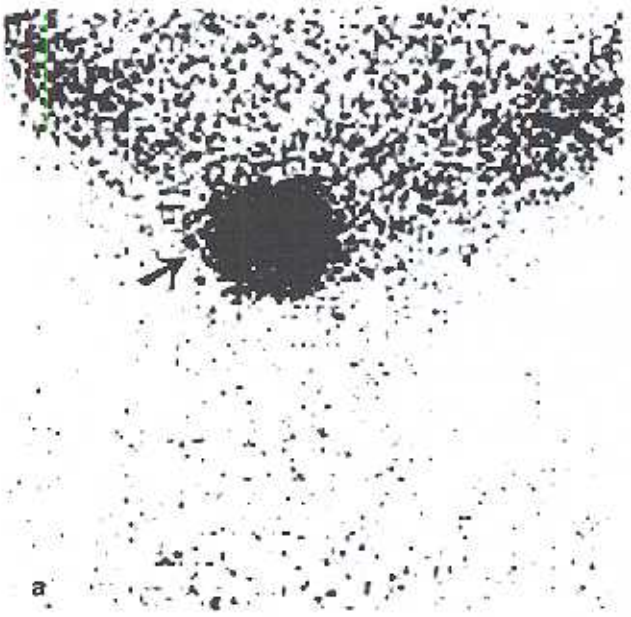


Fig. 2. ^{99m}Tc pertechnetate thyroid scintigraphy. Note the two areas of uptake in an ectopic position (*arrows*). *S*, Salivary gland



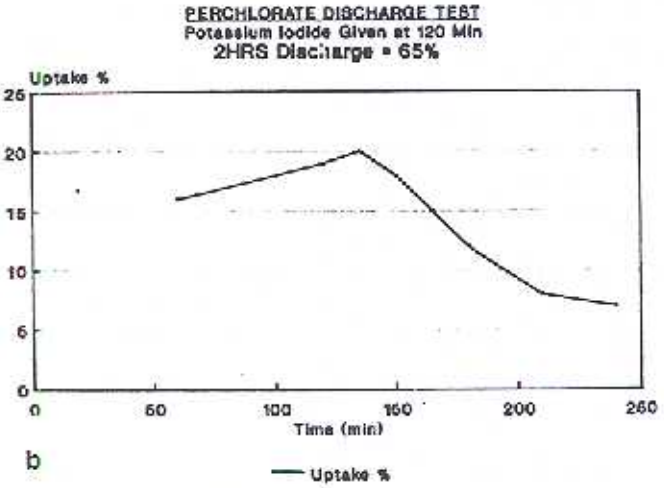


Fig. 3a. ^{99m}Tc pertechnetate thyroid scintigraphy, revealing a large sublingual gland (*arrow*), which is demonstrating increased activity. The PDT (b) was strongly positive

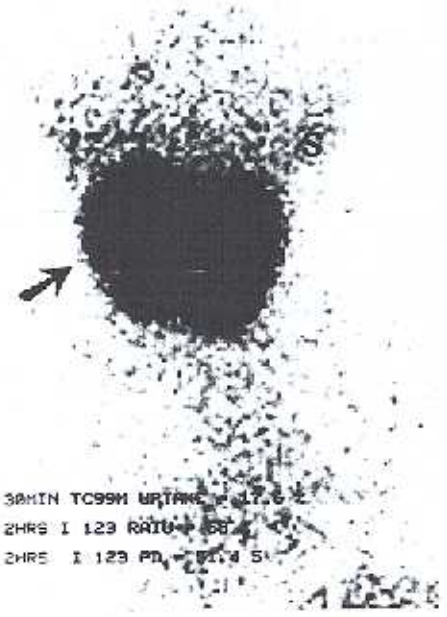


Fig. 4. ^{99m}Tc pertechnetate thyroid scintigraphy revealing a eutopic enlarged gland (*arrow*), which is demonstrating a marked increase in activity. *S*, Salivary gland

was more than 50% in four cases, between 30% and 50% in two and 25% in one).

In 53 (36%) patients the scan revealed an enlarged normally located thyroid which demonstrated high uptake (mean 17%; range, 5%–38%) compared to the salivary gland and background activity (Fig. 4). The gland was clinically palpable in four. The PDT was performed in the first 15 cases and was consistent with organification defects.

Discussion

The presence and location of thyroid tissue in a hypothyroid child has a direct bearing on genetic counselling and prognosis. Athyrosis and thyroid ectopy recur very rarely in the same family, whereas hypothyroidism due to defects in T_4 synthesis or release is inherited as an autosomal recessive trait with an estimated frequency of 25% in siblings [4]. Normal intellectual development is more likely in patients with thyroid tissue, such as those with ectopy or with enzymatic defects, than in those who are athyrotic [9].

Our results (Table 1) are similar to those of O'Connor et al. and indicate that there is little correlation between the biochemical findings (TSH and T_4) and gland anatomy [8]. However, all athyrotic neonates had T_4 levels less than 20 nmol/l (normal: 80–180). Thyroid scan, in conjunction with clinical and laboratory data, provides aetiological, therapeutic and epidemiological information [5–13].

Both ^{99m}Tc and ^{123}I have been used to image the thyroid [5–8, 10–19]. However, we prefer to use ^{99m}Tc as it is freely available locally, it is much less expensive, and the thyroid image can be obtained in a shorter time. Furthermore, the radiation adsorbed dose to the thyroid from ^{99m}Tc sodium pertechnetate is smaller than the expected dose from ^{123}I [10, 13, 17].

The results of the scans showed the full spectrum possible for gland anatomy, ranging from athyrotic, through small or large lingual or sublingual thyroids, to normal or enlarged glands in a normal location. In accordance with previous reports [6–8, 12, 13, 16, 20, 21], thyroid ectopy was the most common finding, and was present in 42.2% of our hypothyroid patients. The finding of ectopic thyroid tissue and increased perchlorate discharge, which suggested an iodine organification defect in some of our patients, is of interest [22]. O'Connor et al. have observed high uptake in some of their patients with lingual thyroids and suggested the possibility

that dyshormonogenesis may coexist with failure of the gland to descend [8]. However, the PDT was not performed in their series to confirm such an observation. Whether these findings represent a true organification defect or a transient state secondary to immaturity of the organification enzymes is of paramount interest and needs further investiation [23, 24]. True organification defect is an autosomal recessive disorder with a 25% likelihood of occurrence in siblings [4]. On the other hand, transient organification defect, if confirmed in a larger series, might contribute to our understanding of the pathogenesis of CH and indicate that some degree of delay in the development of synthetic mechanisms occurs in the dysgenetic gland.

The finding that a high percentage (36%) of patients had normally located glands which demonstrated high uptake and a positive PDT is in contrast to previous reports [6–8, 12, 13, 16]. However, this confirms our previous observation of a high incidence of dyshormonogenesis in this part of the world [2, 25]. A genetic explanation is suggested by the involvement of multiple siblings and the high rate of consanguinity in this population [26]. This fact is worth considering and stresses the importance of identifying the cause of CH in order to provide accurate counselling for the family [4, 11, 12, 19, 25, 27].

In conclusion, quantitative ^{99m}Tc pertechnetate and PDT can add useful aetiological, genetic and prognostic information in the clinical evaluation of infants suspected of having hypothyroidism as a result of neonatal screening.

Acknowledgements. The authors would like to thank the Nuclear Medicine staff at the King Khalid University Hospital for their technical assistance and Miss Alicia C. Evarola for secretarial assistance.

References

1. American Academy of Pediatrics, American Thyroid Association. Newborn screening for congenital hypothyroidism. Recommended guidelines. *Pediatrics* 1987; 80: 745–749.
2. Al-Nuaim A, El-Desouki M, Al-Jurayyan N, et al. Neonatal screening for congenital hypothyroidism, incidence, imaging, feasibility and difficulties of a nationwide program in Saudi Arabia. *Ann Saudi Med* 1992; 12: 129–134.
3. New England Congenital Hypothyroidism Collaborative. Characteristics of infantile hypothyroidism discovered on neonatal screening. *J Pediatr* 1984; 104: 539–544.
4. Rimoin DL, Schimke RN. *Genetic disorders of the endocrine glands*. St. Louis: C.V. Mosby; 1971: 116–138.
5. Heyman S, Crigler JF Jr, Treves S. Congenital hypothyroidism: I^{123} thyroidal uptake and scintigraphy. *J Pediatr* 1982; 101: 571–574
6. Fisher DA. Status of neonatal hypothyroid screening: report from Quebec International Congress on neonatal thyroid screening. In: Stockigt JR, Nagataki S, eds. *Thyroid research VIII*. Proceedings of the Eighth International Thyroid Congress, Sydney, Australia. Canberra: Australian Academy of Science; 1980: 1–7.
7. Connolly JR, Gold H, Kiempfner G, et al. Scanning with Tc 99m pertechnetate in assessment of hypothyroid babies detected by neonatal screening. In: Stockigt BR, Nagataki S, eds. *Thyroid research VIII*. Proceedings on the Eighth International Thyroid Congress, Sydney, Australia. Canberra: Australia Academy of Science; 1980: 30–32.
8. O'Connor MK, Freyne PJ, Cullen MJ. Low dose radioisotope scanning and quantitative analysis in the diagnosis of congenital hypothyroidism. *Arch Dis Child* 1982; 57: 490–449.
9. Rovet J, Ehrlich R, Sorbara D. Intellectual outcome in children with fetal hypothyroidism. *J Pediatr* 1987; 110: 700–704.
10. Bauman RA, Bode HH, Hayek A, Crawford JD. Technetium 99m pertechnetate scans in congenital hypothyroidism. *J Pediatr* 1976; 89: 268–271.
11. Schoen EJ, Dos-Remedios LV, Backstrom M. Heterogeneity of congenital primary hypothyroidism: the importance of thyroid scintigraphy. *J Perinat Med* 1987; 15: 137–142.
12. Wells RG, Sty JR, Duck SC. Technetium 99m pertechnetate thyroid scintigraphy: congenital hypothyroid screening. *Pediatr Radiol* 1986; 16: 368–373.
13. Brooks PT, Archard ND, Carty HML. Thyroid screening in congenital hypothyroidism: a review of 41 cases. *Nucl Med Commun* 1988; 9: 613–617.
14. Arnold JE, Pinsky S. Comparison of ^{99m}Tc and I^{123} for thyroid Imaging. *J Nucl Med* 1976; 17: 261–266.
15. Gulenchyn KY, Brown RG, Green MD, Ash JM. Iodine-123 for pediatric thyroid studies: an evaluation of its role. *J Radioanal Chem* 1981; 65: 251–257
16. Hilditch TE, Jackson HJ. Quantitative ^{123}I-iodide scintigraphy and radiation dosimetry in infants with congenital hypothyroidism. *Eur J Nucl Med* 1985; 11: 132–135.
17. Treves ST, Larsen R. Thyroid. In: Treves ST, ed. *Paediatric nuclear medicine*. New York Berlin Heidelberg: Springer; 1985: 192–201.
18. Casio A, Turba E, Balsamo A, et al. In vivo isotope study of the thyroid with Tc-99m 0_4 in neonatal congenital hypothyroidism. *Eur J Nucl Med* 1984; 9: 351–355.
19. Kim EE, Domstad PA, Choy YC, Deland FH. Avid thyroid uptake of [Tc-99m] sodium pertechnetate in children with goitrous cretinism. *Clin Paediatr* 1981; 20: 437–439.
20. Miyai K, Connelly JF, Foley TP Jr et al. An analysis of the variation of incidence of congenital dysgenetic hypothyroidism in various countries. *Endocrinol J* 1984; 31: 77–81.
21. Virtanen M, Maenpaa J, Pikkarainen J, et al. Aetiology of congenital hypothyroidism in Finland. *Acta Pediatr Scand* 1989; 78: 67–73.
22. Al Jurayyan NAM, Al Nuaim A, El-Desouki M. Association of iodine organification defect and ectopy of the thyroid gland in a patient with primary congenital hypothyroidism. *Saudi Med J* 1992; 13: 65–67.
23. De Iange F, Dodion J, Wolter R, et al. Transient hypothyroidism in the newborn infant. *J Pediatr* 1978; 92: 974–976.
24. Nose O, Harada T, Miyai K, et al. Transient neonatal hypothyroidism probably related to immaturity of thyroidal iodine organification. J Pediatr 1986; 108: 573–576.
25. Al Jurayyan NAM, Abdullah MA, El-Desouki MI, et al. Childhood hypothyroidism in Saudi Arabia: a retrospektive study. *Saudi Med J* 1992; 13: 125–128.
26. Sacdi-Wong S, Al-Frayh AR, Wong HYH. Socio-economic epidemiology of consanguineous matings in the Saudi Arabian population. *J Asian Afr Stud* 1989; 24: 247–252.
27. Cone L, Oates E, Vazques R. Congenital hypothyroidism, diagnostic scintigraphic evaluation and an organification defect. *Clin Nucl Med* 1988; 13:419–420.