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CONGENITAL HYPOTHYROIDISM - A DELAYED DIAGNOSIS IN A NEONATE. A CASE REPORT

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INTRODUCTION

Congenital hypothyroidism is a condition in which a neonate is born with insufficient production of the thyroid hormone[1]. In such children, hypothyroidism will be absent in-utero and at birth because of placental transfer of maternal thyroid hormones to the foetus, if the mother is euthyroid[2,3,4]. Conversely, if the mother has hypothyroidism, such neonates would have experienced hypothyroidism in-utero and will be born with features of hypothyroidism[5,6,7,8]. This is the case in endemic cretinism where the underlying pathology is dietary Iodine deficiency in both mother and foetus. Iodine is necessary for the production of thyroid hormones across all ages.

Other aetiological factors for congenital hypothyroidism are:

- Sporadic thyroid dysgenesis (accounts for 85% of cases of congenital hypothyroidism in areas without endemic Iodine deficiency[1,9,10]).
- Enzymatic defects in thyroid hormones synthesis (5 different enzymes have been identified)[1,9].
- Thyrotropin unresponsiveness[9]
- Hypothalamo-pituitary disease[1,9,11].
- Trans-placental transfer of anti-thyroid drugs or auto antibodies[1,9,12].
- Suppression of foetal hypothalamo-pituitory-thyroidal axis by trans-placental transfer of excess thyroid hormones from a thyrotoxic mother[13].
- Some genetic disorders[14].

Congenital Hypothyroidism (CH) affects 1:4000 newborns worldwide[15]. In areas with severe endemic Iodine (I_2) deficiency e.g. Northern India, the incidence of CH is 75-115 per 1000 live births; whilst in Delhi, Southern India, an area with only mild I_2 deficiency, the incidence of CH is 6 per 1000 live births[16]. In Zaire, Africa, an area with severe endemic I_2 deficiency, CH occurs in 10% of all neonates, giving an incidence of 100 per 1000 livebirths[16]. Conversely, in Pretoria, South Africa, an area without endemic I_2 deficiency, the incidence of CH is approximately 1 per 4000 live births[17].We report a case of congenital hypothyroidism in order to raise the physician's index of suspicion and facilitate early diagnosis. Diagnosis and commencement of treatment of CH before 3 months of age are essential if such infants are to attain optimal intellectual development[1,9].

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CASE REPORT

O.C. is a 4-month-old Nigerian male who presented with constipation since birth, slowly progressive increase in tongue size since birth, jaundice noticed on second day of life (DOL) and lasted 16 days; progressive noisy breathing of 3½ months duration and feeding difficulties of 2½ months duration. Pregnancy and delivery were uneventful. Birth weight was 2.8kg. Mother, a 34-year-old Igbo woman who has been residing in Enugu, Nigeria for the past 10 years, is a trained nurse and is apparently normal. He was admitted into the NBSCU in 2nd DOL and treated for NNJ 2^{o} NNS. His progress notes whilst on admission in the NBSCU were carefully reviewed. No Exchange blood transfusion was done. Jaundice cleared by 16^{th} DOL. No biochemical or clinical screening for hypothyroidism was done. On examination, he had remarkable macroglossia and was small for age. His weight was 3.5kg (58% Expected weight for age); OFC was 38cm (lower limit of normal for age is 40cm); full length was 51cm. Skin was dry and coarse. Breathing was noisy, though dyspnoea and tachypnoea were absent. He had a reducible umbilical hernia of 3cm in diameter; bowel sounds were slightly reduced in pitch. He had normal male external genitalia with both testes within the scrotum. He had reducible bilateral inguino-scrotal hernia (left greater than right); a widened anterior fontanelle (5cm x 6.5cm), a widened posterior fontanelle (2cm x 2cm); global hypotonia and no head control.Thyroid function tests showed markedly elevated TSH (Thyroid Stimulating Hormone), very low free T_4 (thyroxin) and undetectable free T_3. This confirmed the diagnosis of congenital hypothyroidism. X-rays of the limbs were not done. Thyroid scan was requested but not done. Results of other investigations are as shown in table I.He was commenced on Levo-thyroxin 10ug/kg/day for life. The starting dose was 10ug/kg/day. This dose was adjusted as patient gained weight and increased in age. A review 3 weeks after commencing L-thyroxin showed progressive remarkable improvement in all clinical parameters. Clinical photographs before treatment (figures I & II) and six weeks after commencement of thyroxin (figures III & IV) are shown.

Table I: **Laboratory Results**

Age	Investigation	Results
2ND DOL	Total Bilirubin	9.3mg/dL
	Unconjugated	8mg/dL
	Conjugated	1.3mg/dL
2ND DOL	Total WBC	6,900/m^3
	Neutrophils	74%
	Lymphocytes	23%
	Eosinophils	2%
	Monocytes	1%
	Platelets	91,000/mm^3
	Band counts	Not done
2ND DOL	G6 PD status	Not deficient
2ND DOL	Patient's Blood Group	O positive
	Mother's Blood Group	O positive
4 Months	Thyroid Functions tests	
	(a) TSH	22.8ul/ml (0.5 to 4.8)
	(b) T_4	0.7ng/dl (2.5-12.5)
	(c) T_3	0.5ng/ml (0.6-1.6)
	(d) Free T_4	0.2ng/ml (0.8-2.2)
	(e) Free T_3	Undetectable (1.4-4.2)

Figure I: **Photograph of Patient Showing Typical Fascies of Hypothyroidism on Presentation.**

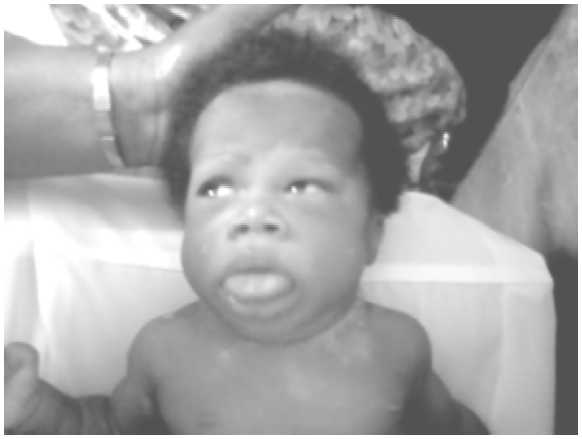


Figure 2: **Same Patient Showing Protuberant Abdomen, Umbilical Hernia and Left Inguino-Scrotal Hernia.**

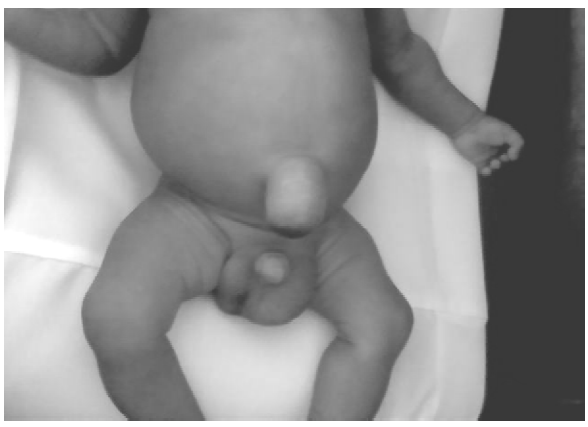


Figure: 3 **Same Patient Showing Marked Improvement after 6 Weeks of Thyroxin Therapy.**

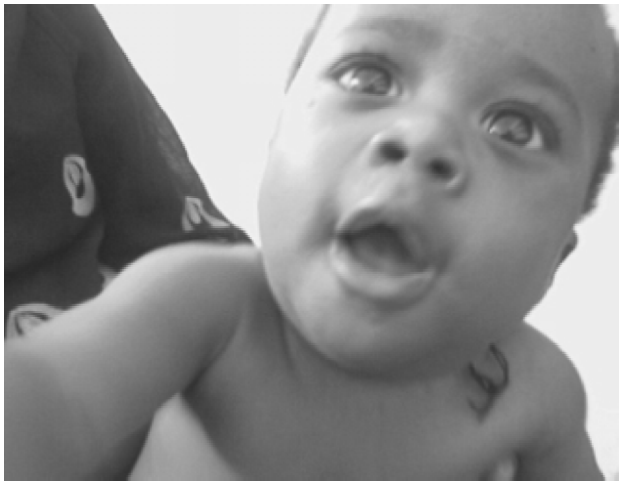
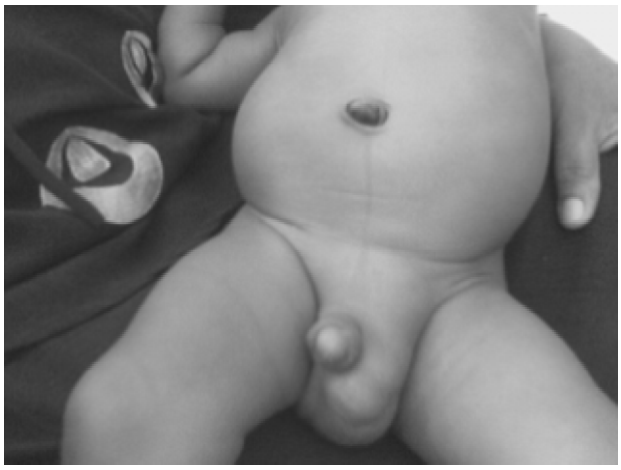


Figure 4**: Same Patient Showing Regression of Umbilical Hernia with Thyroxin Therapy.**



DISCUSSION

This case clearly demonstrates delayed diagnosis of congenital Hypothyroidism (CH) despite early presentation to Paediatricians in a tertiary health institution. Baby O.C. was born in our hospital, presented at the NBSCU on the 2nd day of life with jaundice, and also presented a number of times at the newborn outpatient clinic as the other symptoms evolved, yet the possibility of CH was not considered, until the macroglossia became quite obvious. It is clear therefore, that the absence of a 'typical facies' or gross macroglossia or remarkable global hypotonia or coarse skin and cry at birth or within the first week of life contributed to this delayed diagnosis. So did the Physician's low index of suspicion as the other symptoms evolved. Unachak et al[15] ,in Thailand, in their review of 48 cases of CH seen over a 13 year period found that when CH was diagnosed within the first 3 months of life, the commonest symptoms were neonatal jaundice (NNJ) lasting ≥ 14 days (100%), constipation (85%); typical facies of hypothyroidism

(62.5%), feeding problems (46%). They also Documented delayed diagnosis as follows: 62.5% were diagnosed after 1 year of age, 10.5% between 3 months and 1 year of age and 27% were diagnosed between 1 month to 3 months of life.Maternal thyroid status also contributes to delayed diagnosis of congenital hypothyroidism. This is because trans-placental transfer of maternal thyroid hormones to the foetus, as demonstrated by Contempre` B et al[3] and Vulsma et al[4], supplies the thyroid hormone requirements of the growing foetus. Thyroxin is critical for many aspects of brain development e.g. neurogenesis, neuronal migration, axon and dendrites formation, myelination, synaptogenesis and neurotransmitter regulation[15]. These requirements evolve over months and are most critical in the 2nd trimester[15]. Thyroxin (T_4) production in the foetus starts at about 12 weeks Gestational Age (GA), but only reaches significant levels at about 24 weeks GA. However, maternal T_4 still continues to supply part of foetal T_4 requirement till birth. Up to 30% of T_4 in cord blood is of maternal origin[4,9]. Where these fetal thyroxin requirements are not met, clinical features of hypothyroidism will be present in the neonate at birth. But where maternal thyroid hormones have compensated for the foetus' intrinsic thyroxin production deficiency, clinical features of hypothyroidism will be absent at birth and the infant will remain apparently normal for variable periods thereafter or become only mildly symptomatic sometime during infancy.

This may explain why our patient appeared normal at birth, and the highly suggestive macroglossia and marked global hypotonia slowly evolved over a period of 4 months. Our patient's mother seemed euthyroid and his 2 year old sister was quite normal. Where maternal hypothyroidism is not due to dietary I_2 deficiency or thyroid antibodies (TAB), both of which also affect the foetus, fetal thyroid hormone production may be normal and the effects of intrauterine thyroxin deficiency will be mild[15]. Neonatal screening programmes (TSH assay during the 1st week of life) have been successfully used in developed countries over the past three decades to facilitate early diagnosis of CH. Twenty percent of cases of CH may have normal TSH within the first week of life, but serial monitoring will reveal a progressive increase. This screening is however still too expensive to be carried out routinely in our environment. In resource poor countries, a clinical screening method called Neonatal Hypothyroid Index (NHI) has been proposed[1]. A score of > 3/13 selects children in whom TSH and T4 must be assayed. It is however unclear whether this NHI is applicable to preterms. The optimal post-natal age at which this clinical screening should be done is also Unclear.At 4 months of age our patient O.C. who was a term baby scored 9/13 but at the 2nd day of life scored 2.5/13 and 3.5/13 at one week of life if bowel movement once a day is taken as constipation in a neonate being fed with breast milk and infant formula. Constipation as an indicator in this NHI needs to be clearly defined with respect to patient's gestational age at birth and diet. There is also quite a wide range of "normal bowel habit" in neonates, the definition often referring to what is normal for the individual patient. NHI is an adaptable and sustainable health technology in developing countries. It is suggested therefore that a modified NHI be evolved and correctly used to screen all Nigerian newborns as soon after birth as possible to facilitate early diagnosis of congenital hypothyroidism. The government, NGO's and other charitable organisations can also fund routine screening of all neonates in some specialised centres.

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