



Recurrent Pericardial Effusion Associated with Hypothyroidism in Down Syndrome: A Case Report

Épanchement Péricardique Récurrente Associée à l'hypothyroïdie dans les Le Syndrome de Down: A Propos D'un Cas

M. U. Anah^{*†}, V. O. Ansa[‡], A. U. Etiuma[§], E. E. Udoh[†], E. O. Ineji[†], A. A. Asindi[†]

ABSTRACT

BACKGROUND: The complex of Down Syndrome-hypothyroidism-pericardial effusion is largely unreported in sub-Sahara.

OBJECTIVE: To present and highlight an unusual manifestation of hypothyroidism.

METHODS: A 16-year-old girl with confirmed Down Syndrome presented with complaints of generalised body swelling of eight months' duration. Her work-up consisted of full clinical and laboratory evaluation including ECG and echocardiography.

RESULTS: The patient was diagnosed of Down's Syndrome at birth but was lost to follow-up after at eight years of age. Body swelling was associated with clinical features of heart failure. Echocardiography showed massive pericardial effusion. Serum l-thyroxine was less than 0.5µg/dl and TSH >40iu/l. The heart failure and menstrual irregularities responded to l-thyroxine therapy.

CONCLUSION: This appears to be the first report of the complex of Down syndrome, hypothyroidism and pericardial effusion in a Nigerian child. Thyroid function test is therefore recommended as a part of baseline investigation for Nigerian children with Down syndrome as is the practice. *WAJM* 2011; 30(3): 210–213.

Keywords: Hypothyroidism, Pericardial effusion, Down syndrome, L-thyroxine therapy, Case report.

RÉSUMÉ

CONTEXTE: Le complexe du syndrome de Down-hypothyroïdie-épanchement péricardique est largement signalés en Afrique sub-saharienne.

OBJECTIF: présenter et mettre en évidence une manifestation inhabituelle d'hypothyroïdie.

MÉTHODES: Une jeune fille de 16 ans avec le syndrome de Down a confirmé présenté des plaintes du corps de gonflement généralisé de la durée de huit mois. Son travail a consisté en clinique complet et une évaluation en laboratoire, y compris l'ECG et l'échocardiographie.

RÉSULTATS: Le patient a été diagnostiqué du syndrome de Down à la naissance mais a été perdu au suivi après huit ans d'âge. Enflure du corps a été associée à des signes cliniques d'insuffisance cardiaque. L'échocardiographie a montré un épanchement péricardique massif. g / dl et TSHµL-thyroxine sérique était inférieure à 0,5 > 40iu / l. L'insuffisance cardiaque et les irrégularités menstruelles ont répondu à un traitement par L-thyroxine.

CONCLUSION: Cela semble être le premier rapport du complexe du syndrome de Down, l'hypothyroïdie et un épanchement péricardique chez un enfant nigérian. Test de la fonction thyroïdienne est donc recommandé dans le cadre de l'enquête de référence pour les enfants du Nigeria avec le syndrome de Down comme c'est la pratique. *WAJM* 2011; 30(3): 210–213.

Mots-clés: hypothyroïdie, épanchement péricardique, le syndrome de Down, la L-thyroxine rapport de cas de thérapie,.

INTRODUCTION

Thyroid disorders occur in patients with Down syndrome (DS) with hypothyroidism being more common than hyperthyroidism.¹⁻⁴ This necessitated the American Academy of Paediatrics to recommend routine screening for thyroid function in children with DS⁵ but such a policy does not exist in Sub-Saharan Africa.

The occurrence of pericardial effusion (PE) in patients with DS secondary to hypothyroidism is common but apparently infrequently reported in Africa.⁶⁻¹⁰ The effusion is known to resolve with thyroxine therapy.⁶⁻¹⁰ We report a case of recurrent PE in a child with DS as a first sign of hypothyroidism, which resolved on thyroxine therapy.

CASE REPORT

History

A 16-year-old female with Down syndrome (DS) was admitted into the paediatric ward of University of Calabar Teaching Hospital (UCTH), Calabar, of Southern Nigeria on February 9, 2007 with complaints of generalized body swelling that started with progressive abdominal distension, involving the feet and face of eight months duration, cough of six months duration with difficulty in breathing, easy fatigability, orthopnoea, and paroxysmal nocturnal dyspnoea. Her menarche was five months before presentation but had ceased. She had received all routine immunizations at infancy.

The child was born in UCTH at term to a mother and father whose ages were 36 and 44 years respectively at the time of delivery. Features of DS were apparent at birth and she was being regularly seen on outpatient clinic before being lost to follow-up from the age of eight years.

Physical Examination

On physical examination, the weight was 34kg, height 125cm, occipito-frontal circumference 48cm. She had facial puffiness and pedal oedema. She was not hypothermic and was alert. There was no lymphadenopathy or finger clubbing. The radial pulse rate was difficult to palpate but she had a heart rate of 96 beats per minute. The blood pressure was 90/60mmHg. The jugular venous pressure

was raised. The cardiac apical impulse was not visible and the apex beat was not felt. Heart sounds were muffled and distant. There was no heart murmur.

The liver was palpable eight cm below the right costal margin, firm, with a smooth surface and distinct border but non-tender. There was no demonstrable ascites.

Laboratory Evaluation

Laboratory tests revealed normal haemogram, liver function test, electrolytes and urea; haemoglobin genotype was AA (Table 1). The erythrocyte sedimentation rate was raised (57mm/hour, Westergren). HIV Screening was non-reactive and the Mantoux test was negative. A plain chest radiograph demonstrated cardiomegaly (Figure 1). A transthoracic echocardiographic examination demonstrated massive pericardial effusion (PE) measuring 32mm in the posterior A-V groove with the heart swinging in the fluid. No diastolic collapse of the right ventricle and right atrium was noticed and no structural defect was demonstrable in the heart. The electrocardiogram (ECG) showed low voltages.

The patient was treated with frusemide and spironolactone. On the

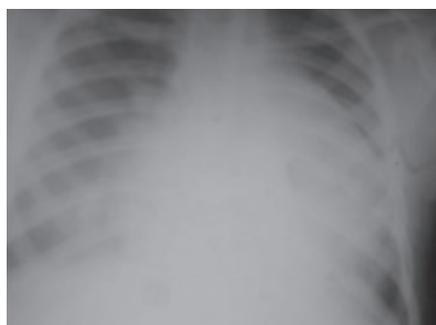
ninth day of admission, a pericardiocentesis was undertaken with 160 ml of straw-coloured fluid drained. The cytology of the fluid showed no malignant cells and the culture yielded no bacterial growth. Facilities for viral serology were not available in our centre. No biochemical analysis was done on the fluid. The patient consequently improved and was discharged home for follow-up. There was a gradual re-accumulation of the pericardial fluid on echocardiographic examinations done fortnightly. BCG vaccine administered for an accelerated reaction was negative. Thyroid function test (TFT) was requested but the parents could not readily pay for the test. She had to be readmitted because the PE had increased enormously three months after the first tap. She was found to be tachypnoeic with a respiratory rate of 34/min, cyanosed with swollen eyes, pulse rate was 64/min, BP 100/70 mm of Hg and the liver 10 cm below the costal margin, firm and tender. The jugular venous pressure was raised. The patient became lethargic but fully conscious. Echocardiography confirmed cardiac tamponade with diastolic collapse of the right ventricle. A second pericardiocentesis was therefore undertaken which yielded 625mls of straw-coloured fluid.

Table 1: Results of Haematological and Biochemical Investigations

	Normal Values	At Admission	3rd Month of Treatment	6th Month of Treatment
Haemoglobin	>12 g/dl	9.7	10.2	11.4
Leucocytes	5.9 X 10 ⁹	6.0	6.4	6.2
Lymphocytes	40%	51.0	57.0	55.0
Neutrophils	60%	45.0	38.0	42.0
Platelet	200-400	220.0	260.0	262.0
ESR	0-20mm/hr	57.0	30.0	20.0
Sodium	132-145mmol/L	139.0	140.0	140.0
Potassium	3.2-5.0 mmol/L	4.3	4.1	4.4
Creatinine	88.6-177 µmol/L	121.0	146.0	143.0
Urea	2.5-6.7 mmol/L	2.3	2.8	2.9
Bicarbonate	22-28 mmol/L	24.0	24.0	24.0
Proteins (Total)	62-82 g/L	61.0	77.0	77.0
Albumin	36-52 g/L	42.0	49.0	50.0
Globulin	18-36 g/L	19.0	28.0	27.0
Trio-Iodothyroxine	0.8-2.1 µg/dl	<0.4	1.2	1.9
L-thyroxine	4-12 µg/dl	<0.5	7.0	7.8
TSH	0.5-5.1 m/u/L	>40	4.7	4.8

Note: The urea, electrolytes and creatinine were of normal values. Thyroid function tests were first done on second admission.

The result of the TFT showed a very low thyroxine ($T_4 < 0.5 \mu\text{g/dl}$) and a very high thyroid stimulating hormone ($TSH > 40 \text{ mIU/l}$) levels confirming hypothyroidism. There was no facility to determine thyroid antibodies. She was commenced on levo-thyroxine $50 \mu\text{g}$ twice daily for 3 months and this was reduced to once daily when the TFT returned to normal (Table 1). Improvements in symptoms, normalization of chest radiograph (Fig. 1), ECG, TFT and echo (Fig. 2) were observed at 3 months of therapy. The menstrual periods became regular and the patient did not re-accumulate fluid. She is still on a regular follow up.



1A



1B



1C

Fig. 1: Chest X-rays of Patient. Massive Cardiac Shadow before Peri-cardiocentesis; Cardiac size before commencement of Thyroxine; reduced Cardiac size following three months of L-thyroxine.

DISCUSSION

Hormonal changes such as hypo/hyperthyroidism in association with DS are common but no clear cut explanation has been offered for this association. Hypothyroidism causes increased capillary permeability and subsequent leakage of proteins into the interstitial space resulting in pericardial effusion.⁶

Down Syndrome is a fairly common condition in Nigeria but to the best of our knowledge, hypothyroidism with PE as a complication has not been reported. This might have made the consideration of infective cause, probably tuberculosis comparatively high and that of the triple complex of DS-Hypothyroidism-PE low in the list of differentials in this patient. Endomyocardial fibrosis was excluded since our patient had a structurally normal heart though Croti *et al*¹¹ had reported inter-atrial communication with PE in Down Syndrome.

It is unlikely congenital hypothyroidism was the cause, because the signs would have presented earlier. In an observational study based on yearly follow-up of patients with DS for 25 years, Karlsson *et al*³ observed that acquired hypothyroidism was commoner after the age of eight years. The age of our patient being 16 years supports the possibility of an acquired type.

Hypothyroidism and DS tend to share the same clinical features hence both conditions can be confused. A history of menstrual irregularity was admitted but this was not linked to hypothyroidism since they could have other causes. Short stature, hypotonia and mental retardation are features common to both conditions.^{12,14}

Our patient had pitting pedal oedema with no clear cut features of myxedema. This was attributed to cardiac failure. Unexpectedly, the pulse rates and the blood pressure were normal but these have been reported by others.^{6,7} Bradycardia and low BP are expected in hypothyroid patients.¹⁴ The pericardial fluid was straw-coloured similar to that seen in tuberculosis as against the typical yellow and opalescent fluid of PE due to hypothyroidism called "Gold Paint" effusion. This is attributed to the fibrin, red blood cells, lymphocytes, proteins and cholesterol content of the fluid. We

did not analyse the fluid.

Our patient had cardiac tamponade before the second pericardiocentesis, a complication known to be rare in this triple complex.^{6,10} Hypothyroidism usually causes slow accumulation of fluid in the pericardium thus allowing for the distensibility of the pericardium to cope adequately. This was not the case with this patient; there was rapid re-accumulation of fluid as the amount (625ml) drained was quite voluminous. Toorians and van Ekelon⁸ had observed a similar rapid re-accumulation of fluid within eight weeks following pericardiocentesis in their patient. No explanation has been advanced for this rapid re-accumulation of pericardial fluid. However, close monitoring and early commencement of thyroxine have been



Fig. 2: Echo demonstrations of Pericardial Effusion. Showing massive PE measuring 32mm but reducing after pericardiocentesis and thyroxine therapy.

shown to reduce this recurrence^{6,9} as was the case with our index patient who did not re-accumulate fluid after commencement of thyroxine.

There is no policy on the screening for thyroid disorders in patients with DS in Africans since hypothyroidism in DS is reported to be rare even among African Americans.¹² The American Academy of Paediatrics policy on routine screening led to increased detection and treatment of hypothyroidism in children with DS.¹² Our patient would have benefitted if there was a policy in place.

In conclusion, this case report is an eye opener to the issue that this triple complex of DS, hypothyroidism and PE may not be rare among Nigerian children. A close monitoring of all DS children for early signs of hypothyroidism and a policy on the routine screening for thyroid disorders in patients with DS are advocated.

REFERENCES

- Gibson PA, Newton RW, Selby K, Price DA, Leyland K, Addison GM. Longitudinal study of thyroid function in Down's syndrome in the first two decades. *Arch Dis Child*. 2005; **90**: 574–57.
- Graneiro de Papendieck L, Chlesa A, Bastida MG, Alonso G, Finkielstain G, Heinrich JJ. Thyroid dysfunction and high thyroid stimulating hormone levels in children with Down syndrome. *J Pediatr Endocrinol Metab*. 2002; **15**: 1543–1548.
- Karlsson B, Gustafsson J, Hedov G, Ivarsson S.A, Anneren G. Thyroid dysfunction in Down's syndrome: relation to age and thyroid autoimmunity. *Arch Dis Child* 1998; **79**: 242–245.
- Selikowitz MA. A five-year longitudinal study of thyroid function in children with Down syndrome. *Dev Med Child Neurol*. 1993; **35**: 396–401.
- American Academy of Pediatrics, Committee on Genetics. Health supervision for children with Down syndrome. *Pediatrics* 2001; **107**: 442–449.
- Werder EA, Torresani T, Navratil F, Arbenz U, Eiholzer U, Pelet B, Burri M, *et al*. Pericardial effusion as a sign of acquired hypothyroidism in children with Down syndrome. *Euro J Pediatr*. 1993; **152**: 397–8.
- Said S, Droste H, Derks S, Fast J. Down syndrome associated with hypothyroidism and chronic pericardial effusion: echocardiographic follow-up. *Neth Heart J*. 2007; **15**: 67–70.
- Toorians AWFT, Van Ekelen WAAJ, Recurrent pericardial effusion with a common clinical disorder. *Neth J Med*. 2007; **65**: 192–194.
- Dinleyici EC, Ucar B, Kilic Z, Dogruel N, Yazar C. Pericardial effusion due to hypothyroidism in Down syndrome: report of four cases. *NeuroEndocrinol Lett* 2007; **28**: 141–144.
- Bereket A, Yang TF, Dey S, Blether SL, Biancanello TM, Wilson TA. Cardiac decompensation due to massive pericardial effusion: a manifestation of hypothyroidism in children with Down syndrome. *Clin Pediatr* 1994; **33**: 749–751.
- Croti UA, Braile DM, Bodini AL, Moscardini AC. Interatrial communication and hypothyroidism in patient with Down syndrome. *Rev Bras Cir Cardiovasc* 2007; **22**: 515–516.
- Aoki Y, Belin RM, Clickner R, Jeffries R, Philips L, Mahaffey, RR. Serum TSH and total T₄ in the United States population and their association with participant characteristics. National Health & Nutrition Examination Survey (NHANES 1999–2002). *Thyroid* 2007; **17**: 1211–1223.
- Carroll KN, Arbogast PG, Dudley JA, Cooper WO. Increase in incidence of medically treated thyroid disease in children with Down syndrome after rerelease of American Academy of Pediatrics Health Supervision Guidelines. *Pediatrics* 2008; **122**: e493–2498.
- Hunter I, Greene SA, MacDonald TM, Morris AD. Prevalence and aetiology of hypothyroidism in the young. *Arch Dis Child* 2000; **83**: 207–210.