Down syndrome associated with hypothyroidism and chronic pericardial effusion: echocardiographic follow-up

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We present a 39-year-old male patient with Down syndrome who was evaluated for fatigue, palpitations and bouts of cyanosis. Physical examination showed features of trisomy-21 (Down syndrome), with a slow pulse rate, distant cardiac sounds and absent apex beat. He had normal jugular venous pressure without pulsus paradoxus. The ECG showed QRS microvoltage and flattened P and T segments. The 48-hour ambulatory ECG depicted normal sinus rhythm with intermittent short PR interval without tachyarrhythmias. The chest X-ray revealed cardiomegaly without pulmonary venous congestion. Although serial transthoracic echocardiographic examination demonstrated pericardial effusion with features of tamponade, there were no overt signs of clinical cardiac tamponade. Biochemically, the serum thyroxine of 3 pmol/l (normal 10 to 25) and thyroid-stimulating hormone of 160 mU/l (normal 0.20 to 4.20) were compatible with hypothyroidism. The patient was treated with L-thyroxine sodium daily, which was gradually increased to 0.125 mg daily. Within a few months he lost weight and became more alert; furthermore, the symptoms of hypothyroidism and the pericardial effusion resolved. It can be concluded that Down syndrome may be associated with hypothyroidism and pericardial effusion. These were alleviated following hormone replace-

ment. Regular evaluation of thyroid function tests is important in Down syndrome. (*Neth Heart J* 2007;15:67-70.)

Keywords: Down syndrome, pericardial effusion, hypothyroidism, hormone replacement therapy

At the beginning of the last century, the pathological association between Down syndrome and thyroid disorders was described by Bournville.¹ However, both hypothyroidism² and hyperthyroidism³ have been reported.^{2,3} The prevalence of hypothyroidism in Down syndrome is estimated at 0.12%.⁴ Hypothyroidism is the commonest form of thyroid disorder to be associated with Down syndrome.

Reports of cases with Down syndrome, hypothyroidism and pericardial effusion have been published earlier.⁵ Clinical and serial echocardiographic follow-up in a case of Down syndrome associated with severe hypothyroidism and accumulation of a large amount of pericardial effusion is presented here.

Case report

A 39-year-old man with Down syndrome was evaluated for fatigue, palpitations and bouts of cyanotic lips. His previous medical history included disintegration treatment for bilateral kidney stones. In 1992 he was investigated for palpitations and found to have pre-excitation syndrome.

On physical examination he had a typical Down syndrome appearance. His pulse rate was slow and regular (56 beats/min) and blood pressure was 100/60 mmHg. The jugular venous pressure was not elevated. The cardiac apical impulse was not visible. The apex beat was not felt. On auscultation, the heart sounds were distant. He had no murmur or pericardial rub. There were a few rhonchi at both the lung bases. There was no peripheral oedema or signs of pulsus paradoxus. He had no signs of celiac disease.

The 12-lead ECG (figure 1) depicted sinus bradycardia (57 beats/min), low QRS voltage with flat P

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Figure 1. (A) The ECG prior to hormone replacement depicting sinus bradycardia with low voltage QRS complexes, flattened P and T segments and prolonged QTc and (B) after hormone replacement showing normalisation of the parameters.

and T waves in the standard and precordial leads, right-axis deviation and right bundle branch block. The QT interval measured 482 ms and QTc 469 ms. Follow-up ECG revealed normalisation of heart frequency (75 beats/min), QRS voltage and QTc interval (409 ms).

Chest X-ray illustrated overt cardiomegaly with a cardiothoracic ratio of 0.67 without pulmonary venous congestion or pleural effusion. Pulmonary embolism was excluded.

Laboratory tests revealed a normal haemogram, liver parameters and electrolytes. The creatinine value was slightly elevated at 134 $\mu\text{mol/l}$ (normal 70 to 110). Serum thyroxine (T_4) level was decreased at 3 pmol/l (normal 10 to 25) and the thyroid-stimulating hormone level (TSH) was increased up to 160 mU/l (normal 0.20 to 4.20). Both were compatible with hypothyroidism. Thyroid autoantibodies were not determined.

Transthoracic echocardiography demonstrated a 'swinging heart' with normal-sized and normokinetic right and left ventricles, a large amount of pericardial effusion (PE) in the anterior and inferior recesses (figure 2) and trivial mitral, tricuspid and aortic regurgitation. Furthermore, features of tamponade such as late diastolic right atrial and early diastolic right ventricular collapse were recorded. Serial echocardiography demonstrated a gradual decrease in the pericardial effusion. Infectious diseases were ruled out.

Ambulatory 48-hour ECG showed normal sinus rhythm with a mean heart rate of 61 beats/min. A short PR interval was intermittently registered. No tachyarrhythmias or extra systoles were seen. He had no bouts of cyanosis during the registration.

The patient was treated with L-thyroxine sodium daily, which was later gradually increased to 0.125 mg daily. Within a few months, he lost more than 25 kg,

Figure 2. (A) Transthoracic echocardiography demonstrated normal-sized and normokinetic right and left ventricles, a large amount of pericardial effusion in the anterior and inferior recesses and (B) after treatment demonstrating a decrease of pericardial effusion.

became alerter, and the symptoms of fatigue and the cyanotic episodes disappeared. Furthermore, the amount of PE had decreased significantly.

Discussion

Down syndrome (Trisomy 21) is the most common chromosomal disorder. In general, it has an incidence of 1 in 750. The incidence of hypothyroidism in Down syndrome is high, but the diagnosis is often delayed or missed for lack of specific clinical clues.⁶ This was the case in our current patient. In a large study of congenital hypothyroidism in neonates with Down syndrome, a prevalence of 0.12% was found.⁴

It has been reported that pericardial effusion is common in hypothyroidism. There is a high incidence between foetal isolated pericardial effusion and trisomy 21.^{7,8}

It has been observed that massive pericardial effusion (PE) in hypothyroid children with Down syndrome completely resolved with medical treatment without pericardiocentesis.^{5,9} This was accomplished in our case; serial echocardiographic examinations documented the decrease in PE.

The rarity of cardiac tamponade in Down patients with hypothyroidism and pericardial effusion is attributed to the slow accumulation of fluid and the remarkable distensibility of the pericardium. Oliver et al. have suggested that the quantity of accumulated pericardial fluid and aetiopathogenetic mechanisms influence the QRS voltage.¹⁰

Hypothyroidism is associated with increased capillary permeability and subsequent leakage of proteins into the interstitial space, resulting in pericardial effusion; however, tamponade is rare.¹¹

The ECG is initially used in patients suspected of having a PE. The electrocardiographic characteristics recognised in PE include low QRS voltage, PR-segment depression, ST-segment elevation, T-wave changes and electrical alternans.¹² In our patient, the

initial ECG manifested low voltage with flat P and T waves during the severe hypothyroidism phase. These changes reverted to normal after thyroid hormone replacement. Incomplete and complete right bundle branch block has been reported in hypothyroidism,¹¹ as was the case in the present patient.

Genetically, Down syndrome accounts for about 5% of patients with congenital heart defects. The number of patients with congenital heart disease and chromosomal anomalies in a newborn population is estimated to be higher at 6 to 10%.¹³ Also of notice is the frequent association between Down syndrome and complete atrioventricular septal defect. In the current case, no congenital cardiac anomalies were detected by echocardiograph.

In a recent study of 86 children without congenital cardiac malformations published by Concolino et al., mild and moderate pericardial effusion was found in 28% of Down syndrome versus 2% of control subjects and four out of 24 patients had hypothyroidism.¹⁴

In view of the above-mentioned findings children and adults with Down syndrome should regularly be tested for thyroid hormone status and undergo echocardiographic screening. Thyroid-stimulating hormone (TSH) measurement appears crucial for diagnosis and treatment.

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