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Brief Report

Prolonged mechanical ventilation associated with hypothyroidism after paediatric cardiac surgery

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Abstract Hypothyroidism in patients undergoing congenital heart defect surgery is known to be possible. This generally temporary condition can progress as it involves yet other factors, increasing the patients' time to heal. The case presented here is that of a 5-month-old girl who was dependent in the long term on mechanical ventilation following cardiac surgery. After having been diagnosed with hypothyroidism, she was extubated on the fourth day of her hormone replacement therapy, and discharged from hospital on the tenth day.

Keywords: Hypothyroidism; prolonged mechanical ventilator support; paediatric cardiac surgery; congenital heart disease

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HYPOTHYROIDISM MAY BE OBSERVED AFTER paediatric cardiac surgery or during hospitalisation in paediatric cardiac intensive care. Acute hypothyroidism can occur in patients with compensated primary hypothyroidism because of surgical stress, and this can delay the healing process by causing cardiac and respiratory dysfunction during prolonged hospitalisation. Hypothyroidism may often be missed because its manifestations can be very similar to those of cardiac failure.[1–3]

Although hypothyroidism is known to be one of the causes of ventilator-dependent respiratory failure, it is uncommon. Differential diagnoses for failure to wean from respirator dependency include impaired ventilator drive, pleural effusion, alveolar hypoventilation, weakness of respiratory muscles and diaphragm dysfunction.[4,5]

Case report

An anastomosis of the hypoplastic main pulmonary artery to the ascending aorta – end-to-side – was performed under cardiopulmonary bypass in a 5-month-old girl with ventricular septal defect and hypoplastic confluent intrapericardial pulmonary arteries. The child could not be kept extubated longer than 72 hours on any of the five extubation attempts between day 4 and 26 after the initial surgery. Pulmonary overflow was considered as a cause, and on post-operative day 39 major aorto-pulmonary collateral arteries were surgically ligated. Following the ligation, three extubation attempts – on days 3, 8 and 10 – were also unsuccessful. On the sixth day after the ligation, generalised oedema, pleural and pericardial effusions, and ascites were observed. The patient's condition was attributed to heart failure, and thus inotropic support (dopamine, 5 μg/kg/min and milrinone, 0.5 μg/kg/min) was started. On the same day, thoracentesis was performed on the right hemithorax, and the diuretic doses were increased. After regression of effusions and the ascites, the occurrence of a non-pitting pretibial oedema led us to investigate the thyroid function. The thyroid-stimulating hormone level was 79.2 mU/ml (normal value 0.4–5.0) and free T4 was 0.6 ng/dl (normal values 0.9–2.6), and these levels were 8.5 mU/ml and 1.1 ng/dl, respectively, before the first surgery. L-thyroxine treatment was

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started at a dose of 10 μg/kg/day on post-operative day 13 after ligation. The patient was evaluated with the diagnosis of subacute/primary hypothyroidism, now manifested by the stress of surgery. The patient had not received thyroid hormone replacement therapy previously. She was extubated on the fourth day of her hormone replacement therapy – 56 days after her first surgery and 17 days after the second. The patient's general condition improved under thyroid hormone substitution and she was discharged 10 days after starting of the treatment. Her thyroid gland was in its proper location at ultrasound and the dimensions were compatible to her age. The diagnosis was considered "dyshormonogenesis" according to thyroid function tests, which were remained in normal limits under treatment.

Discussion

Cardiac insufficiency, sedative drug administration, renal failure, malnutrition and hypothyroidism are among the conditions leading to prolonged mechanical ventilation.[5] The first reason considered for our patient's ventilator dependency was pulmonary overflow, and thus major aortopulmonary collateral artery ligations were performed. However, ventilator dependency continued. She could not be weaned off ventilator support even though other possible causes such as infection, electrolyte imbalance, pleural or pericardial effusion, and heart failure had also been corrected or ruled out. High thyroid-stimulating hormone level at the renewed thyroid function tests led us to think about primary hypothyroidism.

Transient secondary hypothyroidism is known to occur in paediatric cases after cardiac surgery. This condition is related to stress on the hypothalamic–pituitary–thyroid axis.[1,2,6] Long-term intensive care stay and the drugs used during it may also cause the development of hypothyroidism.[1,3] Therefore, using cardiopulmonary bypass, the long-term intensive care follow-up and the use of many different drugs also were risk factors for this patient. Differently from reported cases, however, primary hypothyroidism was found in our patient, with a very high thyroid-stimulating hormone level.

Although hypothyroidism is known as a cause of respiratory failure, it is not a frequent cause of failure to wean from ventilator. None of the four cases reported by Pandya had clinical hypothyroidism; this was a finding during the investigation of neurological and cardiac problems.[4,5] According to Datta and Scalise, the incidence of hypothyroidism in patients who received mechanical ventilation was 3% and they recommended keeping it in mind in all cases of failure to wean, as this cause of failure is treatable.[4]

Clinical consequences of hypothyroidism, such as prolonged mechanical ventilation, heart failure, ascites, pleural effusion and oedema, were not attributed to hypothyroidism in the presented case; they were considered to be consequences of heart failure. With regard to whether these dysfunctions are a result of excessive cardiac load or whether they are at least partly due to the thyroid hormone insufficiency by itself is an open debate. [3] In our patient, the presence of myxoedema, which is a "non-pitting" oedema that is similar to hypothyroidism, following recovery of heart failure led us to control the thyroid function tests. "Non-pitting" oedema for hypothyroidism is different from oedema that is caused by fluid overload. In fluid overload, oedema is referred to as "pitting" when the indentation persists for some time after the release of the pressure, but when the indentation does not persist, "non-pitting", it is a finding of hypothyroidism.

Thyroid dysfunction may occur through various mechanisms. Anti-thyroid drugs such as amiodarone, dopamine or excessive iodine exposure are among the most common causes of hypothyroidism.[6–8] Drugs or a deficiency of thyroxin-binding globulin are the first suspects in the case of hypothyroidism developing in a patient with normal thyroid function.[7,8] The patient presented here had high levels of thyroid-stimulating hormone and low free T4 levels. Low T4 levels were against a diagnosis of a thyroid-stimulating hormone elevation because of a lack of thyroxin-binding globulin as a result of protein loss in ascites and pleural fluid. Hypothyroidism following thyrotropin-releasing hormone deficiency as a consequence of hypothalamic insufficiency, which can be caused by dopamine or other drugs, seemed improbable because of our patient's very high thyroid-stimulating hormone level.

It is known that long-term dopamine therapy can cause iatrogenic hypothyroidism.[9] However, in our patient, very high thyrotropin level following 14 days of dopamine treatment eliminated the possibility of drug-induced hypothyroidism. Hypothyroidism resulting from excessive iodine exposure was also discarded because of the fact that the patient's thyroid hormone substitution treatment is still continuing 8 months after her surgery.

Thyroid dysgenesis, similar to thyroid hypoplasia and ectopic thyroid, can occur following surgery in a decompensated situation. Thyroid dysgenesis was not in differential diagnosis in our patient because of the normal localisation and the size of thyroid gland according to ultrasonography. In addition, decreased T4 synthesis, depending on deficiency of congenital hormone production and efficacy, may be responsible for congenital hypothyroidism[7,10] – inborn errors of thyroid hormone synthesis also

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called dyshormonogenesis. Dyshormonogenesis is a result of various aetiologies including thyroid-stimulating hormone unresponsiveness, defects in trapping, oxidation, organification, and coupling of iodine, and iodotyrosine deiodinase deficiency. Most commonly, dyshormonogenesis is due to defects of thyroid peroxidase activity. Other causes of dyshormonogenesis include Pendred's syndrome, mutations in the enzyme dual oxidase 2, defects in sodium/iodide transport or thyroglobulin action, and defect in the enzyme iodotyrosine deiodinase.[7–9,11] Usually, the diagnosis of dyshormonogenesis is possible with the elimination of other reasons of congenital hypothyroidism.[7,10]

Pre-operatively, our patient's free T4 level was within the normal age ranges and her thyroid-stimulating hormone level was elevated – subacute, compensated hypothyroidism – late-onset dyshormonogenesis was the first-line diagnosis.

Our purpose in presenting this case is to underline the fact that subacute/primary hypothyroidism may become manifest and its clinical manifestations may be missed, as such manifestations are often confused with those of heart failure. Thyroid function tests can help to identify this condition, which is an easily treatable dysfunction in patients following surgery for congenital heart disease, especially if the patients have had prolonged intensive care.

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