Reminder of important clinical lesson

Respiratory failure was improved by growth hormone substitution in a patient with hypopituitarism

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Summary

A 33-year-old man was referred to the Department of Respiratory Medicine in our hospital due to severe hypercapnic respiratory failure in March 2008. His respiratory function test showed severe restrictive pulmonary dysfunction, and respiratory muscle strength assessed by measuring maximal static expiratory and inspiratory mouth pressures was severely impaired. After non-invasive positive pressure ventilation was started, he was referred to the Endocrinology Department as he was diagnosed as hypopituitarism in his childhood. Pituitary MRI demonstrated pituitary stalk agenesis, and hormonal examination showed that he had severe growth hormone (GH) deficiency. GH replacement therapy was started in August 2008 and his arterial blood gas values and respiratory muscle strength were improved in 6 months. The current case demonstrated that GH deficiency could be a cause of severe respiratory failure.

BACKGROUND

Chronic respiratory failure is defined as an abnormal state in which the human body cannot perform normal vital functions because of abnormal arterial blood gas values for O₂ and CO₂ resulting from abnormal gas exchange in the lung.¹ Home oxygen therapy and non-invasive positive pressure ventilation (NPPV) are indicated to improve survival and quality of life in these patients.² While chronic lung diseases such as chronic obstructive pulmonary diseases and sequelae of pulmonary tuberculosis are major causes of chronic respiratory failure, the underlying diseases are not clear in some cases.¹ On the other hand, it is also suggested that deficits of some hormones such as thyroid hormone and growth hormone (GH) could lead to respiratory dysfunction.³

CASE PRESENTATION

A 33-year-old man was referred to our hospital due to severe hypercapnic respiratory failure on 13 March 2008. His height was 164 cm and body weight was 74 kg. Blood pressure was 97/58 mm Hg. Results of blood gas analyses were pH 7.288, PO₂ 40.6 mm Hg and PCO₂ 82.2 mm Hg. In his childhood, he was diagnosed with hypopituitarism and had received hormone replacement therapy (GH, levothyroxine, testosterone propionate), which he discontinued in his 20s except for levothyroxine. He had no other past history of note.

INVESTIGATIONS

Respiratory function test showed severe restrictive pulmonary dysfunction (forced vital capacity 890 ml; forced expiratory volume in 1 s 880 ml). Respiratory muscle strength was assessed by measuring maximal static expiratory (PE_{max}) and inspiratory (PI_{max}) mouth pressures, both of which were severely impaired (PE_{max} 57.5 cm H₂O; PI_{max}

36.2 cm H₂O). Muscle MRI detected no abnormal signal and neuromuscular diseases were not suspected. Sleep apnoea syndrome was not found by apnomonitor test. After NPPV was started, he was discharged in April 2008. He was referred to the Endocrinology Department in June 2008. MRI, as shown in figure 1, revealed pituitary stalk agenesis. Fasting plasma hormone levels were as follows: GH 0.07 ng/ml, insulin-like growth factor 1 59.0 ng/ml, luteinising hormone (LH) undetectable, follicle-stimulating hormone (FSH) undetectable, testosterone 0.13 ng/ml, adrenocorticotrophic hormone (ACTH) 22 pg/ml, cortisol 8.9 µg/dl, thyroid-stimulating hormone (TSH) 1.08 µU/ml, F-T3 3.12 pg/ml, F-T4 1.31 ng/dl. While plasma levels of ACTH increased in response to corticotropin-releasing hormone (baseline: 23 pg/ml, at 30 min 56 pg/ml), urinary excretion of free cortisol was low (18.6 µg/day). Plasma levels of GH and LH/FSH did not increase in response to growth hormone-releasing peptide-2 (GHRP) and luteinizing hormone-releasing hormone (LHRH), respectively (data not shown).

TREATMENT

While multi-hormone replacement therapy was recommended, the patient agreed to only somatropin substitution, which was started in August 2008. After obtaining later agreement, the substitution of testosterone enanthate and hydrocortisone replacement was started in March 2009 and in July 2009, respectively.

OUTCOME AND FOLLOW-UP

After discharge in April 2008, PO₂ ranged between 75.9 and 85.0 mm Hg, and PCO₂ ranged between 46.9 and 47.9 mm Hg until August 2008 when GH substitution started. GH therapy for 6 months increased PO₂ to 93.1 mm Hg while it

Figure 1 MRI of pituitary. Arrow indicates pituitary stalk agenesis.

decreased PCO_2 to 43.5 mm Hg (figure 2). Addition of testosterone or hydrocortisone showed no apparent additional effects on respiratory function. Respiratory muscle strength, assessed by the ratio of PE_{max} and PI_{max} , was increased after substitution of hormones (figure 3).

DISCUSSION

It is suggested that severe hypothyroidism could result in respiratory failure in some cases.^{3 4} The respiratory muscle strength is reportedly weakened in hypothyroidism and the weakness seems to be proportional to the degree of thyroid dysfunction.⁵ However, this is not the case in our patient as the plasma levels of thyroid hormones were within normal ranges with hormone substitution when he was diagnosed as respiratory failure. On the other hand, it is also reported that adult patients with GH deficiency showed moderate impairment of ventilatory function⁶ and that GH replacement therapy reversed that function.⁷ While it has been postulated that respiratory dysfunction in patients with GH deficiency might be due to weakened respiratory muscle strength and a reduction of lung volumes,⁷ there are no reports, to our knowledge, showing that GH deficiency

resulted in severe respiratory failure as in our case. In treating patients with hypopituitarism, it is common practice to substitute hydrocortisone or testosterone, if necessary, before starting GH replacement. However, in our case, the patient refused replacement of hydrocortisone or testosterone at first and we substituted GH first. This resulted in an improvement of respiratory function, suggesting that a GH deficiency caused the respiratory dysfunction. As the ratio of PE_{max} and PI_{max} , which reflects the respiratory muscle strength,⁷ increased after the hormone therapy, it is possible that the improvement in respiratory function was due to increases in respiratory muscle strength. It is unclear whether deficits of glucocorticoids and androgens could affect respiratory function.³ In our case, the addition of hydrocortisone and testosterone had no apparent effects on respiratory function, although we cannot exclude the possibility that replacement of these hormones contributed to the maintenance of improved muscle strength. While patients with hypopituitarism may not often have respiratory dysfunction, our case report suggests that we should examine pituitary hormones, including GH, when the cause of chronic respiratory dysfunction is not clear.

Figure 2 Respiratory function in relation to changes in hormone levels. Changes in IGF-1 (A), testosterone (B), PO₂ (C) and PCO₂ (D) during substitution of hormones are shown.

Figure 3 Changes in respiratory muscle strength assessed by PE_{max} and PI_{max}. Substitution of hormones increased both PE_{max} and PI_{max}.

Learning points

- ▶ GH deficiency could cause severe respiratory failure.
- ▶ Substitution of GH could reverse respiratory function.
- ▶ It is important to check the levels of pituitary hormones when the cause of respiratory dysfunction is not clear.

Competing interests None.

Patient consent Obtained.

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