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Case Report

Hypocortisolism induces chronic respiratory failure

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ABSTRACT

Hypocortisolism is an uncommon condition. Its association with myopathy and respiratory failure has only rarely been described. We report the case of a 52 year-old woman presenting with progressive dyspnoea. Work-up revealed a severe restrictive syndrome with hypoxaemia. Further investigations showed hypocortisolism of pituitary origin. Response to hydrocortisone allowed us to conclude to an unusual case of hypocortisolic myopathy affecting the respiratory muscles.

Educational aims

- To stimulate awareness of the potential impact of an acquired myopathy on respiratory function.
- To stimulate awareness of the potential impact of endocrine diseases on respiratory muscles.
- To incite caution in the prescription and withdrawal of corticoid therapy in patients with a history of pituitary surgery.
- To promote screening of subclinical myopathies in patients with borderline respiratory function in an attempt to find curable causes of respiratory deterioration.

1. Case report

A 52 year-old woman was hospitalized with progressive grade III dyspnoea. The disorder began as a dry cough that became productive with yellow sputum ten days prior to admission. Over the past 8 months, she had presented vomiting, weight loss, asthenia and anorexia.

Her clinical history revealed trans-sphenoidal surgery for a large intra-sellar arachnoid cyst, hypothyroidism due to Hashimoto thyroiditis, mild type 2 diabetes mellitus, and arterial hypertension. The patient was a non-smoker and had never suffered from a respiratory or atopic disease.

Her medication included levothyroxine, metformin (850 mg 3x/day), bumetanide (5 mg/day) and a combined pill with 10 mg of bisoprolol and 25 mg of hydrochlorothiazide for hypertension.

Clinical examination revealed no pyrexia. Blood pressure was 150/50 mmHg and heart rate averaged 104 beats per minute. Haemoglobin saturation without oxygen supplementation reached 92% and respiratory frequency was 20 per minute. Cardiac auscultation was normal. Auscultation of the lungs disclosed symmetrical ventilation with bilateral posterior-basal crackles.

Baseline blood tests (Table 1) showed hyponatraemia, hypokalaemia and an inflammatory syndrome with hyperleukocytosis. Arterial blood gases underlined severe hypoxia (PaO^2 56 mmHg) associated with moderate hypercapnia ($PaCO^2$ 48.8 mmHg). The chest radiograph was normal. However, thoracic CT-scan outlined multiple ground glass infiltrates of pseudo-nodular aspect, mainly in the sub-cortical regions of the middle and lower right lobes.

Cardiac evaluation (ECG, trans-thoracic echocardiography and stress echocardiography) was normal. Ventilation–perfusion scintigraphy excluded a pulmonary embolism. Bronchoscopy, broncho-alveolar lavage and tracheo-bronchial aspiration did not provide any valuable information. Pulmonary function tests demonstrated a restrictive syndrome (total lung capacity: 65% of predicted values) with normal alveolar-capillary diffusion. Ergospirometry disclosed major fatigue in the lower limb muscles and arterial oxygen desaturation. Lastly, after six days with antibiotic therapy, a thoracic CT-scan showed a regression of the infiltrates.

To exclude a neuromuscular disease electromyography (EMG) of the lower limbs was performed but was absolutely normal. Muscle

Abbreviations: ACTH, adrenocorticotropic hormone; CT, computed tomography; ECG, electrocardiogram; EMG, electromyogram.

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Table 1
Comparison of laboratory parameters before and after hydrocortisone therapy.

	Normal values	Before hydrocortisone	After hydrocortisone
Natremia	135–145 mmol/L	130	145
Kalemia	3.1–4.9 mmol/L	2.8	4.6
pH	7.35–7.45	7.53	7.51
pCO_2	35.0–43.0 mmHg	48.8	43.0
PO_2	65–100 mmHg	56	95
TSH	0.20–4.20 μIU/mL	0.11	0.53
Free T3	1.5–4.6 pg/mL	1.9	2.3

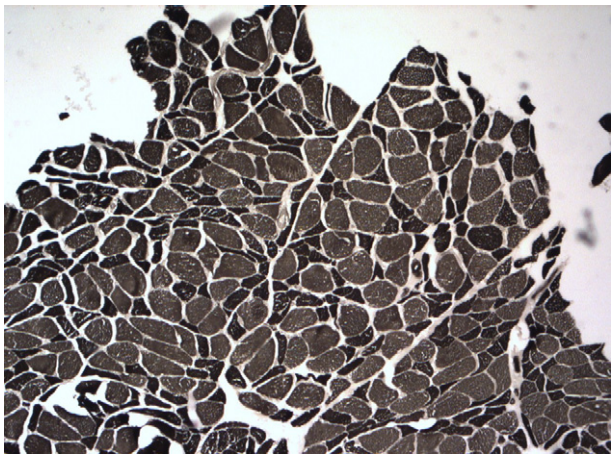

Fig. 1. Biopsy slides (Optical microscopy x50). The histo-enzymologic staining for ATPase. Type 1 (slow-twitch) fibres appear in a lighter shade than the type 2 (fast-twitch) fibres.

enzymes and myoglobin were also in the normal range. Biopsies in the quadriceps and intercostal muscles (Fig. 1) were performed. They showed a mild amyotrophy of non-specific aspect, especially of type II fibres.

The possibility of an endocrine myopathy was brought up given the non-specific aspect of the biopsy and other unaccountable elements. The excision of a supra-sellar arachnoid cyst and recent clinical presentation suggested adrenal insufficiency. Hyperkalaemia was probably absent because, in adrenal insufficiency of pituitary origin, aldosterone levels are not lowered like in primary adrenal insufficiency.[1] Moreover, vomiting and treatment with both a loop diuretic and hydrochlorothiazide could explain further potassium losses. To support this hypothesis, morning cortisolaemia (8 am) was measured and proved to be drastically reduced at 34 μg/L (N: 100–250) along with a decreased level of ACTH at 13 ng/L (N: 10–70).

Our diagnosis is an endocrine myopathy due to secondary hypocortisolism. Our assumption is that, in the context of pituitary surgery, a late exhaustion of the corticotropic cells was revealed by an infectious state. This diagnosis was supported by the rapid and remarkable improvement following hormonal supplementation. Indeed, the restrictive syndrome and hypoxaemia regressed in only six days of intravenous hydrocortisone therapy (300 mg/24 h). After 6 months, total lung capacity had increased to 92%.

2. Discussion

Upon suspicion of a neuromuscular respiratory disease, the maximal inspiratory and expiratory pressures should be measured.[2,3] Thereafter, the EMG and a muscle biopsy are warranted to confirm a muscular disorder.[2] Nonetheless, one cannot expect to yield pathognomonic information pertaining to hypocortisolic myopathy from these investigations. In fact, the diagnosis of endocrine myopathy is suggested by a normal EMG and a non-specific muscle biopsy. It is however possible to observe an amyotrophy, especially of type II fibres, on the muscle biopsy.

As to the diagnosis of secondary hypocortisolism, it will be highly suspected if morning cortisol and ACTH are concomitantly decreased.[4] The insulin tolerance test is the gold standard to ascertain the diagnosis.[4,5]

3. Conclusion

This case is an exemplary illustration of the impact of subclinical endocrine or metabolic disturbances on the respiratory muscles. It is indeed astonishing to witness the complete reversal of the syndrome under hydrocortisone therapy. Screening and treatment of such abnormalities could greatly enhance respiratory muscle function in patients that suffer from chronic respiratory disease in whom no other therapeutical options are available.

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Contributors

Charles Pirlet: Medical student; main author. Emmanuel Beck MD; physician responsible for in-hospital management of the patient in the case report; second author. André J. Scheen MD, PhD; senior endocrinology consultant; supervision and overview of the article. Bernard Duysinx MD, PhD; senior consultant in pulmonary medicine; supervision and overview of the article. Jean-Louis Corhay MD PhD; senior consultant in pulmonary medicine; supervision and overview of the article.

Conflict of interest

The authors have no conflicts of interest to declare.

Appendix. CME questions

- A normal muscle biopsy and a normal EMG exclude the possibility of an endocrine myopathy? (False)
- Concomitantly low levels of ACTH and cortisol confirm the diagnosis of secondary hypocortisolism? (False)
- Hyperkalaemia associated with hyponatraemia, a classic biological finding of primary hypoadrenalism, is uncommon in secondary hypocortisolism because aldosterone secretion is normal? (True)
- Diagnosis of the contribution of a neuromuscular disorder to a restrictive syndrome is based on maximal inspiratory and expiratory pressures? (True)
- The gold standard for the diagnosis of secondary hypocortisolism is the metyrapone test? (False)

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