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Latent dystrophic myopathy revealed by unsuccessful weaning from mechanical ventilation

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Abstract. We report a patient who had difficulty in weaning from mechanical ventilation which was due to an unsuspected latent dystrophic myopathy. The association of latent dystrophic myopathy and unsuccessful weaning has not been previously reported.

Key words: Dystrophic myopathy – Respiratory weaning – Mechanical ventilation – Surgical intensive care

The success of weaning from mechanical ventilation depends mainly on the patient's underlying condition. Unsuccessful weaning attempts are mostly due to inadequate pulmonary gas exchange or insufficient respiratory muscle pump function [1, 2].

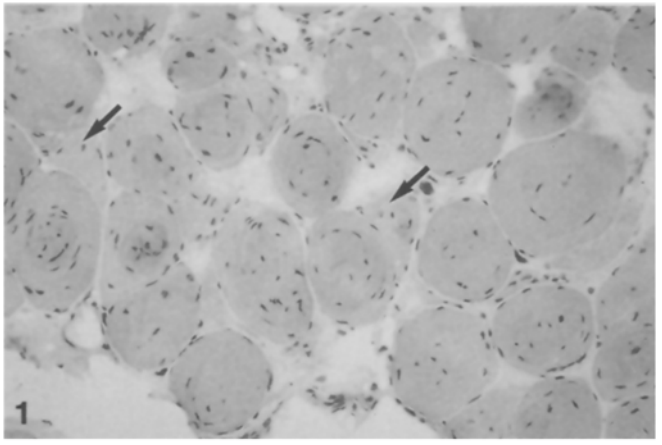
We report a patient who required mechanical ventilation for acute pulmonary failure and who experienced difficulty resuming spontaneous breathing because of an unsuspected latent dystrophic myopathy. The association of latent dystrophic myopathy and unsuccessful weaning has not been reported previously.

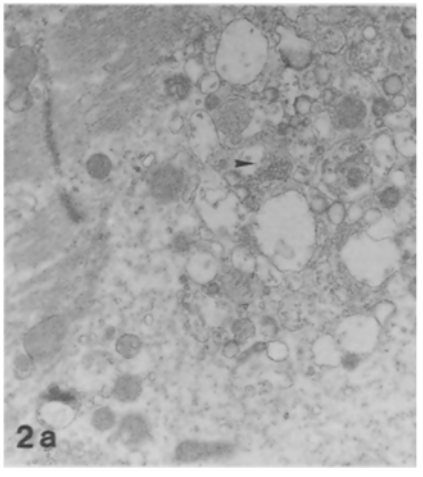
Case report

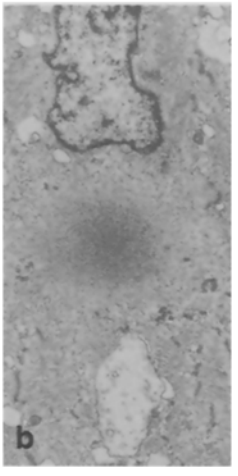
A 39-year-old mildly obese woman was transferred to our ICU for the treatment of an adult respiratory distress syndrome which developed 10 days after the onset of acute pancreatitis. Pancreatitis was due to obstructive gallstone disease and required partial pancreatectomy with necrosectomy.

Past medical history was unremarkable and the patient was not taking any medication prior to admission. On arrival to our ICU, arterial blood gas analysis was as follows: PaO_2 73 mmHg, $PaCO_2$ 39 mmHg and pH 7.37 during mechanical ventilaton with an FiO_2 of 0.7. Chest X-ray showed numerous patchy infiltrates on both lung fields. An abdominal CT-scan revealed an edematous pancreas with changes in the structure of the peripancreatic fat. Laboratory values for hemoglobin, sodium, calcium, potassium, magnesium, urea, creatinine, protein, amylase and lipase were within normal range. CK was 75 iu/l (normal 0–150) and no further increase was noted on daily examination up to the time of discharge. Serum glucose was slightly elevated at 13.4 mmol/l (normal 4.2–6.0). Physical examination was otherwise normal and the neurological status did not reveal any abnormalities. The patient was mechanically ventilated with positive end expiratory pressure (PEEP) of 10 cmH_2O. Peritoneal lavage was continued and the clinical condition steadily improved. Seven days later, weaning from the ventilator was begun. Despite improved chest X-rays and pulmonary gas exchange, weaning progress was difficult and slow. The patient had no pain, and normal bowel movements appeared. She did not receive steroids, paralysing agents or aminoglycosides during her stay in the ICU. Electrolytes, especially phosphorus, calcium, potassium and magnesium remained within the normal range. Enteral nutritional support was adequate as assessed by nitrogen balance and carbohydrates were limited to avoid excess CO_2 production. On day 15, following the 24 h of continuous breathing on CPAP 5 cmH_2O with an FiO_2 of 0.4, arterial blood gases were normal, inspiratory pressure assessed by a manometer connected at the extremity of the endotracheal tube was between -25 and -30 cmH_2O and minute ventilation was 6 $l \cdot min^{-1}$. The patient was extubated. However, shortly thereafter she became severely dyspneic and had to be reintubated. The same procedure was repeated the next day. Despite adequate blood gases the patient became again clinically exhausted 4 h later and reintubation was performed again. There were no signs of sepsis and repeated cultures were negative. Examination of the larynx was normal except for the inability to close the vocal cords completely, although vocal cord movement was otherwise symmetric and normal. A cerebral CT-scan did not reveal any abnormalities. Plasma levels of thyroid hormones and cortisol were within normal range. A third extubation attempt was tried two days later and was again unsuccessful. A tracheostomy was performed. A spinal tap (which was repeated one month later) was unremarkable. Having excluded the usual causes of difficult weaning we therefore considered the possibility of a "critical illness polyneuropathy" [3] as the deep tendon reflexes were reduced in both arms and legs. Electromyography was negative for a polyneuropathy and did not reveal any abnormalities at the neuromuscular junction, but suggested a myopathy. Biceps sural biopsy was performed. Sections of muscle were frozen for histochemical studies and others were fixed in 2.5% glutaraldehyde for ultrastructural studies.

Histologically and histochemically, the muscle fascicles were of variable sizes, sheated by a thickened perimysium. Groups of angulated atrophic fibres situated within and/or at the periphery were observed in each fascicle. The most striking feature was the marked hypertrophy of the majority of the remaining fibres (between 65%–80%) of which some 50%–70% were ring fibres containing numerous central nuclei (Fig. 1). There were a few scattered degenerative fibres and an occasional basophilic regenerating fibre. The endomysium was also thickened. No inflammatory cells were observed. The vessels and nerve fibres were within normal limits. There was very little glycogen as evidenced by the PAS stain. Both the NADH and ATPase (at variable pHs) stains indicated that both types of fibres were involved and this at various degrees within the fascicles. In some there was type I fibre predominance.







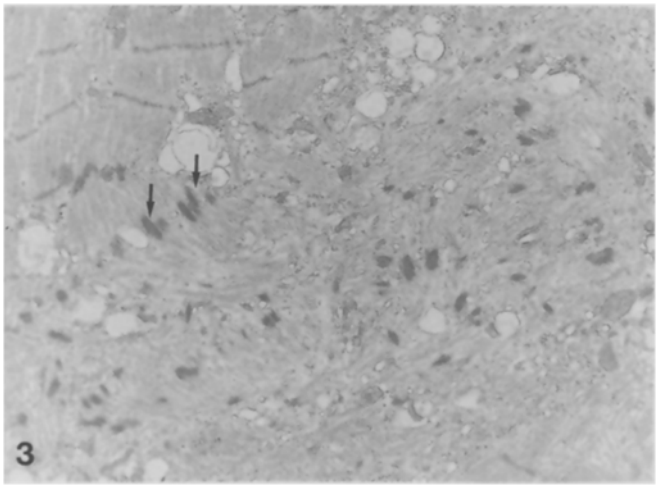


Fig. 1. Great variability in the diameters of the fibres, the majority of which are ring fibres, with numerous central nuclei. Few atrophic fibres, some of which are angulated (*arrows*) (HE 160×)

Fig. 2. a Few lipidic droplets and marked dilatation of the T-system with some honey-combing (*arrow*). Glycogen is markedly decreased (EM 8000×). **b** Filamentous body (EM 6000×)

Fig. 3. Electron micrograph showing disorganization or disarray of the myofibrils with many nemaline rods (*arrows*) (EM 3600×)

Ultrastructural studies revealed areas of myofibrillar disorganization or disarray with numerous nemaline rods and few membrane bound lipid droplets especially in the sub-sacrolemnal regions (Fig. 2). Glycogen granules were sparse. There were focal zones of myofibrillar necrosis with dilatation of the T-tube system with honey-combing, as well as filamentous bodies in places (Fig. 3). The mitochondria were of variable sizes and a few presented with abnormalities of their crista, but no paracrystallin figures were observed. These histological, histochemical and ultrastructural features are consistent with those of a dystrophic myopathic condition.

Intensive respiratory physiotherapy was started and two months later it was possible to remove the tracheostomy cannula. The patient has since resumed her activities as a housewife, but still complains of weakness.

Discussion

The case reported is unusual in that, to our knowledge, latent myopathy discovered during an unsuccessful weaning trial has not been described previously. The nature of the histologic, histochemical and electronic microscopy findings suggest they were present prior to the development of pancreatitis. The diffuse intrafascicular and perifascicular fibrosis attest to a condition of long standing. Furthermore, the many atrophic, angulated fibres observed in a large proportion of the fascicles examined, together with fibre type grouping and the numerous ring fibres, are observed mainly in cases of chronic myopathies such as limb girdle dystrophy and myotonic dystrophy [4].

Usual causes of failed weaning trial were rapidly excluded by clinical, chest X-ray and laboratory exams. The patient had not received drugs such as aminoglycosides known to cause neuromuscular weakness. Guillian-Barré syndrome was excluded in view of the normal spinal tap (repeated after a one-month interval). Pancreatitis has not previously been linked to the development of an acute myopathy although it has been associated with peripheral neuropathy [5]. Acute myopathy following treatment of severe asthma has been reported [6]. In these cases generalized myopathy was observed clinically and delayed weaning from mechanical ventilation was present in all instances. In the majority of these patients (71%) serum creatinine kinase was elevated and muscle biopsy was consistent with rhabdomyolysis. The absence of elevation of serum creatinine kinase during our patient's stay in the ICU and the morphologic changes seen on muscle biopsy are not consistent with an acute myopathy such as those previously described. The possibility of an acute polyneuropathy has been considered in view of the reduced deep tendon reflexes. Indeed a significant number of critically ill patients, in particular those with multiorgan failure were reported to have tetraparesis and difficult weaning periods from mechanical ventilation with neurological signs consistent with an acute peripheral neuropathy [7]. This particular neuropathy is characterized by near normal conduction velocities and distal latencies but reduced compound muscle and sensory nerve action potential amplitudes coupled with abnormal spontaneous activity in muscle, consistent with a pure, primary axonal degeneration of both motor and sensory fibers [8]. However, none of these findings was detected in our case.

This patient showed no respiratory muscle weakness since she was able to develop sufficient maximal inspiratory pressures and to maintain normal blood gases with a near normal minute ventilation; however, after each previous tracheal extubation attempt, she had rapidly developed respiratory muscle fatigue which we believe was the consequence of the prolonged critical illness (pancreatitis and ARDS) superimposed on her dystrophic respiratory muscles.

In conclusion, this case demonstrates that the presence of a latent myopathy, although rare, may be added to the differential diagnosis for unsuccessful attempts at weaning from mechanical ventilation.

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