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BRIEF REPORT

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Acute neuromuscular respiratory failure after ICU discharge

Report of five patients

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Abstract *Objective*: To describe a syndrome of acute neuromuscular respiratory failure (NM-ARF) caused by ICU-acquired acute myopathy and neuropathy.
Design: Case series.
Setting: General Regional University Hospital in Brescia, Italy.
Patients: Five adult patients with NM-ARF after prolonged ICU stay and successful weaning from the ventilator and ICU discharge.
Interventions: None.
Measurements: Clinical signs of NM-ARF, electroneurography and electromyography (ENMG) of peripheral nerves and muscles, and functional assessment of respiratory muscles.
Results: NM-ARF was diagnosed at the time of (one case), or 1–3 days after, ICU discharge. Limb weakness alarmed the physicians, while the signs of the NM-ARF were initially undetected. In the first observed case the acute respiratory failure was near fatal, and necessitated ICU readmission, while in the other cases 2 weeks of aggressive chest physiotherapy permitted resolution of the respiratory failure. History, clinical course and ENMG indicated the diagnosis of critical illness myopathy and neuropathy (CRIMYNE). Three patients recovered fully, while two had persisting evidence of axonal polyneuropathy several months after the onset.
Conclusions: Critically ill patients with prolonged ICU stay, sepsis and MOF are at great risk of developing CRIMYNE, which in turn may be responsible for NM-ARF. This latter complication may arise after resolution of the respiratory and cardiac dysfunctions and successful weaning from the ventilator. As NM-ARF may cause unplanned ICU readmission or even unexpected death, strict clinical surveillance and monitoring of respiratory muscle function is recommended after discharge to the general ward of patients with proven NM-ARF. Early intensive chest physiotherapy can resolve the condition.

Key words Respiratory failure · Neuropathy · Myopathy · Intensive care unit · Readmission · Complications

Introduction

Patients with sepsis and prolonged intensive care unit (ICU) stay may develop critical illness myopathy and neuropathy (CRIMYNE), causing muscle weakness and paralysis [1, 2]. From 50 to more than 80% of such patients may be affected [3, 4, 5], and some are still disabled 1 year after the diagnosis [4].

We describe five patients who had acute neuromuscular respiratory failure (NM-ARF) shortly after, or at the time of, ICU discharge. Electroneurography and electromyography (ENMG) demonstrated an acute my-

Table 1 Clinical presentation of neuromuscular respiratory failure. BOT = breathless on talking. DTR, deep tendon reflexes. MRC score, Medical research Council (0 = complete paralysis; 1 = minimal contraction; 2 = active movements with gravity eliminated; 3 = weak contraction against gravity; 4 = active movements against gravity and resistance; 5 = normal strength). PaO_2, $PaCO_2$ = oxygen and carbon dioxide arterial partial pressures

Patient No.	Signs alarming the physician	Other clinical signs and symptoms	Muscle strength (MRC score)	Chest X-ray	PaO_2 (mmHg)	$PaCO_2$ (mmHg)
1	Severe limb weakness	BOT, tachypnea, intervention of accessory respiratory muscles, impaired cough, absent DTR	3/5	Normal	89 in room air	34
2	None	BOT, tachypnea, intervention of accessory respiratory muscles, impaired cough, muscle atrophy, reduced DTR	3/5	Normal	78 with 4 liters O_2	34
3	Severe limb weakness	BOT, tachypnea, intervention of accessory respiratory muscles, impaired cough, absent DTR	3/5 legs 5/5 arms	Normal	74 in room air	35
4	Feet extension paralysis	BOT, tachypnea, intervention of accessory respiratory muscles, impaired cough, severe limb weakness, reduced DTR	3/5	Normal	87 with 4 liters O_2	33
5	BOT, tachypnea	BOT, tachypnea, dyspnea, intervention of accessory respiratory muscles, impaired cough, reduced chest expansion	4/5	Normal	91 with 30% O_2	34

opathy and axonal neuropathy. These alterations were diagnosed as ICU-acquired, since the patients' histories for previous neuromuscular disorders were negative and follow-up showed complete recovery or substantial improvement of both the clinical and ENMG findings.

Case reports

Patient 1

This 19-year-old man was admitted to the ICU because of multiple trauma. The patient was on mechanical ventilation for 17 days, during which time he had sepsis, acute respiratory distress syndrome (ARDS) and multiple organ failure (MOF). The patient was extubated on day 18 and transferred to the ward on day 21. Two days later he was noticed to have severe weakness, being unable to lift his arms for but a few seconds, and for this reason intensive care and neurologic consultations were required. He was not dyspneic, but was breathless on talking, needing to pause after a few words. When required, he was unable to count to 20 with a single breath. He took 22–25 breaths/min with shallow breathing and with the intervention of accessory respiratory muscles. He was unable to cough effectively, precluding secretion clearing. Chest physical examination was unremarkable and there was no fever. Arterial blood gases and chest X-ray were normal (Table 1).

Two nights later the patient had further respiratory deterioration and required urgent tracheal intubation. He was readmitted to the ICU and, after an 11-day course, eventually recovered normal respiratory muscle function, as shown by normalization of vital capacity (VC) and maximum inspiratory and expiratory pressures (PImax, PEmax) (Table 2). Two days after readmission the ENMG demonstrated a CRIMYNE (Table 3). Repeated investigation at 5 months showed normalization of clinical signs and of ENMG abnormalities.

Patient 2

This 37-year-old woman suffered severe abdominal trauma with urinary bladder rupture and hemorrhagic shock. She had peritonitis, bilateral basal pneumonia, sepsis and MOF. A tracheostomy was performed on day 13 and the patient was weaned from the ventilator (day 56) and finally transferred to the ward (day 60).

On day 63, a consultation was required to remove the tracheal cannula. The patient was lying immobile in bed and was not dyspneic. She was breathing superficially at 25 breaths/min and was using accessory respiratory muscles. When required, she was unable to count to 20 with a single breath. Coughing and clearance of secretions were impaired. The patient was able to lift her arms and legs, although not against resistance. Muscle atrophy was pronounced and deep tendon reflexes were absent. Chest X-ray had normalized and arterial blood gases were near-normal (Table 1).

A 10-day aggressive chest physiotherapy achieved respiratory muscle recovery with normalization of clinical symptomatology and of VC and PI max and PE max (Table 2). ENMG diagnosed a CRIMYNE (Table 3). When the patient was last seen at 3 months after discharge, no clinical signs of myopathy or sensory-motor axonal polyneuropathy were present and the ENMG had normalized.

Patient 3

This 72-year-old woman had acute pancreatitis, bilateral pleural effusion and pneumonia, sepsis and acute respiratory insufficiency requiring ICU admission. After 10 days of antibiotics and mechanical ventilation, the patient was weaned from the ventilator (day 13) and transferred to the ward (day 16). Her lungs had cleared and arterial blood gases normalized. The patient appeared profoundly weak, exhibiting only spontaneous lateral movements of the head. On day 18 consultations were required. The patient appeared breathless when talking, coughing or swallowing, otherwise she lay quietly in bed. She took 30 breaths/min which were superficial, using accessory respiratory muscles. Chest auscultation

Table 2 Respiratory muscle function assessment. Measurements were done in triplicate and the best values are reported. * Vital capacity was estimated clinically, as described in the text. PI max/PE max = maximum inspiratory and expiratory pressures. N. V. = normal values [16]

Patient No.	First examination				Follow-up			
	Days after ICU discharge	Vital capacity (ml/Kg) N. V. 65–75 ml/Kg	PI max (cm H_2O) N. V. Male -111 ± 34 cm H_2O Female -72 ± 26 cm H_2O	PE max (cm H_2O) N. V. Male 151 ± 68 cm H_2O Female 93 ± 30 cm H_2O	Days after ICU discharge	Vital capacity (ml/Kg) (N. V. 65–75 ml/Kg)	PI max (cm H_2O) N. V. Male -111 ± 34 cm H_2O Female -72 ± 26 cm H_2O	PE max (cm H_2O) N. V. Male 151 ± 68 cm H_2O Female 93 ± 30 cm H_2O
1	2	< 2L*	Not done	Not done	13	70	− 97	+ 120
2	3	< 2L*	Not done	Not done	13	60	− 75	+ 95
3	2	25	− 38	+ 58	16	47	− 64	+ 85
4	1	18	− 30	+ 46	15	60	− 70	+ 90
5	0	20	− 31	+ 48	14	75	− 100	+ 140

Table 3 Neurophysiological studies of peripheral nerves and muscles. N-M, neuromuscular transmission studied by repetitive 3-Hz stimulation of the ulnar nerve at the wrist. Denervation signs included fibrillation potentials and positive sharp waves. MUP, muscle unit potential. * Pt No. 5 had his ICU discharge postponed because of proven respiratory muscle failure: the number refers to the planned date of discharge

Patient No.	Date of examination (days after ICU discharge)	Nerve conduction studies					Electro-myography	N-M trans-mission	Summary
		Tested limb	Velocity		Amplitudes				
			Motor	Sensory	Motor nerve-Muscle	Sensory Nerve			
1	6	Lower Upper	Mildly reduced Normal	Normal Normal	Low Low	Low Low	Denervation. Polyphasic, short duration and low amplitude MUP	Normal	Axonal polyneuropathy, myopathy
2	3	Lower Upper	Normal Normal	Normal Normal	Low Low	Low Low	Polyphasic, short duration and low amplitude MUP	Normal	Axonal polyneuropathy, myopathy
3	2	Lower Upper	Mildly reduced Normal	/ Normal	Low Low	Absent Low	Denervation. Short duration and low amplitude MUP	Normal	Axonal polyneuropathy, myopathy
4	1	Lower Upper	Normal Normal	/ Normal	Low Low	Absent Low	Denervation. Polyphasic, short duration and low amplitude MUP	Normal	Axonal polyneuropathy, myopathy
5	1*	Lower Upper	Normal Normal	Normal Normal	Low Normal	Low Normal	Polyphasic, short duration and low amplitude MUP	Normal	Axonal polyneuropathy, myopathy

was unremarkable. She was able to lift her arms, but not legs, and deep tendon reflexes were absent (Table 1). VC, PImax and PEmax were severely reduced. Intensive physiotherapy was maintained for 2 weeks and respiratory muscle function normalized (Table 2).

ENMG diagnosed CRIMYNE (Table 3). At 6 months she was able to walk independently. Residual ENMG signs of axonal sensory-motor polyneuropathy persisted, while myopathic alterations had resolved.

Patient 4

This 33-year-old HIV-positive woman had *Pneumocystis carinii* pneumonia and acute respiratory failure, and was admitted to the ICU. After a clinical course complicated by prolonged sepsis and MOF the pneumonia resolved, the patient was successfully weaned from the ventilator (day 36) and transferred to the ward (day 39). On day 40 generalized profound muscle weakness, bilateral external popliteal nerve paralysis and reduced deep tendon reflexes were noticed. On consultation, the patient was moderately tachypneic and short-breathed. She was using accessory respiratory muscles and was unable to cough effectively. VC, PImax and PEmax were reduced (Table 2) and ENMG documented a CRIMYNE. Two weeks of intensive physiotherapy permitted the resolution of respiratory signs, as well as normalization of VC, PImax and PEmax, however limb weakness persisted and the patient was bedridden at the time of her hospital discharge on day 70. At 5 months the patient had normal arm, but reduced leg strength, was walking with help and was ataxic. ENMG showed signs of axonal sensory-motor polyneuropathy, but not myopathy.

Patient 5

This 21-year-old man suffered severe thoracic trauma with multiple fractures and bilateral lung contusions. He had pneumonia, ARDS, sepsis and MOF. After 11 days of mechanical ventilation and antibiotics, the chest X-ray had cleared and he was successfully extubated. His discharge was planned for the next day and the patient was re-evaluated. He had rapid shallow breathing at 25–30 breaths/min, needing to take a breath after a few words. Recruitment of accessory respiratory muscles was evident and coughing was weak. Limb muscle strength was only slightly reduced, no marked muscle atrophy was seen and deep tendon reflexes were normal (Table 1). However, VC, PImax and PEmax were reduced (Table 2) and his discharge was postponed.

Early in the afternoon, a reduced expansion of the left hemithorax was noticed with reduced sounds on auscultation. Chest X-ray showed left inferior lobe atelectasis, which resolved after urgent fiberoptic bronchoscopy. Chest physiotherapy was initiated soon after and maintained for 14 days, after which the recovery of respiratory muscle function was complete (Table 2). ENMG diagnosed CRIMYNE (Table 3) and was then normal at 1 month.

Discussion

The five patients described here had acute respiratory failure caused by ICU-acquired myopathy and neuropathy. In four of the five patients the diagnosis of NM-ARF was made when they had already being transferred to general wards, and was mostly made by chance. In fact, muscle weakness alarmed the physicians and prompted consultations, while the signs of NM-ARF remained undetected initially.

NM-ARF is a difficult diagnosis to make: dyspnea may be absent, chest X-ray is normal and arterial blood gases worsen only in the late stage of the disease [6]. Furthermore, a long list of myopathies, neuropathies and neuromuscular transmission defects exists, which cause NM-ARF [6]. To our knowledge, this is the first report describing NM-ARF caused by ICU-acquired neuromuscular alterations after successful weaning (4–7 days) from the ventilator. Drugs did not play a role, since neuromuscular blocking agents were only used in small boluses for short-term procedures and steroids were never used.

Compared to respiratory failure due to lung diseases, NM-ARF has an insidious onset and progression. The absence of loud wheezing, hypoxia and hypercapnia may falsely reassure physicians, so that patients are left untreated until overt, life-threatening deterioration appears [6, 7]. This was the case of the first patient described here, whose initial symptoms and signs were overlooked, and who then needed emergency tracheal intubation and ICU readmission. Unplanned ICU readmission [8] and unexpected death [9] are not rare in patients discharged from ICUs. Respiratory "problems" are often cited as causes [9], and this preliminary report suggests that respiratory failure due to CRIMYNE should be considered in the differential diagnosis.

Actually, appropriate testing including VC and/or PImax and PEmax in the appropriate clinical setting provide an accurate method to define the derangement of respiratory muscles and also to plan therapeutic strategies [6, 7]. A rough estimate of VC can be obtained by asking the patient to count to 20 after taking a single breath. Inability to do so corresponds to a greatly reduced VC in the order of 15–18 ml/kg [6, 7], below which tracheal intubation should be performed. Chest physiotherapy is effective in the treatment of the neuromuscular respiratory failure of the Guillain-Barré syndrome when started before critical reduction of VC is reached [7]. This was also the case in this small series of patients and emphasizes the need to make early diagnoses.

Patients with sepsis, MOF or prolonged (> 1 week) ICU stay are at high risk of developing CRIMYNE [3, 4, 5]. Clinical signs vary from mild weakness to flaccid tetraplegia. In some cases, they are completely absent and only ENMG abnormalities are evident [2, 3, 5]. A difficult weaning from the ventilator, after cardiac and/or respiratory dysfunctions have been successfully corrected, suggests a respiratory muscle involvement and appropriate neurophysiologic testing is useful in defining the diagnosis [10]. Successful weaning, however, does not exclude the involvement of respiratory muscles per se, as this case series shows. If clinical signs of neuromuscular respiratory failure are recognized (breathlessness on talking or swallowing, rapid shallow breathing), we suggest that strict clinical surveillance is also maintained after discharge to the general ward. In addition, we recommend serial measurements of VC or PImax and PEmax to monitor the respiratory muscle function: if VC is between 20 and 30 ml/kg (N. V. 65 ml/kg), intensive chest physiotherapy is indicated. Finally, phrenic nerve conduction and needle EMG of the chest wall and diaphragm are required for the ultimate diagnosis [10].

The incidence of NM-ARF after ICU discharge is presently unknown, however, even if rare, it is life-threatening. Its prompt recognition and treatment can therefore be life-saving.

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