A New Syndrome Sheds Light on Old Medical & Rehabilitative Dilemmas: Paraparesis Due to Rhabdomyolysis and Bilaterally Symmetric Compartment Syndrome in Four Patients. Cases Study

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SUMMARY

Via our description of a seemingly heterogenous group of four patients who presented to our rehabilitation facility with a rather unusual clinical presentation of compartment syndrome with development of a flaccid paraparesis and rhabdomyolysis immediately after awakening from a prolonged sleep episode in an unusual posture – which might, in fact, be a ‘new syndrome’ - we have also come to address an important issue linking our group of patients – specifically, the complexities which present to a rehabilitative facility in the cases of unusual and unclear diagnoses. Eventually, all four of our patients remained severely disabled. All had suffered sensorimotor axonal demyelinating polyneuropathies and two patients had subclinical hypothyroidism. Prior to the prolonged sleep episode, they had all consumed alcohol and drugs. Using these four rather demanding diagnostic rehabilitative cases we address the ever-important issue of timely mutual communication and patience. For when a rehabilitative facility is confronted with patients whose diagnoses are not clear, the scope of the long-term comprehensive rehabilitation management faces some major obstacles with respect to how the rehabilitative team can succeed in designing a ‘tailor-made’ rehabilitation program for these patients, which oftentimes proves to be a rather tricky task requiring innovative and creative efforts on the parts of all those involved in the care of the patient. Quite a challenging task, indeed, yet one genuinely necessary to attempt to achieve so that the patient, family and, of course, the ‘payer agency/provider’ can all prepare themselves, realistically so as to obtain the best overall rehabilitative outcome for these patients. We conclude that what is most necessary for these unique patients is patience.

Key words: paraparesis, rhabdomyolysis, prolonged sitting, compartment syndrome, neuropathic pain
BACKGROUND

Patients referred to a department of rehabilitation medicine are usually admitted with a definite diagnosis. After initial treatments at the admitting general hospital, they are transferred to continue the recovery treatment in a department of rehabilitation medicine, usually with firm guidelines and recommendations for further management. However, when a rehabilitative facility is confronted with patients whose diagnoses are not clear, or even perhaps with rare combinations of medical problems, the scope of the long-term comprehensive rehabilitation management faces some major obstacles regarding the design of a ‘tailor-made’ rehabilitation program for these patients, with attention given to prognosis, as well as to predictions on how long patients and family members can expect to devote themselves and their support systems (i.e. family members, friends, etc.) to such oftentimes rigorous rehabilitative schedules fraught with ‘small steps’ of encouraging progress peppered with pauses and intermittent stops and starts along the rehabilitative way. To demonstrate these points, we describe four patients whose clinical course was very unusual. They were all diagnosed and treated in other general hospitals before they were eventually transferred to our rehabilitation medicine ward. We asked ourselves if what we were presented with was an entirely new entity or whether it was coincidence that a prolonged sleep episode in a bizarre posture was a common historical event which immediately triggered the subsequent acute onset of compartment syndrome, rhabdomyolysis, flaccid paraparesis and polyneuropathy in these four patients.

CASE REPORTS

Four patients presented with a flaccid paraparesis and rhabdomyolysis due to compartment syndrome following a prolonged sleep episode or a very prolonged sitting position (due to alcohol consumption and drug abuse). Electrophysiological investigations were indicative of a sensorimotor axonal-demyelinating polyneuropathy. All patients were heavy smokers and two had subclinical hypothyroidism. Incomplete recovery was noted during the rehabilitation and follow-up period.

Case 1

A. S., a recently unemployed, divorced, slightly overweight, 38-year-old man with diet-controlled diabetes, chronic low back pain and a smoking habit, fell asleep overnight while sitting in front of his home computer. Two days later, he was admitted to a general hospital with a clinical picture of anuria, bilateral weakness of his distal lower extremity muscles, rhabdomyolysis, and right anterior thigh compartment syndrome. Hemodialysis, a decompression procedure and skin grafting of the right thigh were performed. Clinical work-up revealed mild severity of both diabetes and hypothyroidism. Muscle biopsy showed a normal histology. CT scan and MRI of the lumbar spine revealed mild disc herniations at L5-S1, L4-5 and S1-2. Electrophysiologically, EMG and NCV studies showed severe axonal neuropathy affecting both legs, slightly more prominent on the left side with signs of denervation in the calf muscles while the proximal muscles seemed spared. Sural nerve biopsy did not show any pathology. No signs of metal poisoning or porphyria were found. Repeated analyses of cerebrospinal fluid (CSF) via lumbar puncture did not show any abnormality. After renal function recovery, he was referred to our rehabilitation department.

Neurological examination revealed: flaccid paraparesis, ‘stockings’-type hypoesthesia, weak patellar and Achilles reflexes, mild depression, and severe neuropathic pain. No pyramidal signs were found. He retained control of his sphincters. Repeat electrophysiological analyses via EMG-NCV studies showed axonal neuropathy in all 4 limbs, while a sleep laboratory test did not reveal sleep apnea syndrome.

Initial and final rehabilitative Functional Independence Measure (FIM) scores for this patient were measured at 94 and 116, respectively.

His pharmacologic treatment included: Amitriptyline 50mg/day, Carbamazepine 600mg/day, Oxycodone 10mg/day and L-Thyroxine 50mcg/day.

A year after the initial hospitalization, he still suffers from neuropathic pain and there is no change in his neurological status. Although he can walk with a left short leg brace and walker, he prefers to use his personal lightweight wheelchair.

Case 2

S. S., a 22-year-old woman, was admitted with an acute paraparesis and rhabdomyolysis. Past history revealed recent hypothyroidism, carrier status for Hepatitis C, and s/p surgical removal of a sacral epidermoid cyst three years ago. She reported being a smoker and occasional use of marijuana. The day prior to her admission, she had experienced high fever, and consumed alcohol and 2 tablets of clonazepam. She fell asleep on the floor for approximately 24 hours. When she was taken to hospital, she was found to be disoriented, anuric and suffering from a mild thigh compartment syndrome. Neurological
examination showed flaccid paraparesis. Laboratory examinations revealed: Hepatitis C positive, LDH=1822u, CK=5050u, SGOT=252. Macrocytic anemia (Hgb 9.3), thrombocytosis of 51400, and normal CSF analysis on lumbar puncture. Electrophysiologically, EMG-NCV studies showed severe sensorimotor axonal-demyelinating polyneuropathy including bilateral median nerves. Levels of Vitamin B1 were borderline and Vitamin B12 levels were within normal range. No trace elements or other metals were found. She was EBV IgG Ag-positive, IgM negative, normal range. No cryoglobulins were found. Renal function remained normal.

Her initial and final rehabilitative Functional Independence Measure (FIM) scores were measured at 96 and 109, respectively. She walks with two short leg braces and two crutches and occasionally uses a personal lightweight wheelchair.

**Case 3**

MG C was a 50-year-old divorced male garage worker who was regularly active in sports and reported no significant past medical history except for his social habits of regularly smoking cigarettes and drinking alcohol. After a heavy bout of vodka and whiskey drinking one night, being unable to drive home, he stayed in his car, in a sitting position, asleep for 14 hours. The next day, in an attempt to move and leave his car, he fell and was subsequently evacuated to the nearest hospital, where he was found to be semiconscious and dyspeptic with heart rhythm disturbances along with anuria due to rhabdomyolysis and compartment syndrome. Initial laboratory findings revealed a creatinine level of 3.4 and a CPK value of 58000 units. Toxicological urine analysis revealed a significantly high level of opiates in his system.

His immediate treatment consisted of ventilation, correction of heart rhythm disturbances and hemodialysis. Progressively, he regained both consciousness and renal function. His CPK level decreased to 173 units and his creatinine level to 1.36. Neurologically, he was found to suffer from left infraspinatus and supraspinatus palsies and a flaccid paraparesis with proximal muscles being more affected than distal muscles. He did not show any autonomic or sensory deficits. He was confined to a wheelchair and complained of severe neuropathic pains. A mild degree of lower limb edema was noted bilaterally. His rehabilitation program consisted of: ADL training, pain control, laboratory follow-up and an attempt to walk again. After 3 months, he is still confined to a wheelchair and can only walk for short distances with the aid of two crutches. Although he has regained a normal sitting balance of posture, and sensation is still found to be normal, no reflexes can be elicited from any of the four limbs, and he remains with a residual flaccid paraparesis.

Significant laboratory findings showed: elevations in WBC (19.1), Hgb (18.2) and blood amylase (123). Liver function tests (LFTs) revealed elevated levels of GGT (201) and LDH (4760), elevated blood ammonia (141) and elevated ferritin (1650).

Kidney function tests revealed: BUN (17mg/dl), creatinine (1.2) sodium (137) and potassium (3.54) along with elevated levels of uric acid (10.4) and C-reactive protein (CRP) (6.5)

Vitamin B12 (1229) levels and magnesium (1.5) levels were both elevated. Coagulation studies were significant for a normal PTT (28) value and an elevated fibrin degradation products (493) value.

He was Hepatitis C-positive (11) and cocaine-negative.

Electrophysiologically, we demonstrated axonal demyelinating sensory motor deficits in 4 limbs, more pronounced in his lower limbs, and an infraspinatus injury.

His final rehabilitative Functional Independence Measure (FIM) score was measured at 100.

**Case 4**

PK, a 58-year-old woman, was referred for consultation from another country. We reviewed the medical reports and all laboratory data during and after her December 2009 hospitalization. Apart from being overweight and a smoker, she had enjoyed good health until she was hospitalized. She reported that after spending a few days in another country (for a week, she had been spending approximately 12 hours uninterruptedly sitting in front of a slot-machine accompanied by some alcohol consumption), she was hospitalized in an IRCU due to an acute-onset multi-organ failure, renal shutdown due to bilateral compartment syndrome, rhabdomyolysis, artificial respiration, and sepsis.

After 5 days at the IRCU her situation had improved substantially, and finally she was found to have some paraparesis which slowly improved and eventually she had a bilaterally symmetric peroneal nerve palsy. All biochemical and hematological values returned to normal levels.

Electrophysiologically, an EMG study revealed the following: SNAP were not found in both peroneal nerves; CMAP were not recorded. A needle-EMG
study showed signs of re-innervation. After thorough immunological, radiological and biochemical work-up, her clinical diagnoses were: capillary leak syndrome, bilateral compartment syndrome, rhabdomyolysis and bilateral peroneal nerve palsy.

A Doppler ultrasound of the venous and arterial systems of both lower limbs showed that these were within normal limits.

She was initially treated for UTI, and she reported normal sphincter control.

Six months later, on examination, her general status was found to be close to normal, yet she was still overweight. She walks with a crutch and a pair of short-leg braces. Without the orthoses, she walks in such a way so as to avoid the ‘shuffle’ gait due to ‘drop-feet’.

Neurologically, normal reflexes were elicited, no sensory deficits were discerned but bilateral ‘drop-foot’ (with some flickers) was noted.

Her final rehabilitative Functional Independence Measure (FIM) score was measured at 126, which is the maximal value for this scale.

Her treatment consisted of:
1. Hydrotherapy (once weekly)
2. Physiotherapy (thrice weekly)
3. Proper diet for weight reduction
4. weekly intravenous injection of Immunoglobulin (Ig) [Octagam, IV injection] 

Tab. 1. Summary of the Clinical Data

<table>
<thead>
<tr>
<th>Patients</th>
<th>case 1</th>
<th>case 2</th>
<th>case 3</th>
<th>case 4</th>
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</thead>
<tbody>
<tr>
<td>Age/Sex</td>
<td>38 / male</td>
<td>22 / female</td>
<td>50 / male</td>
<td>58 / female</td>
</tr>
<tr>
<td>Historical medical background</td>
<td>mild DM, mild hypothyroidism, smoker / low back pain (LBP)</td>
<td>mild hypothyroidism, smoker / Hepatitis C carrier / alcohol / benzo diazepine / s/p surgical removal of sacral epidemoid cyst</td>
<td>smoker / alcohol / opiates</td>
<td>overweight smoker /</td>
</tr>
<tr>
<td>Clinical course</td>
<td>8hrs sleep in a sitting position &gt; ACS &gt; rhabdomyolysis &gt; acute renal failure (ARF)</td>
<td>24hrs sleep on floor / alcohol / clonazepam &gt; ACS &gt; rhabdomyolysis &gt; acute renal failure (ARF)</td>
<td>14hrs sleep in car / alcohol / opiates / &gt; ACS &gt; rhabdomyolysis &gt; acute renal failure (ARF)</td>
<td>12hrs, daily x6 days sitting / alcohol / &gt; multi-organ failure &gt; ACS &gt; rhabdomyolysis &gt; systemic capillary leak syndrome (SCLS)</td>
</tr>
<tr>
<td>Neurologic outcome</td>
<td>paraparesis (PPA), neuropathic pain</td>
<td>paraparesis (PPA)</td>
<td>paraparesis (PPA) neuropathic pain (severe)</td>
<td>bilateral peroneal nerve palsy</td>
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</table>

Rehabilitative Profile

<table>
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<th>Initial and final Functional Independence Measure (FIM) scores</th>
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<td>Walks with aid of a short leg brace (SLB); wheelchair (WC)</td>
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**DISCUSSION**

We have described three young patients who fell asleep in unusual postures, which was followed by the development of a compartment syndrome with rhabdomyolysis and flaccid paraparesis. One patient remained in a sitting position for 12 hours over a total of 6 days. All of them were smokers, two had subclinical hypothyroidism and in all patients, electrophysiological investigations showed sensorimotor axonal-demyelinating polyneuropathy. One had mild diabetes and discs herniations, another one was a carrier of Hepatitis C, and used alcohol, drugs and marijuana on occasion. Three patients remained paraparetic after almost four months of comprehensive inpatient rehabilitation program, using alternately wheelchair or crutches. No autonomic nervous system involvement was found. During hospitalization we did not observe any substance abuse.

Did our patients develop a syndrome which is a new entity or do they rather resemble a coincidence of prolonged unusual posture followed by an acute onset of rhabdomyolysis, paraparesis and polyneuropathy? The patients suffered from depressed mood, smoked cigarettes, consumed alcohol and/or drugs; fell asleep in bizarre postures, and a combination of rhabdomyolysis and compartment syndrome followed. Eventually they were diagnosed as having polyneuropathy and cauda equina syndrome.
What was the influence of mild diabetes or hypothyroidism in two of our patients? Chronic hypothyroidism is associated with various neurological states (dizziness, deafness, myopathy, polyneuropathy, multifocal motor neuropathy and carpal tunnel syndrome) but apparently this subclinical problem in our patients was irrelevant. The patients did not recover neurologically perhaps due to the fact that the acute prolonged neuro-muscular ischemic event caused irreversible nerve damage which had already existed as chronic ‘subclinical polyneuropathy’. In our opinion, the very acute onset paraparesis does not coincide with an ‘intensive /critical care neuropathic’ type of entity.

Rhabdomyolysis may develop after prolonged exercise in people with carnitine palmitoyltransferase deficiency, after or during coma and muscle compression induced by drug or alcohol abuse, after influenza-like illness, as sequelae of Guillain-Barre syndrome and after a severe crushing injury [1-8]. Rhabdomyolysis has been described in patients who regularly take statins, and in alcoholics who develop brachial plexopathy [9-10]. The risk factors for the development of rhabdomyolysis are physical exertion, ischemia or muscle necrosis due to arterial occlusion, deep vein thrombosis (DVT) or prolonged unusual posture during surgery, seizures, abuse of stimulant drugs, trauma, heat stress, heat intolerance, alcoholism and salicylate use [11-15]. Rhabdomyolysis may lead to the release of toxic intracellular material into the systemic circulation via an increase in free ionized calcium in the cytoplasm, which may then go on to cause acute renal failure triggered by renal vasoconstriction and ischemia, myoglobin cast formation in the kidney’s distal convoluted tubules, in addition to myoglobin having a direct renal toxic effect on the epithelial cells of the kidney’s proximal convoluted tubules [16]. Other complications include electrolyte disorders (hyperkalemia, metabolic acidosis, hyperphosphatemia, early hypocalemia, and late hypercalcemia), compartmental syndrome and disseminated intravascular coagulation (DIC). The compartment syndrome may develop after trauma and in diabetes [17-18].

Concerning our fourth patient, systemic capillary leak syndrome (SCLS) (Clarkson’s disease) is a rare disease characterized by leakage of plasma from blood vessels into the interstitial space due to increased capillary permeability. Patients with SCLS can be at risk for ischemia-induced organ failure, rhabdomyolysis, muscle compartment syndromes, and venous thromboembolism. Perhaps the combination of edema, increased hematocrit, and hypotension may lead to spinal cord or cauda equina damage [19]. This rare syndrome may accompany such clinical situations as preeclampsia-eclampsia, systemic edema, hypoalbuminemia, and disseminated intravascular coagulation (DIC), cirrhosis of liver, and, rarely, such as orthotopic liver transplantation which was performed in a 49-year-old man with metastatic liver sarcoma who developed both abdominal compartment syndrome (ACS) and capillary leak syndrome (CLS) after the surgery [20-23]. Severe crises and complications occurring in intensive care units account for 80% overall mortality in such cases. Diagnosis relies on an almost pathognomonic association of recurrent attacks of hypotension and hemoconcentration with paradoxical hypoalbuminemia. A monoclonal gammopathy is found in about 80% of patients. Physiopathology still remains unclear. Paraprotein toxicity has never been demonstrated [24]. Our fourth patient did not suffer from any of these clinical entities. Moreover, she presented to our facility ‘labeled with’ her diagnosis of SCLS, which had entirely been made by other physicians in another country.

In order to bring further support to this discussion, we provide published case reports from the literature which add to our understanding of this probable ‘new syndrome’. An elderly patient with known diabetes, hypertension and a hepatitis B carrier developed an overt hypothyroidism after subtotal thyroidectomy. She developed bilateral lower limb weakness, muscle cramps, and insomnia while she used tranquilizers. Eventually, rhabdomyolysis followed along with acute renal failure and a lower limb myopathy [25]. Another elderly woman was found sitting in the same position for a few hours after a bout of benzodiazepine intoxication. She developed bilateral sciatic neuropathy due to rhabdomyolysis and inflammatory lesions around her nerves [26]. During an operation, in the hyperlordotic position, the patient’s hips were placed above her feet and head, which was complicated by rhabdomyolysis, acute renal failure, and bilateral femoral and sciatic neuropathies [27].

CONCLUSIONS

Did our four patients develop a ‘new syndrome’ which is a new entity or do they just resemble a new entity that by sheer coincidence just happened to present with common historical episodes of prolonged sleeping or sitting in an unusual posture followed by an acute onset of rhabdomyolysis, paraparesis and polyneuropathy? In order to obtain a better understanding and a stronger grasp of these unusual case presentations, which involved quite challenging rehabilitative obstacles, we encourage the
reporting of similar cases which ought to shed more light on this apparent ‘new syndrome’.

A final remark on the rehabilitation process: usually when disabled patients are admitted to a rehabilitation medicine ward, they are referred with a clear diagnosis and prognosis. Consequently, the rehabilitation team can design a durable, ‘tailor-made’ program, so that the patient, family and the paying provider may all prepare themselves accordingly.

However, in a patient without a clear and definite diagnosis, and therefore, quite a vague prognosis, the compounded element of uncertainty and discomfort ensues for the patient, family members, the entire team of care-givers and the paying party. All the more, in such delicate situations, the entire team’s goals need to concentrate on giving the best rehabilitation recommendations in order to treat and maximize any and all functional improvements so as to achieve maximal independence in daily activities for the patient’s current and long-term benefit.

Therefore, the ever-important issue of timely mutual communication and patience comes to the forefront of the management of these patients.

Their rehabilitative programs will need to consist of daily feedback from both patient and the rehabilitative team staff. Consistent encouragement for both patient and family members is very essential. Frequent, periodic briefing of medical insurance representatives on functional progress and projected rehabilitative time-frame schedules should also be viewed upon as a cooperative key to a successful rehabilitative outcome. The facilitation of a mutually communicative environment is really necessary to attempt to achieve so that the patient, family and of course, the ‘payer agency/provider’ can all prepare themselves, realistically, so as to obtain the best overall rehabilitative outcome for these patients. We conclude that what is most necessary for these unique patients is patience.

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