OLGU SUNUMU CASE REPORT

DOI: 10.31609/jpmrs.2020-74611

Bilateral Upper Extremity Peripheral Nerve Injury Due to Compartment Syndrome After Drug Intoxication and Hemodialysis

İlaç İntoksikasyonu ve Hemodiyaliz Sonrası Gelişen Kompartman Sendromuna Bağlı Bilateral Üst Ekstremite Periferik Sinir Hasarı

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ABSTRACT Akut kompartman sendromu (AKS), artmış interstisyel basınç nedeniyle lokal dolaşımı bozan ağrılı bir patolojidir. AKS'ye; kırıklar, kanama riskini artıran tüm patolojiler, girişimsel işlemlerden sonra meydana gelebilen arteriyel yaralanmalar, rabdomiyoliz, koma ve iyatrojenik nedenler sebep olabilir. Bu yazımızda, 21 yaşında genç bir kadının intihar amaçlı ilaç alımı sonrası gelişen bilateral periferik üst ekstremite sinir hasarı olgusunu sunuyoruz. Hastamızda ilaç alımı sonrası rabdomiyoliz, akut böbrek yetersizliği ve hemolitik anemi tabloları ortaya çıktı. Hastanede yatışı sürecinde, kompartman sendromu gelişti. Hasta, fizik tedavi ve rehabilitasyon programına alındı. Tedavi sürecinin ilk dönemlerinde, hastanın sol üst ekstremitesinde, kompleks bölgesel ağrı sendromu tanısı kondu. Dokuz aylık bir tedavi süreci sonunda hastanın sağ eli neredeyse tamamen fonksiyoneldi, ancak sol eldeki sertlik ve atrofi devam etmekteydi.

Keywords: Kompleks bölgesel ağrı sendromu; kompartman sendromu; periferik sinir hasarı; ilaç intoksikasyonu

ÖZET Acute compartment syndrome (ACS) is a painful condition disrupting local circulation due to increased interstitial pressure. Although the most common cause is fractures, vascular injuries without fractures, arterial injuries after interventional procedures, rhabdomyolysis, drunkenness, and coma may also result in ACS. Here we report a case of 21 year-old young woman with bilateral peripheral upper extremity dysfunction after suicidal drug intoxication. She suffered from acute renal failure, rhabdomyolysis and hemolytic anemia. During hospitalisation and dialysis, compartment syndrome and peripheral nerve injury showed up too. After recovering from the life threatening complications, the patient continued her treatment with the physical therapy and rehabilitation program for upper extremity peripheral nerve problems. Unfortunately during this phase she was complicated with complex regional pain syndrome. After a 9 month period of medical and physical therapy, she has a nearly fully functioning right hand but stiffness and atrophy of the left hand still causes disability.

Anahtar Kelimeler: Complex regional pain syndrome; compartment syndrome; peripheral nerve injury; drug intoxication

Acute compartment syndrome (ACS) is a painful condition disrupting local circulation due to increased interstitial pressure and mostly seen at the lower extremities, but upper extremities might be affected too. Although the most common cause of ACS is known to be fractures, isolated vascular injuries, complicated interventional procedures, anticoagulant treatments and pathologies with the increased risk of bleeding, rhabdomyolysis etc. may result in this condition. Once the diagnosis is made, fasciotomy should be performed as early as possible, as delayed decompression will cause irreversible ischemic damage to the muscles.[1-3] Complex regional pain syndrome (CRPS) is an entity characterized by hyperalgesia, allodynia and vasomotor,

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Peer review under responsibility of Journal of Physical Medicine and Rehabilitation Science.

Received: 20 Mar 020 ***Received in revised form:*** 19 Aug 2020 ***Accepted:*** 21 Aug 2020 ***Available online:*** 18 Jan 2021

sudomotor, trophic changes. CRPS is divided into two categories depending on the presence of a primary nerve lesion. CRPS type 1 has no major nerve lesion and is called reflex sympathetic dystrophy. CRPS type 2 has nerve lesion and is called causalgia. The upper limb is more affected than the lower limb in CPRS.[4]

CASE REPORT

A 21-years-old female patient refers to the emergency room a few hours after taking approximately 50 pills of metformin and pheniramidol with suicide intention. She had nausea and womiting but also seemed fully conscious and cooperative. She was hospitalised and monitorised immediately. Her initial laboratory tests revealed elevation in hepatic enzymes, creatin kinase lactate dehydrogenase and urea, creatinine levels. She was diagnosed with acute renal failure (ARF) and rhabdomyolysis so hemodialysis through femoral catheter was initiated at once. Also her low hemoglobin levels, blood smear tests and Coombs tests indicate a drug-induced hemolytic anemia. As she had obscure bilateral upper extremity edema, her parenteral treatment (hydration, eritrocyte suspension etc) was via central venous catheterisation. Her bilateral arm edema progressed and pain started. After consulting to the orthopedics clinics, bilateral upper extremity Doppler ultrasonography (USG) and magnetic resonance imaging (MRI) were performed with suspicion of compartment syndrome. MRI of the bilateral upper extremity was reported as normal including arterial and venous vascular structures and calibration. However there was a diffuse heterogeneous signal increase in T2-weighted fat suppressed sequence within the forearm muscle plans and at the level of the fascia of the muscles (Figure 1). The imaging findings were reported to be consistent with acute-chronic compartment syndrome. Her soft tissue USG displayed edema and fluid echogenity between muscle and fascia plans, too. During follow up, the arms were swollen but the pulses were present so urgent fasciotomy was not planned, however a gradual numbness and weakness started within hours. Neurologic examination revealed that the bilateral ulnar, left radial and median nerves were affected. With further follow up edema and compartment syndrome did not get worse and fasciotomy was not needed. After her recovery of ARF and HA, she was referred to the rehabilitation clinics with muscle weakness and her therapy was immediately started with the diagnosis of bilateral upper extremity multiple nerve injury. The therapy process included therapist-guided exercises, neuromuscular electrical stimulation, transcutaneous electrical nerve stimulation, hot packages and ultrasound therapy. Her first EMG performed including four extremity nerve conduction and upper extremity needle EMG displayed no evidence for polineuropathy or brachial plexopa-

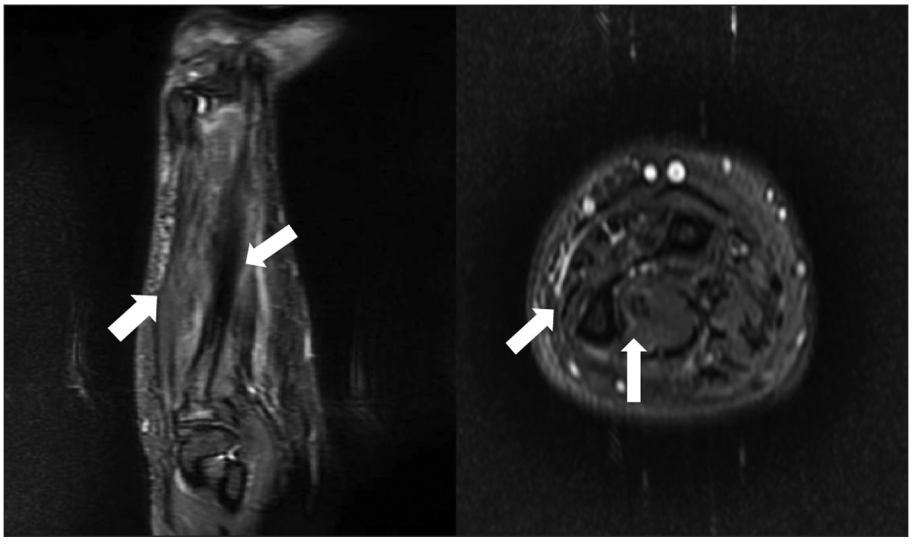

FIGURE 1: T2 weighted fat suppressed sequence shows increased heterogeneous signal intensity of the forearm muscles which indicates edema (arrow).

thy, lower extremity muscles and nerves were normal. However, left radial, ulnar and median nerves had almost complete, axillary and musculocutaneous nerves had partial axonal degenaration in acute-subacute stage. Right radial and axillary, ulnar and median nerves had partial axonal degenaration with no sensory and slightly prolonged motor responses (Table 1).

While the phyical therapy was ongoing, pain and stiffness increased especially on the left arm. Her symptoms and story raised a suspicion of CRPS and the diagnosis was confirmed with a 3 phased bone scintigraphy.

She was already on medication with pregabalin, additionally prednisolone was prescribed which a dramatic effect on the pain and stiffness. However during this period, limitaions on the left hand joints increased with a shortening and contracture of flexor tendons resulting in a flexion contracture of fingers and also atrophy of the intrinsic muscles became prominent.

Follow up EMG after 3 months, compared to the previous EMG was reported as no significant changes

TABLE 1: Electrophysiological findings.

Sensory NCS		**Latency**		**Peak amplitude**		**Velocity**		
Nerve/Sites		**ms**		**µV**		**m/s**		
R-L Median-Digit II		No response^{abc}		No response^{abc}				
R-L Ulnar-Digit V		No response^{abc}		No response^{abc}				
R-L Radial-Thumb		No response^{abc}		No response^{abc}				
L Musculocutaneus- Lat AnBrach		1.46^{a}/1.56^{b}/1.41^{c}		10,5^{a}/11,2^{b}/1.51^{c}				
R Musculocutaneus- Lat AnBrach		2.29^{a}/1.51^{b}/1.51^{c}		34,1^{a} /31,11^{b}/1.41^{c}				
R Sural		2,55^{a}/2.53^{b}/2.41^{c}		12^{a}/12.6^{b}/12.41^{c}		47^{a}/48.1^{b}/47.6^{c}		
L Sural		2,40^{a}/2.38^{b}/2.43^{c}		10^{a}/11.5^{b}/11.41^{c}		45^{a}/47.4^{b}/47.41^{c}		
Motor NCS								
R Median-APB (Wrist)		No response^{ab}/11.56c		No response^{ab}/1.6^{c}				
R Median-APB (Elbow		No response^{ab}/17.60		No response^{ab}/0.9c		No response^{ab}/33.1^{c}		
L Median-APB		No response^{abc}		No response^{ab}/0.9^{c}				
R-Ulnar-ADM (Wrist)		No response^{ab}/5.25^{c}		No response^{ab}/4.6^{c}				
R-Ulnar-ADM (Elbow)		No response^{ab}/11.20^{c}		No response^{ab}/3.7^{c}		No response^{ab}/35.4^{c}		
L-Ulnar-ADM (Wrist)		No response^{ab}/7.40^{c}		No response^{ab}/1.4^{c}		No response^{ab}/28.7^{c}		
L-Ulnar-ADM (Elbow)		No response^{ab}/14.38^{c}		No response^{ab}/1.1^{c}				
R Radial-EIP (Forearm)		2.29^{a}/1.77^{b}/2.19^{c}		1.6^{a}/3.1^{b}/3.3^{c}				
R Radial-EIP (Elbow)		3.39^{a}/1.51^{b}/2.97^{c}		1.3^{a}/2.6^{b}/3.1^{c}				
L Radial-EIP		No response^{abc}		No response^{abc}				
L Axillary-Deltoid		3.33^{a}/4.58^{b}3.54^{c}		2.2^{a}/3.9^{b}/6.5^{c}				
L Musculocutaneus		4.17^{a}/4.58^{b}/4.74^{c}		3.1^{a}/6.7^{b}/5.3^{c}				
R Com.peroneal EDB		4.17^{a}/ 4.11^{b}/4.79^{c}		3.4^{a}/3^{b}/5.8^{c}		42^{a}/43.6^{b}/43.74^{c}		
L Com.peroneal EDB		4.2^{a}/4.24^{b}/4.54^{c}		4.2^{a}/4^{b}/4.66^{c}		43^{a}/42.6^{b}/43.33^{c}		
R Tibial -AH		3.5^{a}/3.4^{b}/3.43^{c}		7.8^{a} /6,7^{b}/7.34^{c}		45^{a}/45.3^{b}/43.81^{c}		
L Tibial -AH		3.4^{a}/3.3^{b}/3.72^{c}		8^{a}/7^{b}/8.71^{c}		46^{a}/46.4^{b}/44.74^{c}		
		Spontaneous Activitiy				**MUAP**		**Recruitment Pattern**		
Summary Muscles	**IA**	**Fib**	**PSW**	**Fasc**		**H.F**	**Amp**	**Dur**	**PPP**	
L Deltoid	N^{abc}	None^{abc}	None^{abc}	None^{abc}		None^{abc}	N^{abc}	N^{abc}	+++^{a}/N^{b}	N^{abc}
L Biceps	N^{abc}	None^{abc}	None^{abc}	None^{abc}		None^{abc}	+^{a}/N^{bc}	+^{a}/N^{bc}	+^{a}/N^{b}	-/N^{bc}
L Triceps	N^{abc}	None^{abc}	None^{abc}	None^{abc}		None^{abc}	N^{a}/N^{bc}	N^{abc}	+^{a}/N^{b}	N^{abc}
R-L Ext Dig Comm	N^{abc}	+++^{abc}	+++^{abc}	None^{abc}		None^{abc}	One^{a}/+^{bc}	No^{ab}/+^{c}	-^{abc}	-^{abc}
R-L First D Inteross	N^{abc}	+++^{abc}	+++^{abc}	None^{abc}		None^{abc}	MUP^{abc}	No^{ab}/MUP^{c}	-^{abc}	-^{abc}
R-L Abs Poll Brevis	N^{abc}	+++^{abc}	+++^{abc}	None^{abc}		None^{abc}	MUP^{abc}	No^{ab}/MUP^{c}	-^{abc}	-^{abc}

R: Right; L: Left; Lat AnBrach: Lateral antebrachial; APB: Abductor pollicis brevis; ADM: Abductor digiti minimi; EIP: Extensor indicis pollicis; EDB: Extensor digitorum brevis; AH: Abductor halluc; No: No activation.

a: First EMG; b: Second EMG; c: Third EMG.

observed in the left median and ulnar nerves, whereas axillary and musculocutenous nerves were significantly and bilateral radial nerves were moderately improved (Table 1).

At the 8 months follow up, her right hand is nearly fully recovered with a minimal clawing and sensory loss due to slight median and radial neuropathy (Table 1). However her left hand is still partially anesthetic, with flexion of 2nd and 3rd fingers due to tethering of flexor tendons and intrinsic muscle atrophy. This is also verified by the last EMG reporting left partial, median and radial, total ulnar neuropathy in the chronic stage. Her physical therapy is still ongoing.

The patient was informed about the case report and written informed consent form was obtained.

DISCUSSION

ACS is, increased pressure in one or more muscle fascial spaces, leading to decreased perfusion pressure resulting in muscular and nerve ischemia. It's a clinical entity characterised by "5Ps": pain, pulselessness, pallor, paresthesia, and paralysis. The most prominent symptom is pain, and pain often does not respond well to analgesics. Other symptoms may not always be present so their absence does not exclude the diagnosis. While paresthesia and paralysis are delayed findings, edema is an early symptom.[5] In many studies, open or closed fractures have been reported as the most common cause of CS. Soft tissue and/or vascular injuries without fractures are other important causes of ACS.[1]

Rhabdomyolysis has been reported to be associated with ACS in as much as 23% of cases. Rhabdomyolysis is caused by the passage of intracellular elements into systemic circulation as a result of the muscle tissue damage. The possible underlying causes are trauma, drugs, toxins, infections, ischemia, electrolyte imbalance and metabolic disorders, genetic diseases, neuroleptic malign syndrome and malign hyperthermia.[1]

ARF is the most common (with an incidence of 10% to 55%) systemic complication of rhabdomyolysis with a poor prognosis.[6]

In our case; ARF has developed due to rhabdomyolysis and hemolytic anemia after drug intoxication. In the literature, there are case reports about lactic acidosis, rhabdomyolysis, hemolytic anemia and ARF due to metformin.[7-9]

The patient's compartment syndrome was linked to rhabdomyolysis but her compartment syndrome was not serious enough to require a fasciotomy however nerve injury gradually evolved. Ischemic neuropathy in distal tissues may result in muscle contracture or necrosis. Besides pressure rise can be exacerbated by reperfusion. It is believed that reperfusion triggers an inflammatory response against the breakdown products of ischaemic tissue, causing further cellular and tissue edema.[1] This may be the reason of further nerve tissue damage. Critical disease polyneuropathy has not been considered in this case because the lower limb nerve conduction velocities was normal and the upper limb was asymmetrically affected (significant influence on the left). The control EMG examination performed 3 months later showed improvement in the upper extremity proximal nerves, needle EMG of the proximal muscles and suspicious denervation findings were detected in the first EMG. For all these reasons, the improvement in some nerves has been interpreted in favor of healing of the mild neuropathy due to edema and inflammatory process. When the hand rehabilitation process started, she was actually recovered from other physical problems, and participating willingly but this time another painful condition/complication disrupted her therapy process.

The series of unfortunate events about our patient starts with the suicidal attempt causing drug intoxication leading rhabdomyolysis and ARF, continues with probable compartment syndrome and ischemic neuropathy and becomes more complicated with coexistence of CRPS. The result of all of these, is the bilateral peripheral upper extremity dysfunction of a 21 year old young girl otherwise healthy.

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