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CASE REPORT

Lead Toxicity due to Ingestion of Lead-Contaminated Opium in a Patient Presenting with Motor Neuropathy and Upper Limb *Paresis*

A case report

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التسمم بالرصاص نتيجة لابتلاع أفيون ملوث بالرصاص عند مريض أظهر اعتلالا عصبيا حركيا وخزل بالطرف العلوي

تقرير حالة

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ABSTRACT: Opium users may present with central or peripheral nervous system-related symptoms, gastrointestinal complications and anaemia; in such cases, lead poisoning should be suspected and chelation therapy initiated as soon as possible. We report a 64-year-old male patient with a 20-year history of opium addiction who was referred to the Imam Reza Hospital, Birjand, Iran, in 2017 with severe motor neuropathy and *paresis* in both upper limbs. His primary symptoms were generalised weakness, abdominal and bone pain, constipation and lower limb paraesthesia that had started several months prior. In addition, he reported severe progressive bilateral *paresis* of the upper limbs of one month's duration. A diagnosis of lead poisoning was confirmed by a blood lead level of 140 µg/dL. The patient underwent chelation therapy after which he improved significantly. At a one-year follow-up visit, he was neurologically intact and symptom-free.

Keywords: Opium Dependence; Lead Poisoning; Lead-Induced Nervous System Diseases; Paresthesia; Case Report; Iran.

الملخص: يظهر مستخدمو الأفيون أعراضا مرتبطة بالجهازين العصبي المركزي والطرفي ومضاعفات معدية معوية وفقر دم؛ وفي هذه الحالات ينبغي الاشتباه في التسمم بالرصاص، والبدء في العلاج بالاتحاد المخلبي بأسرع ما يمكن. ونسجل هنا حالة رجل عمره 64 عاما ظل يستخدم الأفيون لمدة 20 سنة وصار مدمنا له وتم تحويله عام 2017م إلى مستشفى الإمام رضا ببيرجند في إيران، وهو مصاب باعتلال عصبي مفرط وخَزَل بالطرفين العلويين. وكانت الأعرض الرئيسة عنده هي وهن عام، وآلام في البطن والعظام، وإمساك، ومَذَل في الطرفين السفليين، وهي أعراض بدأت عند هذا المريض قبل عدة شهور قبل تحويله للمستشفى. كذلك حدث للمريض خَزَل بالطرفين العلويين قبل نحو شهر. وأثبت فحص للدم وجود تسمم بالرصاص، إذ أن تركيزه بلغ 140 ميكروجرام/100 مل من الدم. وتم إجراء علاج مخلبي للمريض أدي لتحسن حالة المريض بصورة ملحوظة. وعند مراجعة المريض للمستشفى بعد عام على ذلك العلاج وجد أنه سليم عصبيا وليست لديه أي أعراض.

الكلمات المفتاحية: إدمان الأفيون؛ التسمم بالرصاص؛ أمراض الجهاز العصبي التي يسببها الرصاص؛ مَذَل؛ تقرير حالة؛ إيران.

Exposure to certain toxic agents results in neurotoxicity which may lead to cognitive and memory disabilities, mood changes and even predispose the affected patient to psychiatric problems such as depression, anxiety and irritability.[1] In factories producing glazed tiles, canned food, paint and cosmetics, workers may be affected by the presence of inorganic lead; in addition, drinking water and dust may be contaminated from industrial sources and motor vehicles.[2,3] Another source of potential exposure is the presence of organic lead in opium.[4,5] Lead may be intentionally added to the drug to increase its weight for profit-related reasons or it may be introduced accidentally during the production process.[4–7] Subsequently, the lead is ingested by opium users either orally or via inhalation.[6,8]

In recent years, lead poisoning due to the ingestion of lead-contaminated opium has become a major health concern in Iran.[4–9] According to Ghane *et al.*, more than 4,000 patients with lead poisoning due to opium ingestion were referred in under one year to clinical centres in Iran with abdominal pain and constipation.[10] Moreover, the researchers estimated that over 260,000 out of >700,000 opium users remained untreated and at risk of lead poisoning.[10] This case report describes a patient who presented to Imam Reza Hospital, the main referral centre for poisoning cases in the South Khorasan province of Iran, with severe lead-induced motor neuropathy due to the ingestion of lead-contaminated opium.

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Case Report

A 64-year-old male patient was referred to the Imam Reza Hospital, Birjand, in 2017 with generalised weakness, abdominal and bone pain, constipation and lower limb paraesthesia that had first started several months prior. The patient had then developed severe *paresis* in both upper limbs 30 days previously. He reported a 20-year history of oral opium use consisting of approximately 5 g daily. A urine drug analysis was positive for opium. Upon examination, the cranial nerves were normal, as were lower limb deep tendon reflexes; however, deep tendon reflexes in the upper limbs, biceps and triceps were absent. No sensory impairment was detected. The muscular power in the upper limbs was 2/5 and 1/5 in the proximal and distal areas, respectively, while the lower limbs were normal. The median and ulnar nerves were moderately affected, while the radial nerve was severely affected; the patient also had bilateral wrist drop.

Imaging studies yielded normal results, including brain and cervical magnetic resonance imaging (MRI), computed tomography (CT), a chest X-ray and abdominal ultrasonography. Brain CT and MRI scans revealed no evidence of a mass, haemorrhage, hydrocephalus or abnormalities in the basal *ganglia* and posterior *fossa* structures. No established infarct and intra- or extra-axial collections were detected in the major vessel vascular territory. The basal cisterns and *foramen magnum* were patent. The chest X-ray showed an increase in bilateral bronchovascular markings with no other abnormalities. Whole body bone scintigraphy was performed to rule out malignancy; this showed only minor tracer uptake throughout the skeleton. An endoscopy and colonoscopy revealed a 7-mm polypoid lesion in the D1-D2 junction of the duodenum and internal haemorrhoids in the anus. Electromyography confirmed chronic motor-sensory polyneuropathy with axonal features which were more severe in the upper limbs. Critically, the patient's blood lead level was 140 µg/dL (normal range: <10 µg/dL). Table 1 shows the results of various other laboratory tests. Nerve conduction and F-wave parameters are shown in Tables 2–4.

Based on his blood lead level, the patient was diagnosed with lead poisoning and admitted to hospital. He was initially treated with 4 mg/kg of dimercaprol via deep intramuscular injection every four hours, followed by 1,300 mg/day of intravenous calcium disodium ($CaNa_2$) edetate four hours after the first dose of dimercaprol. After five days of parenteral treatment, his blood lead level was 60 µg/dL. He was discharged and prescribed 10 mg/kg of oral succimer, initially every eight hours for five days followed by every 12 hours for 14 days. After 21 days of treatment, his clinical symptoms began to improve, particularly the abdominal pain, generalised

Table 1: Laboratory test results of a 64-year-old male opium addict with severe lead-induced motor neuropathy

Variable	Result	Normal range
White blood cell count in $\times10^3/mm^3$	8.1	4–10
Haemoglobin in g/dL	9.6	14–18
Haematocrit in %	30.5	Males: 45–52 Females: 37–48
MCV in femtolitres	83.6	80–96
MCH count in pg	27.1	27–33
MCHC in %	32.5	32–36
Platelet count in $\times10^3/mm^3$	206	150–450
Vitamin B_{12} in pg/mL	1,178	160–950
Folic acid in ng/mL	6	2–20
Serum iron in µg/dL	36.8	65–176
TIBC in µg/dL	176	240–450
Ferritin in ng/mL	338.9	12–300
Serum vitamin D in ng/mL	9.55	20–50
T3 in pg/mL	4	2.3–4.2
T4 in ng/dL	9.9	4.5–11.5
TSH in µIU/mL	0.5	0.5–4.7
T3RU in %	36.7	24–37
AST in U/L	50	<37
ALT in U/L	55	<41
Alkaline phosphatase in U/L	188	80–306
Total bilirubin in mg/dL	1.2	<1.1
Direct bilirubin in mg/dL	0.4	<0.6
Creatinine in mg/dL	1	0.5–1.4
Prothrombin time in seconds	13	10–13.5
Partial thromboplastin time in seconds	28	25–35
INR	1	<1.1
Wright agglutination test	Negative	Negative
2ME	Negative	Negative
ANAs	Negative	Negative
Rheumatoid factor	Negative	Negative
Anti-ds-DNA in IU/mL	2.37	<10
Serum albumin in g/dL	3.6	3.5–5
α-globulin in g/dL	0.2	0.1–0.3
α-2-globulin in g/dL	0.8	0.6–1
β-globulin in g/dL	0.7	0.7–1.2
γ-globulin in g/dL	1.1	0.7–1.6

MCV = mean corpuscular volume; MCH = mean cell haemoglobin; MCHC = mean corpuscular haemoglobin concentration; TIBC = total iron-binding capacity; T3 = triiodothyronine; T4 = thyroxine; TSH = thyroid-stimulating hormone; T3RU = T3 resin uptake; AST = aspartate aminotransferase; ALT = alanine aminotransferase; INR = international normalised ratio; 2ME = 2-mercaptoethanol; ANAs = antinuclear antibodies; ds = double-stranded.

Table 2: Motor nerve conduction parameters of a 64-year-old male opium addict with severe lead-induced motor neuropathy

Nerve and site/segment	Latency in ms	Amplitude in mV	Distance in mm	Velocity in m/s
Right median APB				
Wrist	3.6	1.4	-	-
Wrist-elbow	8.9	1.3	240	44.5
Left median APB				
Wrist	3.3	1.0	-	-
Wrist-elbow	8.2	0.959	240	39.3
Right ulnar ADM				
Wrist	2.7	2.2	-	-
Wrist-below elbow	7.0	1.9	260	40.8
Left ulnar ADM				
Wrist	2.4	1.7	-	-
Wrist-below elbow	7.1	1.5	260	39.4
Right radial EIP				
Forearm	Absent	Absent	-	-
Elbow	Absent	Absent	-	-
Below spiral groove	Absent	Absent	-	-
Left radial EIP				
Forearm	Absent	Absent	-	-
Elbow	Absent	Absent	-	-
Below spiral groove	Absent	Absent	-	-
Right DPN EDB				
Ankle	3.5	1.8	-	-
Ankle below FH	9.1	1.7	-	-
Below FH-PF	9.8	1.8	350	41.3
Left DPN EDB				
Ankle	5.1	1.8	-	-
Ankle below FH	12.1	1.9	-	-
Below FH-PF	12.8	1.8	340	38.4
Right tibial AHB				
Medial ankle	6.3	3.1	-	-
Medial ankle-PF	14.3	2.9	380	37.7
Left tibial AHB				
Medial ankle	5.1	3.9	-	-
Medial ankle-PF	13.6	4.3	380	44.3

APB = abductor pollicis brevis; ADM = abductor digiti minimi; EIP = extensor indicis proprius; DPN = deep peroneal nerve; EDB = extensor digitorum brevis; FH = fibula head; PF = popliteal fossa; AHB = abductor hallucis brevis.

weakness and weakness in the upper limbs. However, at a three-month follow-up appointment, the patient reported that the upper limb weakness still persisted; moreover, his blood lead level was 44 µg/dL.

Table 3: Sensory nerve conduction parameters of a 64-year-old male opium addict with severe lead-induced motor neuropathy

Nerve	Latency in ms	Amplitude in uV	Distance in mm	Velocity in m/s
Right median	4.0	14.6	130	43.1
Left median	3.6	9.64	130	47.2
Right ulnar	3.8	16.9	110	51.4
Left ulnar	3.5	14.3	110	50.4
Right radial	3.3	13.1	90	56.4
Left radial	3.1	15.3	90	60.5
Right sural	3.1	3.55	-	-
Left sural	2.7	3.0	-	-

Table 4: F-wave parameters of a 64-year-old male opium addict with severe lead-induced motor neuropathy

Nerve	Latency in ms				F/M amplitude in uVms	F %
	M	F-M	F min	F max		
Right median APB	4.3	24.2	28.6	31.1	0.11	50
Left median APB	3.7	22.0	25.7	32.1	0.14	60
Right ulnar ADM	0.1	28.2	28.3	33.0	0.07	100
Right tibial AHB	6.4	48.3	54.7	62.3	0.05	75
Left tibial AHB	0.1	54.1	54.2	54.7	0.03	66

min = minimum; max = maximum; APB = abductor pollicis brevis; ADM = abductor digiti minimi; HB = abductor hallucis brevis.

Due to a shortage of succimer, D-penicillamine treatment was initiated at a dose of 250 mg every eight hours for 10 days. After this, a neurological examination was normal, including examination of the power in the upper limbs, although the patient still complained of some upper limb weakness. He was referred to a rehabilitation clinic to undergo methadone maintenance therapy. One year later, his blood lead level was 20 µg/dL and the upper limb weakness had completely resolved.

Discussion

Symptoms of acute lead poisoning include nausea, headaches, cognitive problems and emotional impairment, while chronic lead exposure may cause fatigue, a decline in brain and cognitive function, motor impairment, psychiatric problems and, in some cases, a decline in nerve conduction velocity.[11,12] Critically, initial symptoms of irritability, headache, fatigue, memory loss and tremors may progress to weakness, limb paralysis, seizures, delirium and hallucinations, coma and, eventually, death.[13] As such, the early detection and immediate treatment of lead poisoning is imperative.

Neuropathy due to the ingestion of lead-contaminated opium is uncommon, with most patients presenting with anaemia and gastrointestinal symptoms.[14,15] A comb-

ination of motor and sensory nervous system impairment, as seen in the current case, is even less common. Lead-induced neuropathy commonly affects the radial and peroneal nerves and *extensor* muscles, resulting in wrist and foot drop, while sensory processing disorders are less frequent.[2,16] Beigmohammadi *et al*. reported a 40-year-old male oral opium addict who presented with weakness of the limbs due to severe lead poisoning (blood lead level: 200 µg/dL).[17] The patient had digestive symptoms (including stomach aches and constipation) and severe weakness of the upper and lower limbs, although sensation was normal. Despite treatment with $CaNa_2$ edetate, dimercaprol and oral succimer, the patient remained quadriplegic, although both his blood lead levels and gastrointestinal symptoms improved.[17]

Toxic-metabolic polyneuropathy may be induced by extrinsic or intrinsic metabolites which are toxic to the peripheral nerves, resulting in damage to the axial cylinders of the axons. The severity of this damage is dependent on the level of toxicity, duration of exposure and genetic characteristics of nervous tissue metabolism.[18] Clinically, the damage manifests as both sensory impairment and muscle weakness, although muscle wasting and severe trophic disorders may also occur. In these cases, electroneuromyography would show a decrease in the amplitude of peripheral nerve sensory potentials and muscle action potential.[18] In patients with axonal-type polyneuropathy, there is often sufficient retention of motor function—in the absence of severe *paresis*—while sensory and trophic impairments are disabling. Axonal nerve damage develops slowly and gradually, although it is potentially reversible with appropriate treatment.[18]

In the current case, the patient developed both motor and sensory neuropathy due to long-term exposure to high levels of lead. However, all neurological symptoms completely resolved after treatment with chelating agents. Most patients with sensory complications are resistant to treatment and a full recovery is not expected, even after chelation therapy.[16] This case emphasises the importance of the timely diagnosis and treatment of cases of lead toxicity in order to reverse central and peripheral nervous system-related symptoms.

Conclusion

Opium addicts are predisposed to developing lead toxicity resulting from the ingestion of lead-contaminated opium. This may result in the development of serious symptoms such as cognitive, sensory and motor impairment, with delays in diagnosis and treatment potentially resulting in irreversible neurological damage. As such, lead poisoning should be suspected among opium users with central or peripheral nervous system-related symptoms, gastrointestinal complications and anaemia. Chelation therapy should be initiated as soon as possible in such cases.

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