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Case Report

The copper conundrum: a case of toxicity and altered mental status in a young male with opioid dependency

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ABSTRACT

Copper is a trace element with higher concentrations in the brain, liver, and kidneys. Its toxicity is rare in humans because of its homeostatic mechanisms. This case highlights a 30-year-old male with a history of opioid abuse and occupational exposure to metallurgy. Despite treatment, a gradual neurological worsening prompted us for heavy metal screening and nerve conduction velocity study (NCV) which revealed copper toxicity and demyelinating polyneuropathy. Following the initiation of D-penicillamine therapy, he showed gradual improvement. The coexistence of opioid abuse and dependency posed challenges in the clinical presentation, necessitating a comprehensive approach to effectively manage both opioid withdrawal and evaluation for other toxic substances.

Keywords: Toxicity, Copper, Opioid, Polyneuropathy

INTRODUCTION

Copper, a trace element essential for various physiological processes, is tightly regulated in the body to prevent toxicity.[1] We describe a case of a 30-year-old male with a history of opioid abuse and occupational exposure to metal pipes, highlighting the unique challenges posed by the coexistence of copper toxicity and opioid abuse in the clinical setting. The rarity of copper toxicity emphasizes the importance of early recognition and tailored management strategies in drug abuser.

CASE REPORT

A 30-year-old male, employed in the metal pipe industry, had a chronic history of headaches for 3 years. He had been regularly using analgesics including tramadol and codeine syrup to manage his headaches and suffered from opioid abuse and dependency. Ten days back, he developed a sudden onset severe headache at night, and the next morning, was found unconscious. Initially admitted to another hospital, he was treated with Naltrexone with the suspicion of opioid toxicity, which resulted in a gradual improvement in his sensorium. Two days later, he developed a generalized tonic-clonic seizure (GTCS). At this time, he presented with a low-grade fever, tachycardia, and blood pressure (BP) of 180/100 mmHg. Initial evaluation showed leukocytosis of 18,000/µl and non-oliguric acute kidney injury (AKI) (creatinine level of 3 mg/dl). He was treated with anti-epileptics and broad-spectrum antibiotics were initiated for suspected aspiration pneumonia. Subsequently, he was referred to our center for further management. Upon examination, he was drowsy and restless, with a GCS score of E3V1M6. He had tachycardia with a BP of 150/80 mmHg, axillary temperature of 100.4°F, and oxygen saturation of 95% on room air. Pupils were 4 mm dilated with sluggish reactivity to light. There was no neck rigidity, and bilateral planters were flexor. Multiple IV injection marks were noted on his non-dominant arm (Figure 1). To address his symptoms, Fentanyl infusion was initiated. Initial investigations showed neutrophilic leukocytosis, elevated inflammatory markers, non-oliguric acute kidney injury, transaminitis, and deranged coagulation profile (Table 1). Blood and urine cultures were sterile. The fever workup, including serology for common flu strains and tropical fevers, was negative (Table 1). Hepatitis, herpes, and human

immunodefiency virus (HIV) serologies were negative. The possibility of meningoencephalitis was considered; however, magnetic resonance imaging (MRI) brain, electroencephalography, and cerebrospinal fluid (CSF) study were unremarkable (Table 2).

Table 1: Baseline investigations of patient in our hospital.

Tests	Report
Hemoglobin	13.6 g/dl
Total leucocyte count	16680/ul
Platelet count	425 thous/ul
Creatinine	1.79 mg/dl
Sodium	147 mmol/l
Potassium	4.93 mmol/l
Uric acid	8.35 mg/dl
Total/direct bilirubin	0.64/0.32 mg/dl
AST/ALT	411/246 IU/l
ALP/GGT	80/311 IU/l
S. Albumin	4.54 g/dl
S. Ammonia	44.23 umol/l
ESR	42 mm in 1st hour
CRP	47 mg/l
CPK	12,452 U/l
Malaria antigen test	Negative
Dengue NS1/IgM/IgG	Negative
Scrub typhus IgM	Negative

Table 2: CSF examination of the patient test.

Tests	Report
CSF cell count (100% lymphocyte)	3/ul
CSF protein	30.70 mg/dl
CSF glucose	80 mg/dl
CSF LDH	23 U/l
CSF ADA	0.07 U/l
CSF culture	Negative
CSF bio-fire multiplex PCR	Negative
CSF ZN stain/Xpert MTB	Negative
CSF India ink preparation	Negative
CSF autoimmune encephalitis panel	Negative

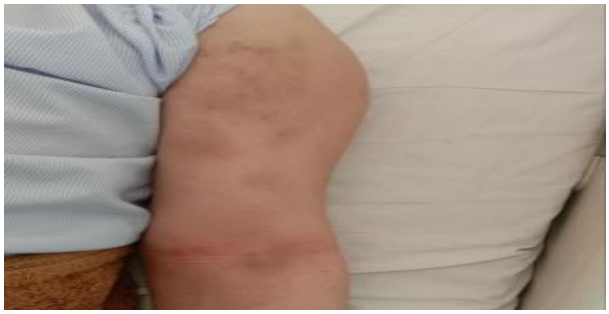

Figure 1: Photograph depicting multiple IV injection marks on the left arm.

Given the background of possible drug abuse and occupational exposure, a drug toxicology and heavy metal screen were conducted, which revealed elevated urine and serum copper levels measuring 127 µg/l and 176.6 ug/dl respectively. Notably, serum ceruloplasmin levels were normal, indicating copper toxicity. NCV showed bilateral symmetrical demyelinating motor neuropathy in the lower limbs. He was treated with D-penicillamine with gradual improvement on follow-ups.

DISCUSSION

Copper, a trace element is found in higher concentrations in brain, liver, and kidneys.[1] It serves as an essential catalyst for various redox reactions. Hence, in excess, free copper ions can lead to oxidative stress leading to cellular and DNA damage causing impaired cell growth.[2] Copper toxicity can be classified as primary, resulting from inherited metabolic defects as in Wilson disease, or secondary, caused by increased intake or reduced excretion due to underlying diseases.[3] The incidence of copper poisoning varies across regions, being more prevalent in South Asian countries, particularly in rural populations.[4]

Our case involves a 30-year-old male with a history of opioid abuse and occupational exposure to metallurgy. On his initial presentation, opioid toxicity was suspected and managed. He later developed GTCS. The possibility of opioid withdrawal was considered. However, him being a drug abuser, we further pursued and investigated possible drugs and heavy metal exposure which uncovered copper toxicity.

Copper toxicity in this case could be due to occupational exposure, commonly found in metalworking industries. Nanoparticulate, produced during industrial processes like welding fumes, electric motors, and electronic cigarettes, can be released into the environment.[5-7] They have a high risk of accumulating in the brain over time, but studies on their potential impact on neurodegeneration are lacking.[8] Although direct copper nanoparticle-induced toxicity to the human brain hasn't been established, research suggests that combustion-derived nanoparticles enter the brain through olfactory nerve, causing neuroinflammation and cognitive impairments.[9]

The presentation of acute copper toxicity depends on the mode of copper overload. Ingestion-related cases commonly exhibit symptoms associated with erosive gastropathy. Neurological symptoms such as depression, fatigue, irritability, excitation, and difficulty focusing are reported and may accompany these gastrointestinal effects. Severe toxicity can cause rhabdomyolysis, cardiac and renal failure, methemoglobinemia, hemolysis, hepatic necrosis, encephalopathy, and death. Chronic copper toxicity is rare and can result in neurological and hepatic manifestations, which align with the patient's symptoms and abnormal laboratory findings.[10]

Miyakawa et al were pioneers in investigating the role of copper in peripheral neuropathy among patients with Wilson's disease demonstrating demyelination and axon involvement in biopsy. Their hypothesis pointed towards disruptions in copper metabolism affecting Schwann cells and myelin sheath.[11] Subsequently, Leven et al and Jung et al also documented cases of peripheral neuropathy in individuals with Wilson's disease, further emphasizing that the role of copper metabolism in these fibers must be reconsidered.[12,13]

CONCLUSION

This case report highlights the rarity of copper toxicity and its unusual manifestations, attributed to the precise homeostatic control in the body. The presence of opioid abuse and dependency complicated the clinical presentation. The importance of early recognition of copper toxicity in drug abusers and tailored treatment strategies is emphasized, as is the need for further research on occupational copper exposure and its potential impact on neurodegeneration.

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