SUCCESSFUL THERAPY WITH 2,3 MESO DIMERCAPTOSUCCINIC ACID (CHEMET®) IN A WORKER WITH SEVERE LEAD POISONING

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SUMMARY: Working conditions for the majority of the world's workers do not meet the minimum standards and guidelines set by national and/or international agencies (1). Lead is believed to be the most toxic metal at the workplace. Therefore, the risk can be substantially reduced by effective local exhaust ventilation systems. This case report describes disappearances of severe basophilic stippling, anemia with decreased reticulocyte count, restoration of essential enzyme activity and resolution of symptoms in a 24 year old male working in the production of lead batteries plant using 2,3 meso dimercaptosuccinic acid 30 mg/kg body weight every eight hours for five days.

Key Words: Lead (Pb), Blood Lead Level (BPb), Meso 2,3 dimercaptosuccinic acid (Chemet®), δ aminolevolinic Acid Dehydratase (ALAD).

BACKGROUND

Inhalation of lead fumes and dust in the workplace is regarded as the most common source of lead toxicity. Primary target organs from occupational lead (Pb) exposure in battery manufacturing workers are the hematopoietic system, central and peripheral nervous systems, reproductive, gastrointestinal, renal, hepatic and cardiovascular systems (2). Inadequate prevention and control measures at the workplace constitute as the major factors contributing to occupational health hazards to lead workers (3). This case report emphasizes on the significant use of oral meso 2,3 dimercaptosuccinic acid (Chemet®) in severe lead poisoning.

CASE PRESENTATION

A 24 year old male reported to the clinic complaining of metallic taste in the mouth, severe abdominal pain in the form of cramps, vomiting, lack of appetite, constipation, fatigue, joint and muscle pains, decreased memory, apathy, irritability, lack of concentration and decreased libido. Upon admission, physical examination revealed a thin, pale young male with fine tremors and normal vital signs. Brown coloration of the fingers and toe nails, and blue lines (lead lines) at the gingivodental junction were observed (Figures 1 and 2) respectively. Diffuse hypotonia and depressed deep tendon reflexes were detected.

Occupational history revealed that he has been working at a battery plant (operator of a plate formation machine) for 2 years without any prevention measures taken. Laboratory investigation showed a: Hemoglobin (Hb) 8.4 g/dL; Hematocrite (Hct) 0.29; Reticulocyte count 0.138; White Blood Count (WBC) 10,000; Blood lead level (BPb) 384 ug/dl (acceptable range 50 ug/dl); 24 hour Urinary Lead: excretion 1345 ug/dl (Table 1).

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Table 1: Laboratory results prior to chemet therapy.

Hb	8.4 g/dl	normal 16 ± 2
Hct	0.29	normal .046 ± 0.05
Reticulocyte count	0.138	normal 0.005-0.015
WBC X 10^9 / L	10.000	normal 4.0-10
B - Pb	384 ug/dl	normal <40 ug/dl
24 / h Urinary - Pb	1345 ug/dl	normal <80 ug/dl

Table 2: Additional laboratory results prior to chemet therapy.

Coproporphyrine III		5,712 ug/24 hour
ALA-D		53 Units/Activity

Delta aminolevulinic acid dehydratase (ALAD) 53 Units /Activity and 24/hr. and Urinary Coproporphyrin III: 5,712 ug/24 hour (Table 2). Bone marrow smear revealed several areas showing myeloid elements of unremarkable sequence; erythroid elements of all stages of maturation with severe basophilic stippling and occasional megakaroyocytic elements (Figure 3). Liver and kidney function tests were within normal levels. ECG showed sinus rhythm with normal axis. Electromyelograph showed mild to moderate reduction of recruitment and long duration polyphasic potential. Nerve conduction velocity revealed low amplititude of peripheral motor nerve with slow times which are consistent with mild axonal neuropathy of chronic nature such as chronic lead poisoning. Semen analysis was carried out and it revealed a count of 37 million/ml with low motility of which 40% were dead; 20% sluggish and 40% active. The patient received a five day course of Chemet® 30 mg/kg body weight eight hourly. Prior to treatment base line serum chemistry, iron, total iron binding capacity, calcium and magnesium were also measured and were within normal levels.

Table 3: Laboratory results following chemet therapy (five day course).

Hb	12.7 g/dl	normal 16 ± 2
Hct	0.42	normal .046 ± 0.05
Reticulocyte count	0.017	normal 0.005-0.015
B - Pb	97 ug/dl	normal <40 ug/dl
24 / h Urinary - Pb	16.580 ug/dl	normal <80 ug/dl

Table 4: Results of enzyme activity following chemet therapy.

Coproporphyrine III		25 ug/24 hour
ALA-D		230 Units/Activity

The patient was discharged on the 7th day of admission post Chemet® therapy with restoration of normal values as observed in Tables 3 and 4 respectively. Figures 4 and 5 show the disappearance of the brown coloration of fingers and toe nails as well as the restoration of normal gingival tissue. Treatment was resumed for another five days after one month without further exposure to lead and a follow up measurement of blood lead level were determined.

Figure 1: Brown coloration of the fingers and toe nails prior to Chemet therapy.

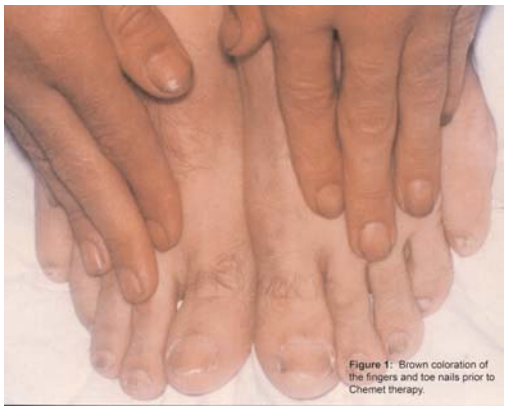


Figure 2: Blue lines (lead lines) at the gingivodental junction prior to Chemet therapy.

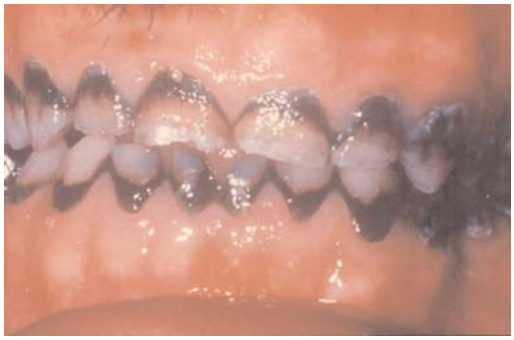


Figure 3: Bone marrow smear showed several areas showing myeloid elements of unremarkable sequence; erythroid elements of all stages of maturation with severe basophilic stippling and occasional megakaroyocytic elements prior to Chemet therapy.

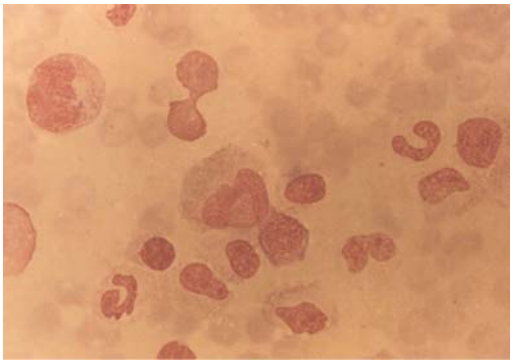


Figure 4: Disappearance of the brown coloration of the fingers and toe nails following to Chemet therapy.

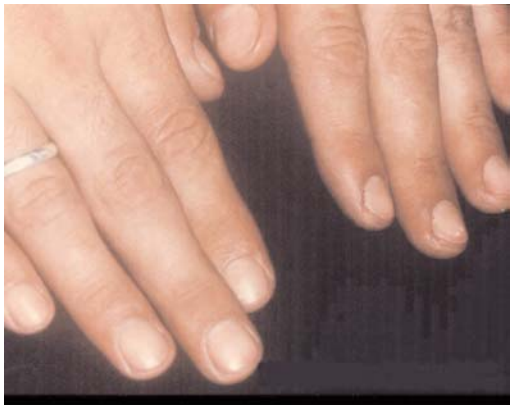
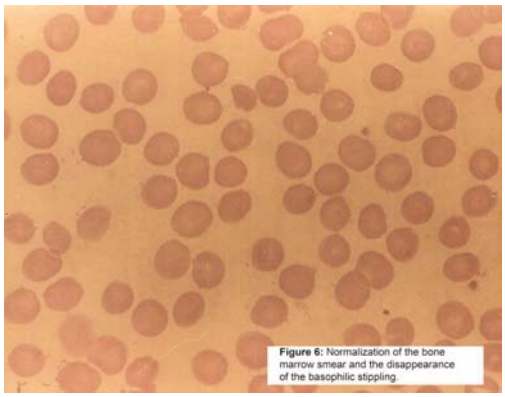


Figure 5: Disappearance of the blue lines following to Chemet therapy.

Figure 6: Normalization of the bone marrow smear and the disappearance of the basophilic stippling.



DISCUSSION

Lead is a ubiquitous substance found in air, soil and water and recognized more than thousand of years for its toxic effects on human health (4). Incidences of occupational exposure to lead fume and dust remain the most common cause of chronic lead poisoning. Chronic lead toxicity in adults results primarily from workplace exposure. Lead exerts its toxic effects through several biochemical mechanisms via the disruption of certain enzymes necessarily for heme biosynthesis. The hematological abnormalities of lead poisoning such as normochromic and normocytic anemia, reticlutocytosis and basophilic stippling of the erythrocytes were the prominent findings in this case. These abnormalities can be attributed to (a) inhibition of heme biosyenthesis and (b) short life span of circulating erythrocytes thus resulting in stimulation of erythropoiesis. High excretion of ALAD and coproporphyrin III in the urine are attributed to lead induced derangement of heme synthesis. Enzymes of significant sensitivity to lead toxicity are ALAD and 5´ pyrimidine nucleotidase. Inhibition of ALAD and coproporphyrin causes significant accumulation of ALAD and coproporphyrin in the urine. While reticulocytosis and basophilic stippling results from the inhibition of 5´ pyrimidine nucleotidase.

Clinical manifestations of lead poisoning varies from one individual to another, thus may present with the classical clinical picture of which abdominal pain, constipation or diarrhea, nausea, vomiting, pallor, fatigue, irritability, loss of memory and lack of concentration are frequently seen in individuals with chronic lead poisoning. However, the diagnosis is not confirmed unless high blood lead levels are determined.

The mainstay in the treatment of chronic lead poisoning is chelation therapy. Calcium disodium ethylenediaminetetraacetate (CaNa2EDTA) has been used substantially until oral therapy with Chemet® has been

introduced in early 1990s (5). Chemet® appears to offer several advantages over EDTA (6). It is an oral chelating agent well tolerated, proved to be effective and safe for the treatment of acute lead poisoning in children with blood lead levels above 40 ug/dl and adults respectively (7,8). It is an analog of dimercaprol, forms water soluble compounds which have the ability to form complexes with intracellular lead due to its lipophilic nature which are subsequently excreted via the kidney (9).

CONCLUSION

Using oral Chemet® has proven to be efficacious in reducing blood lead concentration and increasing urinary lead excretion as shown in Table 3. Figure 5 shows complete disappearance of basophilic stippling which suggest the restoration of 5´ pyrimidine nucleotidase an enzyme necessary for the maturity of erythrocytes (10). Furthermore, this case indicates that the lead content of the blood, soft tissue, and other skeletal compartments were depleted by Chemet®, thus many of the toxic effects of lead were reversible once chelation therapy was initiated.

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