Toxicology Reports 11 (2023) 444–448

Contents lists available at ScienceDirect

Toxicology Reports

journal homepage: www.elsevier.com/locate/toxrep

"Heavy Metal": Management of lead toxicity following a gunshot injury with retained lead fragments, a case report

Ilaria Costantini [a,1], Massimo Carollo [b,*,1], Lorenzo Losso [c], Elia Morando [a], Matilde Bacchion [a], Giovanni Mantelli [a], Mauro Pizzuto [d], Letizia Spagnuolo [d], Maria Vittoria Ventura [d], Giorgio Ricci [a]

[a] USD Poison Control Center, Azienda Ospedaliera Universitaria integrata, Verona, Italy
[b] Department of Diagnostics and Public Health, University of Verona, Verona, Italy
[c] Department of Medical Toxicology Unit and Poison Control Centre, University of Florence, Florence, Italy
[d] Department of Medicine, University of Verona, Verona, Italy

ARTICLE INFO

Handling Editor: L.H. Lash

Keywords:
Lead poisoning
Toxicology
Poisons
Poison control centers
Chelation therapy

ABSTRACT

There is limited literature on managing chronic lead exposure from non-removable sources such as lead fragments. In this case report, we present the complexities and clinical considerations involved in treating an elderly patient who sustained a comminuted knee fracture due to a gunshot wound, complicated by retained lead fragments. This case highlights the absence of comprehensive guidelines for managing chronic lead exposure when complete fragment removal is impractical. It also emphasizes the importance of a multidisciplinary approach to decision-making, while considering patient autonomy in such unique clinical scenarios.

1. Introduction

Lead poisoning may result from acute or chronic exposure to lead, leading to its body accumulation. Such exposure can be occupational, environmental, or accidental. The prevalence of occupational lead poisoning (e.g., fumes released during the melting process of lead or during battery manufacturing) in the Western world ranges from 10 to 20 cases per 100,000 individuals, although can significantly vary based on the geographic location [1,2]. In contrast, environmental lead poisoning can be insidious and stem from common sources such as lead-based paint, cosmetics, tap water contaminated by lead pipes, airborne emissions (especially in areas still using leaded gasoline), and the systemic release of lead from retained bullets. Lead can be absorbed through various routes, including the respiratory, gastrointestinal, dermal, and osteoarticular systems [3,4].

The United States Centers for Disease Control and Prevention (CDC) has established an upper limit for blood lead level (BLL) at 10 μg/dL and 3.5 μg/dL for adults and children, respectively [5,6]. However, the World Health Organization (WHO) asserts that there is no safe level of lead exposure and recommends identifying and quickly addressing the source of exposure for individuals with BLLs exceeding 5 μg/dL [3,5,6].

It has been demonstrated that BLL is correlated with the duration of exposure and the severity of intoxication, with symptoms being more likely and severe in adults with BLLs exceeding 80 μg/dL. Early recognition of symptoms, such as headache, disorientation, weakness, poor appetite, vomiting, constipation, abdominal and joint pain, and anemia, can help to quickly manage and limit the severity and neurological consequences of lead poisoning [3,5].

Concerning lead poisoning resulting from retained projectiles or fragments of bullets, the likelihood of toxicity is generally low when the fragments are situated within soft tissue, as they tend to become encapsulated and isolated by scar tissue formation. Conversely, some studies have shown that intra-articular lead fragments, in particular, should be removed due to the potential for metal degradation and increased absorption through the synovial [2,4,5].

To date, the management of retained lead fragments primarily involves surgical removal or chelation therapy. In adults, indications for initiating chelation therapy include a BBL exceeding 45 μg/dL (with a stronger recommendation when BLL > 100 μg/dL) or the presence of severe encephalopathy at any BLL [3,5].

* Corresponding author at: Department of Diagnostics and Public Health, University of Verona, Piazzale Ludovico Antonio Scuro, 8, 37134 Verona, Italy.
E-mail address: massimo.carollo@univr.it (M. Carollo).
[1] Co-first authors: Dr I.C. and Dr. M.C. contributed equally to this work

https://doi.org/10.1016/j.toxrep.2023.11.004
Received 21 September 2023; Received in revised form 30 October 2023; Accepted 7 November 2023
Available online 8 November 2023

Lead chelation should start with dimercaprol (BAL), followed by another dose of BAL four hours later, along with either succimer (meso-2,3-dimercaptosuccinic acid, DMSA, if oral administration is feasible) or $CaNa_2$-EDTA (if intravenous infusion is necessary). DMSA promotes urinary excretion of the metal and antagonizes enzymatic inhibition [6,7]. While BAL treatment is gradually phased out, one of the other chelating agents is continued, typically for a duration of five days. Thereafter, chelation therapy should be discontinued due to declining urinary lead excretion and continued chelator usage is associated with increased risk of adverse drug reactions [2,6,7]. Indeed, the utilization of chronic chelation therapy is hindered by potential toxicity, diminished long-term effectiveness, and insufficient evidence [3,6]. To our knowledge, no certain information concerning chronic treatment of bullets that cannot be surgically removed is available. We present the case of a patient with a not-surgically removable source of lead.

2. Case report

An 81-year-old man presented to the Emergency Department with a firearm injury, resulting in significant tissue loss and complex comminuted fracture of the right knee (Fig. 1 and Fig. 2), which occurred accidentally during a hunting expedition. His medical background comprises a pacemaker implantation for atrial fibrillation, a vascular prosthesis to treat aortic aneurysm, and hypertension.

At the initial assessment, he did not report pain, weakness, nor any other significant symptoms associated with lead intoxication. Laboratory tests did not show significant alterations in the blood cell count or transaminase levels, but there was an impairment in renal function indicated by a creatinine level of 1.59 mg/dL and an estimated glomerular filtration rate (eGFR) of 40 mL/min/1.73 m^2 (Table 1). Conventional X-rays confirmed an extensive traumatic component, including a comminuted patellar fracture with involvement of both adjacent joint surfaces (Fig. 1). Numerous lead pellets were evident, extending from the supracondylar region to the whole leg. No radiological signs of chronic lead intoxication were found. An urgent surgical stabilization of the right knee bridge was performed with an external fixator. Only one month later, a BLL test revealed lead intoxication, with a BLL of 55.2 μg/L. This prompted communication with our poison control center (PCC), which recommended initiating chelation therapy alongside surgical removal of the fragments. Three weeks later, the patient underwent a surgical intervention to partially debride the wound, followed by knee arthroplasty. Complete surgical removal of all lead fragments was not feasible, fragments were numerically reduced in postoperative radiographic images, but they were still present in significant amounts (Fig. 3). The option of limb amputation was discussed with the patient, who emphatically declined the procedure. The surgery had been successful, and there was a high likelihood of functional recovery. The sole rationale for considering amputation was to reduce the lead burden.

Fig. 2. Photography of the wound (right knee) before the surgical intervention of debriding, followed by knee arthroplasty.

Few days later, the patient exhibited ideomotor slowing and slurred speech. Consequently, the medical team recontacted our PCC. We promptly visited at the patient's bedside and observed that, in the *interim*, the neurological pathologic signs had already resolved. We noted that chelation therapy had not yet started due to challenges in sourcing the recommended medications. The neurological symptoms experienced by the patient were very non-specific and could be related to a wide differential diagnosis in an elderly patient. The fact that they resolved spontaneously suggest that another cause may have been the instigator of these symptoms. Therefore, considering the patient's age, the absence of lead intoxication symptoms, and the presence of irretrievable lead fragments, a conservative approach was adopted and chelation therapy was neither initiated nor further prescribed. The patient was scheduled for close follow-up, including bimonthly blood tests and clinical reassessments through both home monitoring and outpatient visits. Serial follow-up lead concentrations and clinical exams have revealed gradual (spontaneous) decrease in BLL with a plateau around 35–40 μg/L eight months after the accident, and no documentation of any signs or symptoms of lead poisoning. The patient remains fully autonomous and active, and the follow-up is ongoing. *Ad vitam* follow-up using telemedicine support was planned, with in-person ambulatory or outpatient visits as necessary.

3. Discussion

While numerous case reports of lead intoxication have been documented in the medical literature, there remains a paucity of cases

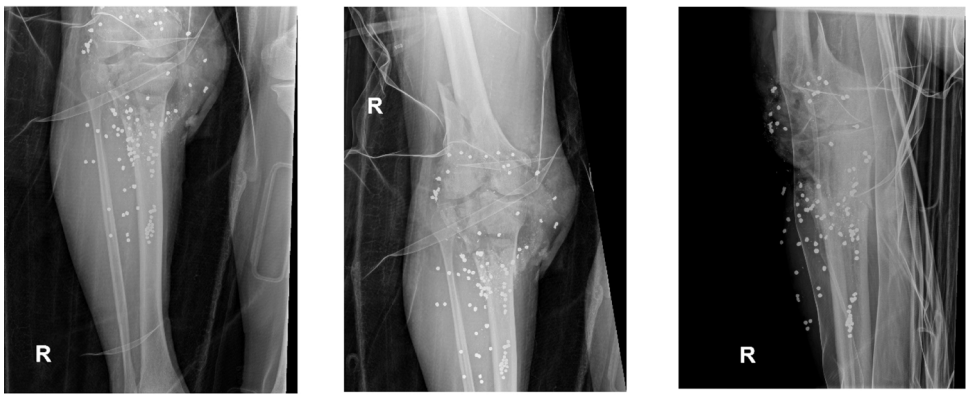

Fig. 1. Radiographies at first evaluation in the Emergency Department.

Table 1
Relevant patient's laboratory tests during hospitalization and home monitoring.

Date	Requesting Department	WBC (10^9/L)	RBC (10^12/L)	Hb (g/L)	MCV (fL)	HCT (L/L)	Platelets (10^9/L)	D-Dimer (μg/L)	Creatinine (mg/dL)	eGFR	Sodium (mmol/L)	Potassium (mmol/L)	BUN (mg/dL)	AST (U/L)	ALT (U/L)	Lead (μg/dL)
10/29/22	ICU Admission	5.7	3.74	120	92.5	0.35	102	1470	1.59	40	144	4.6	19	18	15	-
11/26/22	Traumatology	-	-	-	-	-	-	-	-	-	-	-	-	-	-	55.2
12/23/22	Orthopedics	7.7	4.49	138	92.4	0.41	284	-	-	-	-	-	-	-	-	53.3
01/24/23	Orthopedics †	15.5	3.51	105	89.7	0.31	200	-	1.30	51	133	4.8	16	-	-	-
01/31/23	Orthopedics	-	-	-	-	-	-	-	-	-	-	-	-	-	-	37.3
03/08/23	Orthopedics	-	-	-	-	-	-	-	-	-	-	-	-	-	-	44.5
05/10/23	General practitioner	9.1	4.96	164	100.0	0.50	290	-	1.35	49	-	-	32	22	59	37.7
08/02/23	General practitioner	9.8	4.90	160	92.2	0.48	265	-	1.35	49	-	-	30	29	37	39.8

Abbreviations: ALT = Alanine Aminotransferase; AST = Aspartate Aminotransferase; BUN = Blood Urea Nitrogen; Hb = Hemoglobin; eGFR = estimated glomerular filtration rate (CKD-EPI equation); HCT = Hematocrit; ICU = intensive care unit; MCV = Mean Corpuscular Volume; RBC = Red Blood Cells; WBC = White Blood Cells
† One day post-surgery

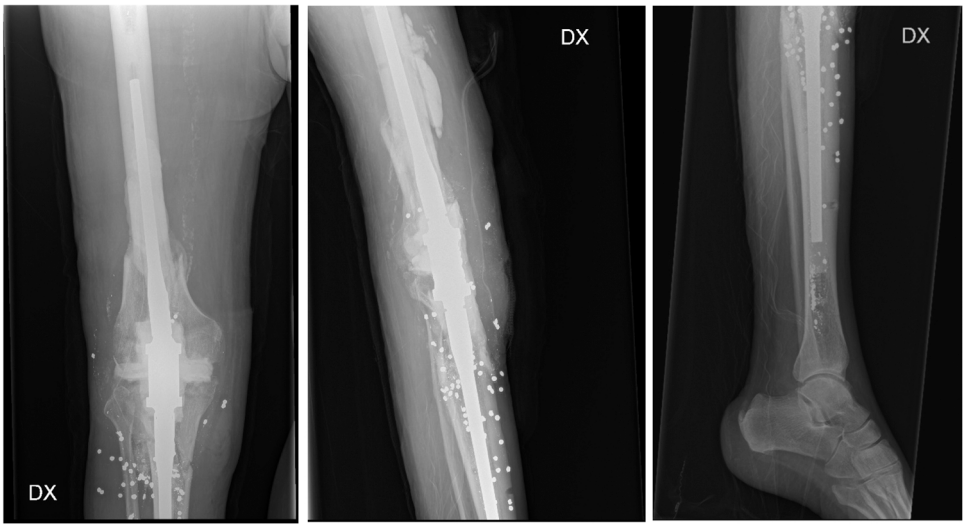

Fig. 3. X-ray radiograpies of the right lower limb after surgical interventions.

specifically addressing firearm injuries involving retained intra-articular lead fragments or multiple spread fragments. In instances of knee or intradiscal lead fragment retention, case reports have documented the implementation of chelation therapy alongside surgical removal, even in scenarios where peak BLL were relatively lower [8,9]. In another case, a 20-year-old male with gunshot wounds, characterized by multiple radiopaque fragments distributed across the left chest and inner arm, was precluded from undergoing bullet removal surgery due to the extensive surgical dissection required. Consequently, chelation therapy utilizing DMSA was initiated, culminating in a decrease in BLL from 24.0 to 13.3 μg/dL following seven treatment courses [10]. In general, there is no consensus on how to handle cases of multiple scattered fragments leading to chronic exposure. The symptoms can range from being asymptomatic to posing an increased risk of severe outcomes [11,12].

In the presented case, the patient sustained a severe firearm injury resulting in substantial tissue loss and a complex comminuted fracture of the right knee. A conservative strategy supplemented by close monitoring was elected, taking into account the patient's age, surgical risks, and overall asymptomatic status, leading to the decision to forgo chelation therapy. This case report raises several clinical considerations. Primarily, it highlights the substantial variation in lead intoxication symptoms contingent upon individual and circumstantial factors. Remarkably, our patient remained nearly asymptomatic throughout the ongoing follow-up period, and he exhibited only neurological symptoms several weeks following the incident and the detection of elevated BBL. This delayed symptom manifestation may carry considerable implications for lead intoxication diagnosis and management, potentially causing patients to remain unaware of their lead exposure until symptoms become overt.

Another pivotal consideration pertains to the initial absence of lead toxicity assessment, despite the presence of numerous lead pellets within the patient's body. This highlights the challenge in recognizing cases of lead intoxication, particularly when symptoms are either absent or mild. The implementation of targeted tests such as BLL analysis assumes paramount significance in identifying such cases. Lastly, emphasis is placed on the value of a multidisciplinary approach in clinical decision-making. In this specific scenario, the involvement extended beyond orthopedic specialists, toxicologists, and the general practitioner, encompassing both the patient and their family. The patient's choice to decline amputation in favor of adopting a conservative approach to lead fragment management accentuates the delicate balance between optimal medical choices and patient autonomy in decision-making.

In summary, the medical literature lacks extensive documentation on lead intoxication from retained firearm fragments in joints. As such, a multidisciplinary approach, which includes patient choice, is essential for monitoring and treatment decisions. Notably, chelation therapy should not be mandatory.

Conflict delineations

No funding was received to assist with the preparation of this manuscript. The authors have no conflicts of interest to declare that are relevant to the content of this article. This study has not been previously presented at any conferences or in abstract form.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

Data will be made available on request.

References

[1] W.A. Alarcon, State Adult Blood Lead Epidemiology and Surveillance (ABLES) program investigators. elevated blood lead levels among employed adults - United States, 1994-2013, MMWR Morb. Mortal. Wkly Rep. 63 (55) (2016) 59–65, https://doi.org/10.15585/mmwr.mm6355a5.
[2] A.L. Wani, A. Ara, J.A. Usmani, Lead toxicity: a review, Inter. Toxicol. 8 (2) (2015) 55–64, https://doi.org/10.1515/intox-2015-0009.
[3] G. Ricci, G. Mantelli, E. Morando, M. Bacchion, I. Costantini, Handbook di tossicologia in emergenza urgenza, Edizioni Med. - Sci. (2023).
[4] M.T. Quail, Retained bullet or bullet fragments: a potential source of elevated blood lead levels, Nursing 48 (10) (2018) 15, https://doi.org/10.1097/01.NURSE.0000545014.98790.6e.
[5] A. Apte, K. Bradford, C. Dente, R.N. Smith, Lead toxicity from retained bullet fragments: a systematic review and meta-analysis, J. Trauma Acute Care Surg. 87 (3) (2019) 707–716, https://doi.org/10.1097/TA.0000000000002287.
[6] E.K. Kershner, N. Tobarran, A. Chambers, B.K. Wills, K.L. Cumpston, Retained bullets and lead toxicity: a systematic review, Clin. Toxicol. (Phila. Pa.) 60 (10) (2022) 1176–1186, https://doi.org/10.1080/15563650.2022.2116336.
[7] Agency for Toxic Substances and Disease Registry (ATSDR). Medical Management Guidelines for Lead. Centers for Disease Control and Prevention. Published 2014. Accessed August 20, 2023. https://wwwn.cdc.gov/TSP/MMG/MMGDetails.aspx?mmgid=1203&toxid=22.
[8] J.E. Towner, T.A. Pieters, P.K. Maurer, Lead toxicity from intradiscal retained bullet fragment: management considerations and recommendations, World Neurosurg. 141 (2020) 377–382, https://doi.org/10.1016/j.wneu.2020.05.112.

[9] D. Weiss, D. Lee, R. Feldman, K.E. Smith, Severe lead toxicity attributed to bullet fragments retained in soft tissue, bcr2016217351, BMJ Case Rep. 2017 (2017), https://doi.org/10.1136/bcr-2016-217351.
[10] J.S. Yen, T.H. Yen, Lead poisoning induced by gunshot injury with retained bullet fragments, QJM 114 (12) (2022) 873–874, https://doi.org/10.1093/qjmed/hcab144.
[11] C. Witt, C. Kienast, G. Bölke, et al., Long-term indoor gunshot exposure of special police forces induces bronchitic reactions and elevated blood lead levels-The Berlin shooting range study, J. Cachex. Sarcopenia Muscle 14 (1) (2023) 452–463, https://doi.org/10.1002/jcsm.13147.
[12] S.E. Farrell, P. Vandevander, J.M. Schoffstall, D.C. Lee, Blood lead levels in emergency department patients with retained lead bullets and shrapnel, Acad. Emerg. Med. 6 (3) (1999) 208–212, https://doi.org/10.1111/j.1553-2712.1999.tb00157.x.