

Basophilic stippling in red blood cells in the bone marrow: indication for lead poisoning diagnosis

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Abstract

A 40-year-old man presented at our hospital with anaemia that had been undiagnosed for 2 years. Blood tests, endoscopy, and contrast-enhanced computed tomography were performed, but a definitive diagnosis could not be made. A subsequent bone marrow biopsy revealed basophilic stippling in transformed red blood cells, which led to a differential diagnosis of lead poisoning. Additional tests revealed elevated levels of lead in the blood. Basophilic stippling is generally found on a peripheral blood smear in lead poisoning patients; however, in this case, basophilic stippling was found only on the bone marrow smear and not in the blood smear. Even if basophilic stippling is not found in the peripheral blood, lead poisoning cannot be excluded.

Keywords

Lead poisoning, anaemia, blood smear, basophilic stippling, bone marrow biopsy, transformed red blood cell

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Introduction

Lead poisoning is still reported in Japan, although the frequency of these reports has decreased.¹ Numerous clinical symptoms of lead poisoning can be observed depending on the blood lead concentration.² Lead poisoning is associated with

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various symptoms such as anaemia, high blood pressure, joint and muscle pain, difficulty with memory or concentration, convulsions, coma, headache, abdominal pain, mood disorders, and tremors.²

This report presents a rare case of lead poisoning accompanied by fatigue due to anaemia that had been undiagnosed for 2 years. Basophilic stippling occurs in lead poisoning,¹ and it can be an indication for a lead poisoning diagnosis. Basophilic stippling occurs because of imperfect ribonucleic acid (RNA) resolution and abnormal ribosomal structure, and it reflects haemoglobin composition, heme, and combined iron disorder. This case report describes a didactic case in which basophilic stippling in the bone marrow was an indication for the diagnosis of lead poisoning.

Case report

A 40-year-old man presented at our hospital with anaemia that had been undiagnosed for 2 years, and his chief complaint was chronic fatigue. A medical examination at the patient's workplace revealed that the patient's anaemia had begun 2 years before presenting at our hospital. The cause of this patient's anaemia had been investigated at other hospitals but had not been definitively diagnosed. Approximately 3 months before the consultation at our hospital, the same medical examination at the patient's workplace revealed severe anaemia (haemoglobin [Hb], 8.1 g/dL; mean corpuscular volume [MCV], 82.9 fL). The physical examination yielded normal results, except for pallor of the palpebral conjunctiva. Some blood test results were abnormal (Hb, 8.1 g/dL; MCV, 82.6 fL; aspartate aminotransferase [AST], 81 IU/L; and alanine aminotransferase [ALT], 103 IU/L) (Table 1). Plasma electrolyte, ferrum, and ferritin levels and thyroid function were normal. Peripheral blood smears did not show any abnormal findings. Faecal

occult blood and urinary occult blood test results were negative. Upper and lower endoscopy, small intestinal capsule examination, and whole-body contrast-enhanced (CT) were performed, but a source of bleeding could not be identified. Results for tumour markers, immunoglobulins, electrophoresis tests, viral markers, antinuclear antibodies, zinc, or copper were unremarkable.

Because a diagnosis could not be made, a bone marrow biopsy was performed to allow a closer inspection. The biopsy results revealed no abnormalities in chromosomes or leukocyte cell surface markers, but the smear revealed basophilic stippling around the erythrocytes (Figures 1, 2, and 3). Further, myelodysplastic syndrome (MDS) markers were negative because iron staining results showed no ring sideroblasts. The presence of basophilic stippling in red blood cells is the best marker to identify lead poisoning. During an additional interview, we found that the patient worked at a construction site (painting business). Due to the possibility of lead poisoning at the workplace, we performed additional blood tests (lead concentration, 131.5 µg/dL; protoporphyrin, 82.6 µg/dL; and urinary aminolevulinic acid, 104 mg/L). These abnormally high results revealed the cause of the patient's anaemia (Table 2).

After admission, chelation therapy (dimercaprol 2.5 mg/kg for 7 days) was started, and no conspicuous adverse events were observed. After chelation therapy, the lead concentration in the blood decreased over time, anaemia symptoms resolved, and no side effects or anaemia recurrence was observed. No treatment other than chelation therapy was administered.

This study conforms to the CARE reporting guidelines.³

Discussion

Lead poisoning is a common disease of environmental origin. Adult lead poisoning

Table 1. Blood and biochemistry test results.

Blood test	Result	Normal range
White blood cells (/ μ L)	6810	(4000–8000)
Neutrophils (%)	64.3	(40.0–75.0)
Lymphocytes (%)	27.6	(30.0–50.0)
Red blood cells (/ μ L)	293×10^6	$(380 \times 10^6\text{--}480 \times 10^6)$
Haemoglobin (g/dL)	8.1	(12.0–16.0)
Haematocrit (%)	24.2	(37.0–47.0)
Mean corpuscular volume (fL)	82.6	(88.0–99.0)
Mean corpuscular haemoglobin (pg)	27.6	(29–35)
Mean corpuscular haemoglobin concentration (%)	33.5	(29–35)
Red cell distribution width (fL)	50.8	(35.2–50.5)
Reticulocyte (%)	5.3	(0.5–1.5)
Platelets (/ μ L)	29.2×10^4	$(13.0 \times 10^4\text{--}35.0 \times 10^4)$
Total protein (g/dL)	7.2	(6.7–8.3)
Albumin (g/dL)	4.6	(3.8–5.3)
Total bilirubin (mg/dL)	1.2	(0.2–1.0)
Aspartate aminotransferase (IU/L)	81	(12.0–32.0)
Alanine aminotransferase (IU/L)	103	(8.0–36.0)
Lactate dehydrogenase (IU/L)	187	(127.0–221.0)
Creatine kinase (IU/L)	49	(50.0–206.0)
Blood urea nitrogen (mg/dL)	24.2	(8.0–20.0)
Creatinine (mg/dL)	0.87	(0.3–1.2)
Sodium (mEq/L)	142	(134.0–147.0)
Potassium (mEq/L)	4.1	(3.2–4.8)
Chloride (mEq/L)	106	(98–108)
C-reactive protein (mg/dL)	0.09	(0.0–0.3)

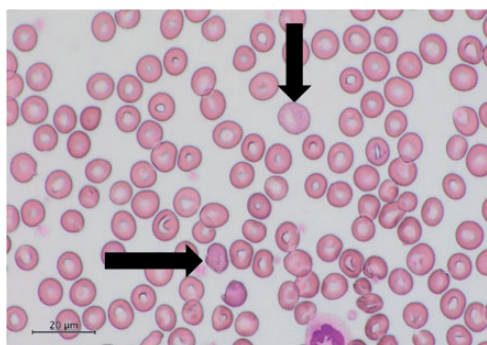


Figure 1. Bone marrow smear: Large and small red blood cells of unequal morphology and transformation. Some the red blood cells exhibit basophilic stippling (black arrows). (May Giemsa stain; magnification $\times 400$).

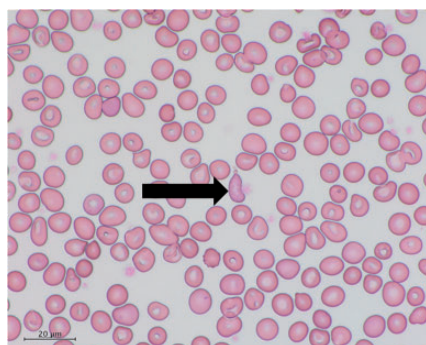


Figure 2. Bone marrow smear: Large and small red blood cells of unequal morphology and transformation. Some the red blood cells exhibit basophilic stippling (black arrows). (May Giemsa stain; magnification $\times 400$).

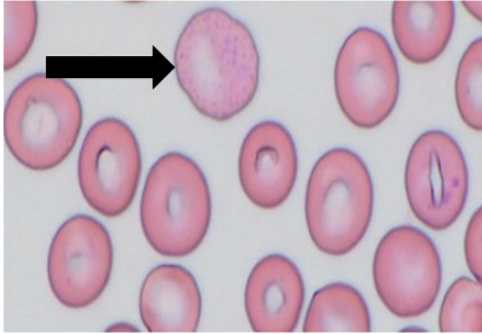


Figure 3. Basophilic stippling (expansion of the image in Figure 1).

Table 2. Additional blood and biochemistry test results.

Blood test	Result	Normal range
Lead ($\mu\text{g/dL}$)	131.5	(0.0–5.0)
Copper ($\mu\text{g/dL}$)	73	(40.0–75.0)
Zinc ($\mu\text{g/dL}$)	48	(30.0–50.0)
Urinary aminolevulinic acid (mg/L)	104	(0.0–2.2)
Protoporphyrin ($\mu\text{g/dL}$)	505	(30–86)

results primarily from exposure and inhalation in the workplace.⁴ Paediatric lead poisoning results primarily from the ingestion of lead from environmental media, including paint chips, dust, soil, drinking water, ceramics, and medications.^{4–7} In Japan, the Japan Paint Manufacturers Association began to abolish the use of lead in paint in 1996. For water pipes, lead has not been used in areas that were built after 1989, and the number of lead poisoning cases in Japan has decreased. Similar measures have been implemented in developed countries such as the United States, but currently, over 3% of American children have blood lead concentrations that are above normal.⁸

Most of the lead is deposited in the bone, and it has a biological half-life of 10 years.⁹ Lead poisoning is associated with various

symptoms. The patient's symptoms in the present case included only anaemia and general fatigue. Typical symptoms of lead poisoning (e.g., abdominal pain, tremors, and muscle pain) were absent. These typical symptoms are observed more widely in accordance with the lead concentration in the blood, but the safety margin and cut-off value remain unclear.⁹

Diagnosing this patient was difficult because he presented with only anaemia and general fatigue, as mentioned above, and because lead poisoning symptoms are mostly vague and nonspecific, misdiagnosis may occur.^{10,11} Additionally, many case studies have assumed that stomach ache is the chief complaint in lead poisoning, and lead poisoning patients who have anaemia as the chief complaint, as in this case, are rare.^{1,11}

Abnormal test results, normochromic anaemia, and liver dysfunction were observed. In this case, anaemia was identified by medical examination at our hospital. However, after upper and lower endoscopy, a small intestinal capsule, and iron prescription were ineffective in identifying the cause of the anaemia, and a whole-body contrast-enhanced computed tomography examination was performed. No subjective symptoms were observed, except for mild fatigue. The only indication for the diagnosis of anaemia in this case was the bone marrow biopsy.

The bone marrow smear revealed that basophilic stippling around erythrocytes had developed in the cytoplasm, which is a red blood cell anomaly (Figures 1, 2, and 3). Many lead poisoning case reports identified basophilic stippling around erythrocytes in peripheral blood smears.^{1,11,12} However, in this case, basophilic stippling was present only in the bone marrow smear, which is an unprecedented occurrence that made the diagnosis difficult. In the absence of basophilic stippling around the

erythrocytes, a bone marrow biopsy is considered to be critical to exclude lead poisoning.

Basophilic stippling occurs because of imperfect RNA resolution and abnormal ribosomal structure, and it reflects haemoglobin composition, heme, and combined iron disorder.¹ Basophilic stippling occurs in lead poisoning, benzene poisoning, and pernicious anaemia.¹² Initially, the current patient reported no clear history of lead exposure. However, an additional interview indicated that he was likely exposed to lead at a construction site. For anaemia, it is important to carefully interview a patient about their occupational history.

Lead poisoning is also considered to be a differential diagnosis. Thus, the concentration of lead in the blood was measured, and abnormally high values were observed. The concentration of lead in the blood was over 100 µg/dL, which is an abnormally high value that may cause convulsions and coma.² Despite a high blood lead level of 131.5 µg/dL, the patient only presented with anaemia, which is considered to be rare.

Lead poisoning has also been shown to decrease reproductive function in both men and women.^{2,9} If the lead concentration in the blood is 40 µg/dL or higher, lead poisoning negatively affects the sperm count, causes sperm malformation, and decreases its motility rate.^{2,9} Reduced levels of lead in the blood in prepubertal male mice improved reproductive function, although this has not been confirmed in humans.¹³ The patient's sperm was examined, but there was no effect on the sperm motility rate or malformation (Table 3).

As mentioned above, the effect of human chelation therapy on the sperm count and motility needs to be verified, and further research is required.

The most important part of treating lead poisoning is reducing the lead intake. When lead poisoning is observed, chelation therapy is the only viable treatment method. For symptomatic patients or those with a blood lead level of 70 µg/dL, immediate chelation therapy is strongly recommended.^{1,14,15} Chelation therapy involved administration of calcium ethylenediaminetetraacetic acid (EDTA), which has a high affinity for lead and binds to it in the blood, and the lead is removed from the blood via excretion in the urine. Although magnesium EDTA is sometimes used, we used calcium EDTA in this case. This is a common choice in Japan because there are fewer side effects, such as arrhythmia, with calcium compared with magnesium EDTA, and a large amount of evidence supports its use.^{2,9} Renal tubular disorders can be a side effect of this treatment, but no side effects were observed in this case.

Conclusion

We report the case of a patient with lead poisoning with chronic anaemia that had been undiagnosed for 2 years. Basophilic stippling around the erythrocytes was observed on bone marrow smears, which led to the diagnosis. It is important to recognize lead poisoning to identify undiagnosed anaemia. Furthermore, it is also important to obtain a bone marrow smear as an indicator to confirm the diagnosis of

Table 3. Sperm analysis.

	Sperm concentration (/mL)	Motility rate of sperm (%)	Malformation rate of sperm (%)
Normal range	More than 15,000,000	More than 40	Less than 96
Results	38,400,000	64.7	25.5

lead poisoning in the absence of basophilic stippling around the erythrocytes.

Consent

The patient provided written informed consent for publication of this case report.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

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