



Tuberculosis in the Bone Marrow: A Case Report

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Mycobacterium tuberculosis of bone marrow is considered one of the rare extrapulmonary tuberculosis (TB). Herein we report one case of tuberculosis of the bone marrow. A 82-year-old Thai woman presented with fever, fatigue, and weight loss of 4 kg in one month. The physical examination revealed only pallor and the ejection murmur at the upper parasternal border. Her chest film was unremarkable but the computed tomography of the chest revealed the reticular infiltration at both lower lungs and multiple small mediastinal lymphadenopathies. Although her blood smear did not show the leukoerythroblastic blood picture with the tear drop red blood cells (RBCs) or pancytopenia, her bone marrow biopsy showed a few granulomas with positive acid fast bacilli (AFB). The common risk factors such as diabetes, human immunodeficiency virus (HIV) infection, low CD4 counts, chronic kidney disease, malnutrition, and immunosuppressant therapy which might contribute her to be vulnerable to TB, were not found. The definite diagnosis was TB in the bone marrow and she clinically responded well to the 4-drug antituberculous regimen. Our case suggests that even though the leukoerythroblastosis with the tear drop RBCs or pancytopenia, the clues of the bone marrow involvement, is not found, the study of the bone marrow should not be precluded from the plan of the investigations for the diagnosis in a case of fever of unknown origin.

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Introduction

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. The clinical presentations include the constitutional symptoms such as low-graded fever, fatigue and weight loss, and the local symptoms depending on the organ involved. Although *M. tuberculosis* can infect any organ, the lung is the most common site while the extrapulmonary TB constitutes about 15 to 20% of all cases of TB in immune-competent hosts and accounts for more than 50% of the cases in human immunodeficiency virus (HIV) positive patients. And the common sites of extrapulmonary TB include the lymph nodes, the pleura,¹ the bone and joint,² the peritoneum, the meninges, etc.³

TB involving the bone marrow is one of the rare extrapulmonary TB, and most cases have the tuberculous lesions in other parts of the body. All cases had high fever, no specific symptoms, and no acid fast bacilli (AFB) on the sputum staining. Most cases had the abnormal liver function tests, and 7 of 11 patients had no tuberculous lesion in the chest film.⁴ TB in the bone marrow was presumed to be the part of the hematogenous disseminated TB.⁴ So far, TB in the bone marrow was very rare in Thailand.⁵ Herein we report a case of TB in the bone marrow in a Thai woman who had no common risk factor.

Case Report

A 82-year-old Thai woman presented with the low-graded fever, fatigue, anorexia and weight loss for 4 kg in one month. She had neither cough nor hemoptysis. The physical examination revealed body temperature of 38.2°C, pallor and systolic ejection murmur grade II at the upper sternal border.

Results of blood tests were as follows: hemoglobin (Hb), 7.9 g%; white blood cell (WBC), 10 150/mm³; platelet, 311 000/mm³; total lymphocyte, 1431.1/mm³; CD4, 468 cell/mm³; Hb analysis [Hemoglobin E trait (AE), Hemoglobin E (Hb E)], 30.2%; fasting blood sugar (FBS), 94 mg%; creatinine, 0.8 mg%; cholesterol,

146 mg%; albumin, 2.5 g%; globulin, 4.2 g%; total bilirubin, 1.1 mg%; alkaline phosphatase, 715 U/L; aspartate aminotransferase (AST), 114 U/L; alanine aminotransferase (ALT), 97 U/L; γ -glutamyl transferase (GGT), 515 U/L; ferritin, 188.6 ng/mL; cortisol, 19.3 μ g/dL; cancer antigen 125 (CA 125), 171.8 U/mL (normal 0 - 35); normal CA 15-3, CA 19-9, α -fetoprotein (AFP), and carcinoembryonic antigen (CEA).

Protein electrophoresis revealed normal α 1-globulin, α 2-globulin, β -globulin, β 2-microglobulin, immunoglobulin A (IgA), and IgM; γ -globulin, 2.4 g% (normal 0.7 - 1.5), IgG, 23.3 mg/mL (normal 7.0 - 16.0); and no monoclonal gammopathy.

Hepatitis B surface antigen (HBsAg), hepatitis C virus antibody (anti-HCV), and HIV antigen/antibody were all negative, and melioidosis titer was 1:40.

The real-time polymerase chain reaction (PCR) for *Mycobacterium tuberculosis* complex (MTBC) and nontuberculous mycobacteria (NTM) in the bronchial fluid from the bronchial wash was negative.

The chest film was unremarkable but the computed tomography (CT) of the chest and abdomen showed the reticular infiltration at the periphery of both lower lungs, multiple mediastinal, para-aortic, aortocaval and mesenteric lymph nodes, size 0.5 - 1.5 cm, generalized multiple small nodules 0.5 - 0.7 cm at the spleen, minimal right pleural effusion and minimal ascites.

The bone marrow biopsy was moderately hypercellular trilineage with normal maturation, presence of few granulomas (Figure 1), positive bacilli on acid fast staining (Figure 2), and negative Grocott's methenamine silver (GMS) stain for fungus.

The given definite diagnosed were TB in the bone marrow, Hb E heterozygosity, mild hepatitis. The patient was treated with the 4-drug antituberculous regimen; isoniazid (INH), rifampicin (RMP), pyrazinamide (PZA), and ethambutol (EMB). She clinically responded well to the therapy; the defervescence within a week, increased body weight, normal liver function test, decreased size of the lymph nodes and splenic lesions on the subsequent CT study.

Figure 1. Moderately Hypercellular Trilineage Bone Marrow Biopsy With Focal Presence of Granulomas By Haematoxylin and Eosin Stain, x10

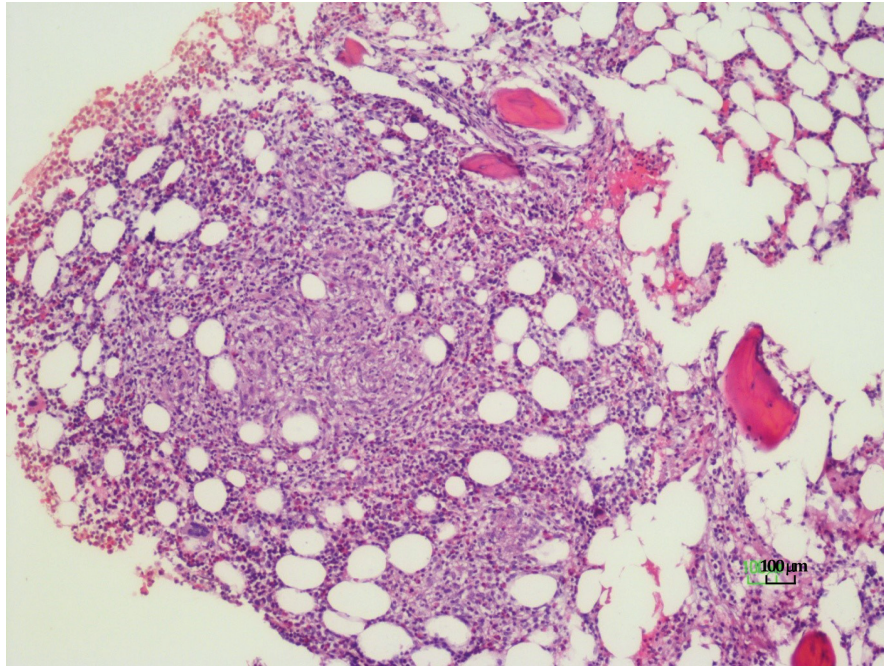
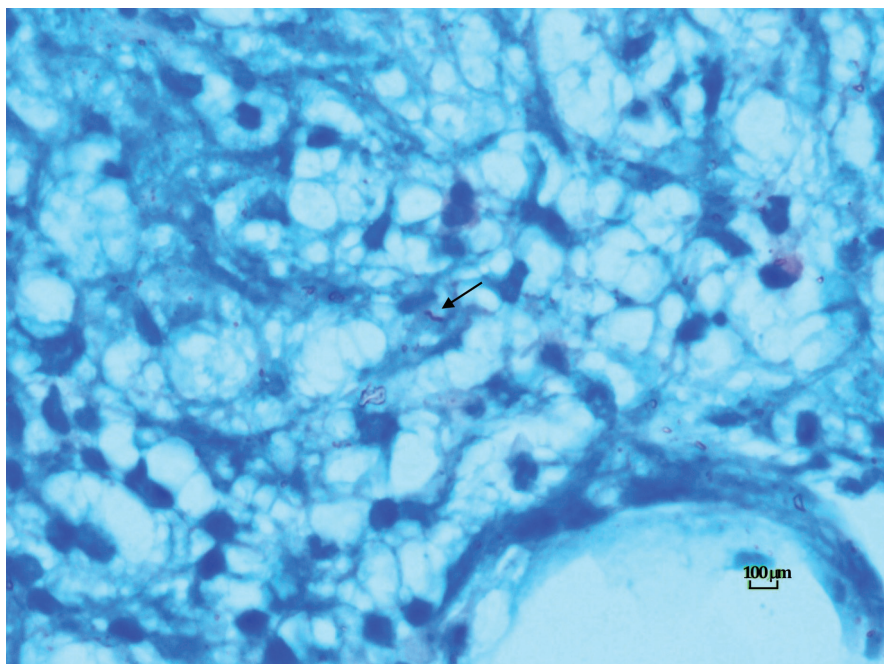


Figure 2. Positive Smear With an Acid Fast Bacilli (Arrow) By Kinyoun Stain, x100





Discussion

The diagnosis of TB in the bone marrow in our case was solely based on the finding of the AFB and the granuloma in the bone marrow biopsy specimen.⁶ It can also be diagnosed by using the PCR method for the bone marrow aspirate specimen that will be more sensitive and it takes 2 days for yielding result which is much more rapid than the culture method.⁷ In a study of 22 patients with culture-proven *M. tuberculosis* infection of the bone marrow, the pathological findings were found to be the granuloma in 19 cases (86%) and the caseating granuloma in 3 (14%). The outcome of treatment was favorable for 11 patients (50%) while 10 (45%) died during the hospitalization.⁸

As the mycobacterial infection in other organs, *M. tuberculosis* is much more common than nontuberculous mycobacteria in cases of mycobacterial infection in the bone marrow.⁹ Our case was found positive for AFB staining and presumed to be *M. tuberculosis* although the culture or PCR for definite identification of *M. tuberculosis* had not been performed

The underlying conditions which are commonly found in patients with TB of the bone marrow include the solid organ transplantation (18%), diabetes (14%), and HIV infection (9%). However, 55% of cases do not have these factors.⁸ Likewise, our case was tested and found free from these factors but she had slight lymphopenia and her CD4 was 468/mm³ that might precede and

activate TB as seen in HIV-infected patients or follow TB especially in the disseminated form.¹⁰

Pancytopenia is a common finding in cases of disseminated TB involving the bone marrow and the viscera¹¹ but our case had only anemia with lymphopenia. On the contrary, the bone marrow findings in cases with pulmonary TB were the depressed erythropoiesis in 69% of the patients, micronormoblastic change in 18%, megaloblastic change in 16.6%, no granuloma, no caseation necrosis, and no growth of *M. tuberculosis*¹² on culture. In military TB, all cases had granuloma, either caseating or noncaseating, in the bone marrow.¹³ The PCR for detecting *M. tuberculosis* in the bone marrow aspirate is more sensitive than the culture.¹⁴

The infection¹⁵ or tumor¹⁶ invading the bone marrow can cause leukoerythroblastosis, viz, young WBC and nucleated RBC with tear drop RBC in the peripheral blood or pancytopenia. But none of them was found in our case. This seems that in case of fever of unknown origins, the bone marrow study is still helpful for the diagnosis despite lack of any clue in the peripheral blood.

Conclusions

A 82-year-old Thai woman presented with fever, weight loss, and mild hepatitis. Despite lack of leukoerythroblastosis, tear drop RBCs and pancytopenia, her bone marrow biopsy was found to have granuloma with positive AFB. The diagnosis of tuberculosis of the bone marrow was concluded.

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วัณโรคในไขกระดูก: รายงานผู้ป่วย

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เชื่อว่าวัณโรคก่อโรคที่ปอดได้บ่อย แต่การติดเชื้อในไขกระดูกถือเป็นวัณโรคนอกปอดที่พบได้น้อย บทความนี้ได้รายงานผู้ป่วยหญิงชาวไทย อายุ 82 ปี มีอาการคือ มีไข้ อ่อนเพลีย น้ำหนักลด 4 กิโลกรัม ใน 1 เดือน การตรวจร่างกายเบื้องต้นพบเพียงภาวะซิคและได้ยินเสียงแบบฟุด (Ejection murmur) ของหัวใจที่บริเวณด้านข้างของกระดูกสันอกส่วนบน ผลเอกซเรย์ปอดไม่พบความผิดปกติ แต่ผลเอกซเรย์คอมพิวเตอร์ทรวงอกพบว่า มีลักษณะเป็นเส้นร่างแหที่ส่วนล่างของปอดทั้งสองข้าง และมีต่อมน้ำเหลืองโตเล็กน้อยรอบอวัยวะแกนกลางทรวงอก แม้ว่าการตรวจเสมียร์เลือด (Peripheral blood smear) จะไม่พบเซลล์ตัวอ่อนของเม็ดเลือดแดงและเม็ดเลือดขาว (Leukoerythroblastosis) ไม่พบเม็ดเลือดแดงทรงหยดน้ำตา ไม่มีการลดลงของเซลล์เม็ดเลือดทุกชนิดทั้งเม็ดเลือดแดง เม็ดเลือดขาว และเกล็ดเลือด แต่ผลการเจาะไขกระดูกพบกลุ่มเซลล์ (Granuloma) ที่ย้อมพบเชื้อแบคทีเรียทรงแท่งติดสีทนกรด (Acid fast bacilli, AFB) บ้างยี่สิบโดยทั่วไป เช่น วัณโรค การติดเชื้อเอชไอวี การมีค่า CD4 ต่ำ โรคไตเรื้อรัง ภาวะทุพโภชนาการ และการได้รับยากดภูมิคุ้มกัน ซึ่งจะส่งเสริมให้ผู้ป่วยติดเชื้อวัณโรคง่ายขึ้น อย่างไรก็ตาม บ้างยี่สิบดังกล่าวไม่พบในผู้ป่วยรายนี้ สุดท้ายผู้ป่วยรายนี้ได้รับการวินิจฉัยว่าเป็นวัณโรคในไขกระดูก ได้รับการรักษาด้วยยารักษาวัณโรคสูตรมาตรฐาน 4 ขนาน และตอบสนองดี ดังนั้น ผู้ป่วยรายนี้จึงเป็นตัวอย่างที่ดีแม้ว่าจะตรวจไม่พบเซลล์ตัวอ่อนของเม็ดเลือดแดงและเม็ดเลือดขาว และเม็ดเลือดแดงทรงหยดน้ำตา ซึ่งเป็นสัญญาณเตือนถึงการรบกวนไขกระดูก จึงไม่ควรละเว้นการส่งตรวจไขกระดูกออกจากแผนการสอบสวนเพื่อการวินิจฉัยโรคในผู้ป่วยที่มาด้วยไข้ไม่ทราบสาเหตุ

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