Case Report

Disseminated tuberculosis masquerading primary myelodysplastic syndrome

Syahrul Sazliyana Shaharir, Nor Rafeah Tumian, Andrea Ban Yu Lin, S Fadilah Abdul Wahid

Department of Internal Medicine, Universiti Kebangsaan Malaysia Medical Centre, Cheras, Kuala Lumpur, Malaysia

Abstract

Tuberculosis is notoriously known to be a great mimicker of other diseases and may cause various haematologic abnormalities, especially with marrow involvement. A 61-year-old man who presented with right empyema and pancytopenia was diagnosed to have disseminated tuberculosis supported by the presence of caseating granuloma with Langhan's giant cells in the marrow and demonstration of acid-fast bacilli in the pleural fluid. Trilineage dysplasia from marrow aspirate was initially attributed to be reactive to the infection. A cytogenetic study was repeated after he showed poor response to a year of anti-tuberculosis treatment. The underlying primary myelodysplastic syndrome was unmasked when his cytogenetics showed trisomy 8. This case report has demonstrated the various haematological manifestations of tuberculosis and highlighted the importance of cytogenetic study in differentiating between primary and secondary myelodysplastic marrow changes.

Key words: disseminated tuberculosis; cytogenetic; hematological; myelodysplastic syndrome

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Introduction

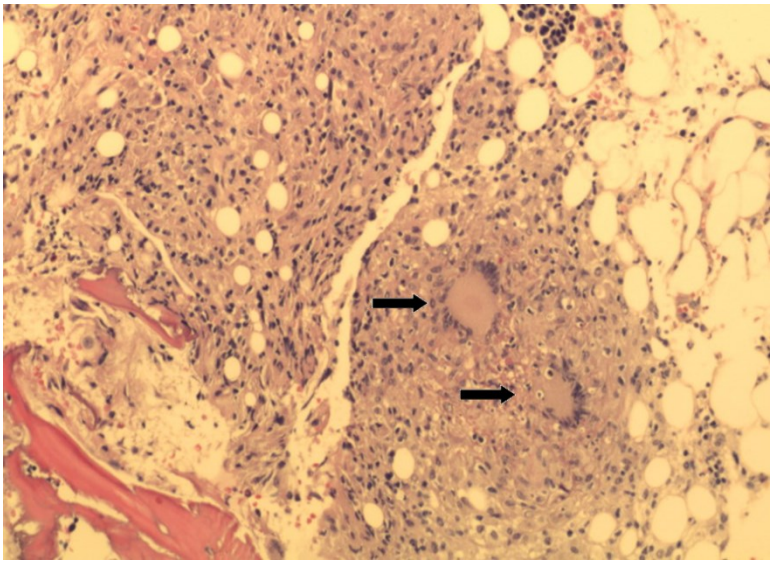
Disseminated tuberculosis (TB) is reputably capable of inciting various haematological abnormalities and the spectrum ranges from pancytopenia, myelofibrosis, and myelodysplasia to a rare leukemoid reaction [1-3] It is extremely important to differentiate between primary and secondary myelodysplastic changes as they signify different prognosis and management of the patient. Primary myelodysplastic syndrome (MDS) is a clonal myeloid disorder and approximately 30% to 70% of cases have cytogenetic changes [3]. The most frequent cytogenetic abnormality is a loss of genetic material in the form of deletions and monosamies such as -5/5q-, -7/7q-. 20q- and –Y [4,5]. A gain of genetic material may also occur with the appearance of total or partial trisomies such as trisomy 8 [5]. Although radiation, cytotoxic, and toxic agents may also cause cytogenetic abnormalities, the genomic changes usually are more complex, involving two or more chromosomal abnormalities [5,6].

We report an interesting case whose dysplastic marrow was initially attributed to the underlying disseminated TB infection until the cytogenetic study, which was repeated a year later, revealed trisomy 8. Literature reviews of haematological changes in TB will be discussed further in this case report.

Case report

A 61-year-old non-smoker gentleman with no previous medical illness presented with a two-month history of fever, cough, progressive shortness of breath, and constitutional symptoms. Clinically there was right pleural effusion with multiple cervical and supraclavicular lymphadenopathies, the largest measuring 1.5 x 1.5 cm. Other systems were unremarkable. Blood investigations revealed pancytopenia with a white cell count of 3.9 x 10^9/L, hemoglobin count of 8.2g/dL (macrocytic anemia, MCV 92.1), and platelet count of 67 x 10^9/L. Computed tomography (CT) of the thorax confirmed large right empyema with consolidation in the apical segment of left lower lobe. Subsequently a chest tube was inserted and acid-fast bacilli were demonstrated in the pleural fluid smear. Bone marrow aspirate smear was hypocellular with trilineage dysplasia but no excess blast and ring sideroblast. Granulomatous inflammation with caseation and Langhan's giant cells were identified in both the cervical lymph node and bone marrow biopsy specimens (Figure). However, cultures from the pleural fluid, peripheral blood, and

Figure. Trephine marrow biopsy shows presence of caseating granulomas with Langhan's giant cells (black arrows)



marrow failed to yield any growth. The initial cytogenetic study was inconclusive as there was no metaphase spread. Further investigations showed low folic acid (3nmol/L) but normal B12 level (189pmol/L), and his retroviral screening was negative.

At this point, the initial impression was that the myelodysplastic changes were caused by the combination of disseminated TB and folic acid deficiency. Therefore, he was treated with the first-line anti TB therapy consisting of daily Isoniazid 300 mg, Rifampicin 600 mg, Ethambutol 800 mg, and Pyrazinamide 1250 mg od, with oral folic acid 5 mg once daily. Despite treatment, he had five admissions in a year due to recurrent empyema which required chest tube drainage. The pleural fluid was persistently positive for acid-fact bacilli and TB polymerase chain reaction (PCR), but the culture failed to yield any growth. He remained pancytopenic despite normalization of folic acid level and required regular pack cell transfusion every two to six weeks. In view of the refractory infection, a second-line anti TB regime consisting of oral ciprofloxacin 750 mg twice daily and IM Streptomycine 1 g twice weekly were added to the first-line treatment. He continued to show poor response; therefore, a cytogenetic study was repeated. Finally, a diagnosis of myelodysplastic syndrome (MDS) refractory anemia with multilineage dysplasia (WHO classification 2001) was confirmed when the cytogenetic studies came back as trisomy 8.

The primary MDS had compromised the patient, making him extremely susceptible to a disseminated infection and thus have poor response to the combination of first and second-line antiTB treatment.

After approximately 14 months of intensive phases of first- and second-line anti-TB therapy, the repeated samples of the residual pleural fluid acid-fast bacilli and TB PCR were finally negative. Subsequently, he was converted to a maintenance phase of Isoniazid 300 mg daily and Rifampicin 600 mg daily. The empyema was resolved but it was complicated with pleural thickening and no improvement in the hematological parameters. He was put on lifelong maintenance antiTB treatment because of his immunocompromised state with a history of difficult disseminated TB infection. The MDS was treated conservatively with regular blood transfusion in view of his advanced age and the underlying infection.

Discussion

This patient is interesting because the diagnosis of MDS, which was finally revealed with the cytogenetic abnormality, and was masked by the presence of disseminated TB. A great mimicker, TB often poses diagnostic confusion and management dilemmas for clinicians. Further diagnostic complacency is not uncommon as the infection may co-exist with many other primary haematological diseases, and TB itself may cause similar haematological abnormalities as has been illustrated in our case. Only a few sporadic case reports of disseminated TB in MDS can be found in the literature, and the reported prevalence ranges between 7.7% and 10.5% [7-13]. These figures and reports most probably do not reflect the true burden of

the disease as a lot of cases, especially from TB endemic countries such as Malaysia and other developing countries, are largely underreported.

Karel Pelger first described abnormal segmentation of neutrophils in advanced TB; hence non clonal myelodysplasia may mimic primary haematological or bone marrow disorder [14,15]. To differentiate between primary and secondary dysplatic marrow, cytogenetic studies play a pivotal role, not only in the diagnosis, but also in determining the prognosis and treatment [3]. In MDS, the cytogenetic changes may be observed at the onset of symptoms or evolve over time as the disease progresses [7]; therefore, a normal karyotype study at the diagnosis warrants a repeat later in the course of the disease. Furthermore, a lack of improvement or worsening in the haematological parameters despite anti-TB treatment, as has been demonstrated by our patient, should prompt further investigation of the underlying primary haematological disease.

According to the very few case reports available, TB with MDS generally has poor prognosis and is invariably fatal because of the fulminant disseminated infection [8]. Generally, there is a lack of consensus in the treatment of disseminated TB in MDS; however, since our patient remained immunocompromised with persistant pancytopenia and a history of a refractory TB infection, he was prescribed lifelong maintenance anti-TB treatment to prevent further recurrence. In regard to the underlying MDS, he was treated supportively with regular blood transfusion. Hematopoeitic growth factors such as erythropoietin, granulocyte-colony stimulating factor (G-CSF), and granulocyte-macrophage colony stimulating factors (GM-CSF) may not be suitable options or cost effective if the patient has already become transfusion dependent; therefore, the success of the above-mentioned treatment is most likely poor [16] .

In conclusion, TB continues to pose challenges to clinicians and may masquerade as many hematological diseases. Therefore, performing a cytogenetic study is an important tool in revealing the primary hematological diagnosis.

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Corresponding author

Syahrul Sazliyana Shaharir
MD (UKM), MRCP (UK), MMed Internal Medicine (UKM)
Department of Internal Medicine
Universiti Kebangsaan Malaysia Medical Center (UKMMC)
Jalan Yaacob Latiff 52100
Cheras, Kuala Lumpur
Telephone: +60123730137
Email: sazliyana@hotmail.com

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