CASE REPORT

A new diagnosis of acute myeloid leukaemia complicated by peripancreatic tuberculous lymphadenitis

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SUMMARY

A 29-year-old woman presented with neutropenic sepsis and was found to have a new diagnosis of acute myeloid leukaemia. Following initiation of induction chemotherapy the patient became increasingly unwell with ongoing sepsis despite broad-spectrum antibiotic treatment. An extensive septic screen failed to identify a source, other than the finding of a peripancreatic mass on imaging. Following the introduction of antituberculous treatment the patient showed signs of clinical improvement and a subsequent biopsy confirmed the mass to be tuberculous lymphadenitis. The patient completed three cycles of combination chemotherapy achieving a complete remission and also successfully completed 12 months of antituberculous treatment.

BACKGROUND

This case acts as an important reminder to consider underlying tuberculosis (TB) infection in certain populations, when undergoing myelosuppressive chemotherapy. Tuberculosis is an increasingly prevalent condition in certain parts of the U.K., with an estimated 8300 new cases throughout the country in 2013.¹ The risk of reactivating latent TB with the use of biological antitumour-necrosis factor agents in rheumatological disorders is well recognised, with a chest X-ray and tuberculin skin test required to actively exclude underlying TB infection, in most cases, prior to the initiation of treatment.² However, the effects of immune suppression due to the myelosuppressive effect of acute leukaemia and subsequent cytotoxic chemotherapy, on latent TB are less well recognised. Confirming a diagnosis of TB can be challenging, particularly in the case of extrapulmonary disease, but is important due to the length of potentially toxic treatment that one is committed to after initiating therapy. Our case highlights this clinical dilemma and is the first reported case of a successfully treated concomitant presentation of acute leukaemia and TB in the UK.

CASE PRESENTATION

A 29-year-old Nigerian woman presented to our emergency department with a history of fever, weight loss and occasional headaches. These symptoms had increased in severity over the preceding week. The patient had no medical history of note and took no regular medications. A systems enquiry excluded any respiratory or gastrointestinal

symptoms. Clinical examination, other than confirming fever, was non-contributory.

INVESTIGATIONS

Admission bloods showed pancytopenia with a haemoglobin of 83 g/L, white cell count $8.3 \times 10^9/L$, neutrophils $0.8 \times 10^9/L$ and platelets of $85 \times 10^9/L$. A peripheral blood film showed 78% blast cells with a high nucleocytoplasmic ratio. Bone marrow aspirate and trephine were in keeping with acute myeloid leukaemia (AML) M2. The diagnosis was confirmed with immunophenotyping while cytogenetic analysis revealed t(8;21).

The patient was started on broad-spectrum antibiotics and enrolled on to the AML 17 trial, starting on induction DA (daunorubicin and cytarabine) chemotherapy. She had ongoing high temperatures and significantly elevated inflammatory markers despite a change of antibiotic therapy to meropenem, followed by the successive addition of amikacin, teicoplanin and amBisome. An extensive septic screen failed to identify a source of her sepsis. She became increasingly thrombocytopenic and transfusion dependent and was noted to have developed antihuman leucocyte antigen (HLA) antibodies. A CT scan of the chest, abdomen and pelvis was performed at the time of adding AmBisome, which showed evidence of a multiloculated mass around the head of the pancreas, which had the appearance of confluent necrotic lymph nodes (figure 1). Biopsy of this mass was initially not possible due to severe neutropenia and thrombocytopenia with suboptimal increments even to HLA-matched platelets.

Figure 1 CT image of the abdomen showing peripancreatic mass.

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Figure 2 Peripancreatic biopsy showing granulomatous inflammation.

DIFFERENTIAL DIAGNOSIS

Having confirmed the underlying diagnosis of AML and initiated treatment, the primary area of concern regarded treating the persistent sepsis, and attempting to identify the source. The differential diagnosis for this included a resistant bacterial organism, however multiple cultures did not show any growth and an extended septic screen was negative. An invasive fungal infection was also considered, however high-resolution CT scanning of the chest was normal and there was no clinical improvement following the addition of AmBisome. Finally, there was also the concern that the clinical picture may represent refractory leukaemia. The identification of the peripancreatic mass, with an appearance of necrotic lymph nodes, led to the suspicion of tuberculous lymphadenitis and treatment was initiated empirically in view of the clinical deterioration.

TREATMENT

In view of the imaging and her deteriorating clinical condition, the patient was started on quadruple antituberculous therapy with rifampicin, isoniazid, pyrazinamide and ethambutol. She began to improve clinically 4 days after this, as her blood counts also began to recover after the addition of lenograstim. A trans-hepatic biopsy of the abdominal mass was then performed. Histopathological examination showed evidence of granulomatous inflammation (figure 2), with Ziehl-Neelsen staining positive for acid-fast bacilli (AFB) (figure 3). Subsequent AFB culture was negative, likely due to the fact that the patient had been on antituberculous therapy for 5 days before it was possible to perform a biopsy. The possibility of non-tuberculous mycobacteria was considered in view of the negative culture result, however by this stage the patient had shown a good clinical response to standard antituberculous therapy and as such this was deemed less likely.

OUTCOME AND FOLLOW-UP

The patient continued chemotherapy, achieving a complete remission after the first cycle and went on to have two further cycles of consolidation treatment. She also completed 12 months of combined antituberculous treatment and serial imaging showed a resolution of the peripancreatic mass.

DISCUSSION

This case acts as an important reminder to consider underlying TB infection in certain populations, when undergoing myelosuppressive chemotherapy. The diagnosis should be kept in mind particularly in those with prolonged neutropenia and

Figure 3 Ziehl-Neelsen showing multiple acid-fast bacilli.

ongoing sepsis, who fail to respond to initial broad-spectrum antibiotic therapy. TB is an uncommon infection in acute leukaemia, particularly in the developed world. A recent retrospective study of 130 cases of acute leukaemia in India found 6.9% of patients to have active TB.³ The majority of these patients had AML and responded well to antituberculous therapy with no significant delays in initiation of antituberculous treatment reported. A Chinese study, looking retrospectively at 44 cases of leukaemia complicated by TB found a higher prevalence compared with the general population, with the majority of cases involving pulmonary TB.⁴ A previous case of AML complicated by anergic TB, which was identified at postmortem examination, was reported in the UK in 1996.⁵

The case highlights a number of clinical dilemmas. First, the decision to initiate antituberculous therapy empirically should not be taken lightly, as one is generally committed to a minimum of 6 months of potentially toxic treatment. Obtaining tissue to confirm a diagnosis is not possible in many cases due to severe neutropenia, the risk of introducing further infection, and the risk of haemorrhage in severely thrombocytopenic patients. In this case the lack of any respiratory symptoms and the difficult site of the lesion in terms of obtaining a biopsy, as well as the absence of any known TB contacts, made the decision to start treatment particularly difficult. Furthermore, the use of Amikacin as Gram-negative antibiotic cover may in some cases partially treat and obscure the diagnosis, as it is a commonly used second-line agent for resistant TB. In this case the clinical deterioration of the patient and suspicious imaging provided sufficient grounds to begin antituberculous treatment.

Learning points

- ▶ Tuberculosis should be considered in all patients undergoing myelosuppressive chemotherapy with persistent sepsis, which is not responding to standard therapy.
- ▶ Investigations should consider the possibility of occult extrapulmonary disease.
- ▶ Where possible diagnosis should be confirmed microbiologically or histologically to avoid unnecessary and potentially toxic treatment.

Contributors PH wrote the paper. TY reviewed and critically analysed the paper.

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