An unusual cause of a marked leukocytosis and an abnormal blood film

Introduction

This article presents a case of a young woman undergoing treatment for breast cancer. She presented with diarrhoea, bleeding per rectum and was noted to have a marked leukocytosis (>40x10^9/litre). Endoscopy showed only haemorrhoids but her marked leukocytosis persisted. Her blood film showed several metamyelocytes and myelocytes, with toxic granulation, but the patient had no signs of sepsis. Haematologists were initially concerned about an underlying haematological malignancy. The final diagnoses were diarrhoea as a side effect of her recent chemotherapy, per rectum bleeding secondary to haemorrhoids and marked leukocytosis secondary to granulocyte-colony stimulating factor (given with her neo-adjuvant chemotherapy in a different hospital). This case highlights the importance of a clear history, in addition to an up-to-date knowledge of current treatments and their side effects.

Discussion

Without the details of the neo-adjuvant chemotherapy that this patient had received, the diagnosis was unclear. Possible unifying diagnoses included a chemotherapy-induced colitis, infective colitis or inflammatory bowel disease (although the latter was less likely in view of the acute onset and would not explain the marked leukocytosis).

Alternatively, there could have been more than one diagnosis – a more common cause for per rectum bleeding (e.g. haemorrhoids or an anal fissure) and the high leukocyte count could be the result of a primary leukocytosis (e.g. acute or chronic myeloid leukaemia), a secondary leukocytosis such as acute infection or

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Table 1. Full blood count results

Investigation	Result	Reference range
Haemoglobin (g/litre)	101	118–148
Platelets (x10^9/litre)	118	150–400
White cell count (x10^9/litre)	43.4	3.5–11.0
Neutrophils (x10^9/litre)	22.6	2.0–7.5
Lymphocytes (x10^9/litre)	3.9	1–3.5
Monocytes (x10^9/litre)	3	0–0.8
Metamyelocyte (%)	8.3	10.0–25.0
Promyelocyte (%)	0.4	2.0–4.0

Case Report

A 27-year-old woman with a history of breast cancer presented to the acute medical unit with a 2-day history of diarrhoea and a 1-day history of fresh per rectal bleeding. Otherwise, she felt systemically well and denied any fevers, abdominal pain, vomiting or pain on defaecation.

The patient was undergoing neo-adjuvant chemotherapy for right-sided breast cancer (epirubicin and cyclophosphamide) and had received the fourth cycle 8 days before presentation. Past medical history also included haemorrhoids. She took no other regular medications.

On examination, she had a mild tachycardia (101 bpm) but other routine observations were within normal limits. She was alert and generally well. Examination of the cardiovascular and respiratory systems was normal. Her abdomen was soft and non-tender, without palpable masses, and a per rectum examination revealed some fresh blood; there were no visible or palpable masses or haemorrhoids. She had a peripherally inserted central catheter line in her left arm. The insertion site was not clinically inflamed.

Her full blood count was abnormal (*Table 1*). Renal and liver function tests, clotting screen and C-reactive protein were within normal limits. Chest and abdominal radiographs were normal. A repeat of the full blood count confirmed the leukocytosis (50.3x10^9/litre). A blood film was performed which was markedly abnormal, containing several metamyelocytes, myelocytes, toxic granulations and neutrophilic leucocytosis. It demonstrated a very left-shifted granulopoesis.

The patient remained systemically well and the per rectum bleeding and diarrhoea settled. Flexible sigmoidoscopy showed internal haemorrhoids but the rest of the examination was normal. In view of her persistent marked leukocytosis and abnormal blood film, a haematology opinion was sought. They were initially concerned about a possible underlying haematological malignancy, until a vital piece of information became apparent. She was reviewed by the acute oncology team on the day following admission, who confirmed that she had been given granulocyte-colony stimulating factor following the last chemotherapy cycle. She was discharged with oncology follow up.

inflammation, or medication, in particular haematopoietic growth factors (for example granulocyte-colony stimulating factor).

Granulocyte-colony stimulating factor had been used in this patient because of the myelotoxicity of the chemotherapy. Myelotoxicity may cause further treatment to be deferred (therefore risking sub-optimal treatment) and increases the risk of neutropenic sepsis. To help maintain dose intensity and frequency, granulocyte-colony stimulating factor is administered as either primary or secondary prophylaxis. Patients on regimens with a high risk of neutropenic sepsis (e.g. fluorouracil, epirubicin, cyclophosphamide, docetaxel for breast cancer or neo-adjuvant chemotherapy), or those for whom maintaining dose intensity is essential, receive primary prophylaxis. Secondary prophylaxis is given after the first episode of febrile neutropenia. The aim of the granulocyte-colony stimulating factor is to increase the white cell count and reduce the length of the nadir. This reduces the risk of neutropenic sepsis and therefore the risk of prolonged and life-threatening infection (von Minckwitz et al, 2009).

The granulocyte-colony stimulating factor used is a single 6 mg pegylated dose 24 hours after the completion of chemotherapy. The dose is normally self-administered subcutaneously, but if the patient cannot do it him-/herself, district nurses will administer. Patients should be made aware that granulocyte-colony stimulating factor can cause side effects such as bone pain, fever and flu-like symptoms. The granulocyte-colony stimulating factor can increase the blood counts to unusually high levels and may give a false impression of infection. This leukocytosis may be more marked when granulocyte-colony stimulating factor is given in conjunction with dexamethasone (as in this case). The dexamethasone is used for its antiemetic properties and is initially given as 8 mg intravenously on the day of treatment, then 4 mg twice a day orally for 3 days (Clatterbridge Cancer Centre, 2012).

Snyder and Stringham (2007) reported a white cell count of 100 x10^9/litre or greater in less than 1% of patients receiving pegfilgrastim (a type of granulocyte-colony stimulating factor), but there is no specific range or duration of leukocytosis to be expected available in the literature. To the authors' knowledge, there are only two cases of pegfilgrastim-induced leukocytosis reported in literature, one in an adult and one in the paediatric age group (Jaiswal et al, 2013).

This case not only highlights the importance of treating the patient and not the test (as the patient was systemically well and had no markers of sepsis), but also to be mindful of patients who have recently received chemotherapy, and to find out whether they may have also received granulocyte-colony stimulating factor as primary prophylaxis, e.g. the patient may recall giving him-/herself or receiving a subcutaneous injection after chemotherapy. **BJHM**

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LEARNING POINTS

- Be mindful of patients who have recently received chemotherapy – their symptoms or investigation results could be related to their chemotherapy regimen.
- Granulocyte-colony stimulating factor (G-CSF) may be administered as either primary or secondary prophylaxis to reduce the risk of neutropenia resulting from the myelotoxicity of chemotherapy.
- Remember to treat the patient, not the test. Is the patient systemically well? Do the results fit the clinical picture?