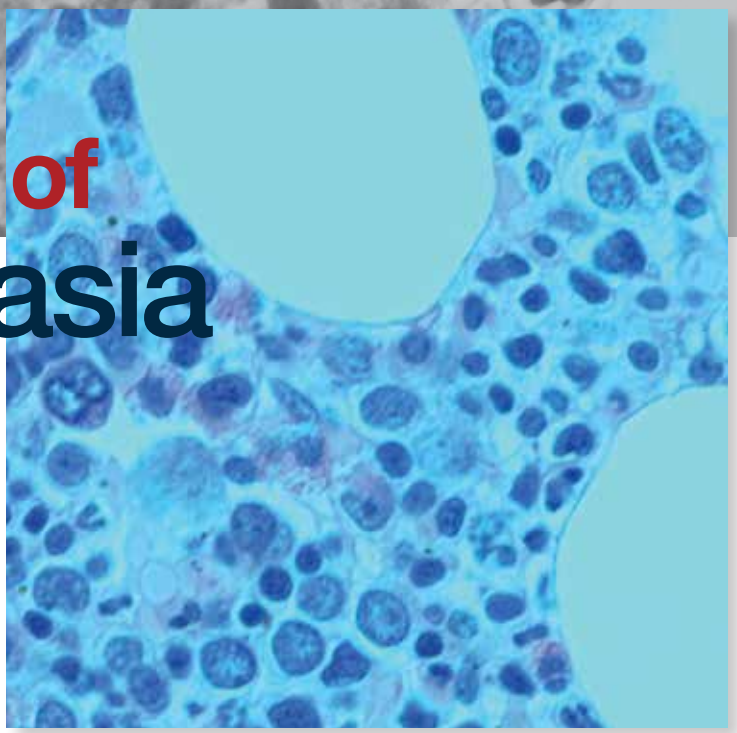
A presentation of myelodysplasia



Commentary by
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Is leucocytosis in this middle-aged man in the absence of infection an inflammatory condition, a major systemic disorder due to his recently developed gout or something more serious?

MedicineToday 2014; 15(4): 54-55

CASE SCENARIO

Bill, aged 59 years, is a nonsmoker and has, on average, six to eight drinks on four days of each week. He has had hypertension, hypercholesterolaemia and osteoarthritis at least since he first attended your practice two years ago, and has recently developed gout. He takes intermittent colchicine and regular allopurinol for his gout, and is also taking indomethacin, irbesartan and hydrochlorothiazide. There is no recent history of fever or infections, and although he has plethoric facies there are no notable physical findings.

A recent blood test showed a haemoglobin level of 141 g/L (normal range 130 to 170 g/L), a platelet count of 140 x 10^9 per L (normal, 150 to 400 x 10^9 per L) and an elevated white cell count of 15.4 x 10^9 per L (normal, 4.0 to 10.0 x 10^9 per L); the white blood differential count was neutrophils 11.2 x 10^9 per L (normal, 2.0 to 7.0 x 10^9 per L), lymphocytes 1.8 x 10^9 per L (normal, 1.0 to 3.0 x 10^9 per L) and monocytes 1.8 x10^9 per L (normal, 0.2 to 1.0 x 10^9 per L). A repeat blood test has confirmed the leucocytosis.

A haematologist's opinion was sought because of the recent onset of gout associated with leucocytosis in the absence of infection.

A bone marrow study ordered by the specialist showed changes consistent with a myelodysplasia with a normal cytogenetic profile 46XY. No intervention was offered and he continues under observation.'

COMMENTARY

From time to time patients are referred to a consultant because of leucocytosis as the dominant abnormality in the blood count. In an otherwise well person it is usually easy to exclude causes such as infection, an inflammatory condition or a major systemic disorder such as malignancy on clinical grounds or with limited imaging to target areas of symptoms. In a person with leucocytosis, the development of gout may be significant because gout results from the increased turnover of purines and accumulation of uric acid that is caused by enhanced white cell production occurring in the bone marrow and other sites. There are no other pointers in the presentation so everything depends on the investigations.

The white cell differential is informative with a dominant neutrophilia and slight monocytosis, and the platelet count has shown mild thrombocytopenia. The normal lymphocyte count effectively excludes chronic lymphocytic leukaemia, the most common of the blood malignancies in a person of this age

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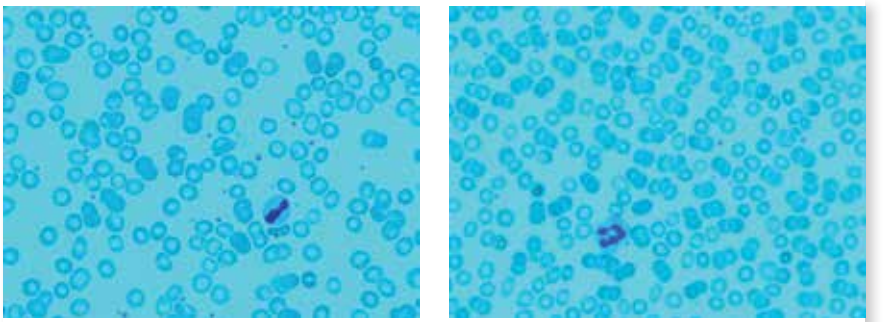
group. Granulocytosis and thrombocytopenia, although mild in degree in this patient, when consistent are important pointers to a more serious disorder and cannot be ignored. Although an acute attack of gout may well be associated with granulocyte leucocytosis, this patient's gout is in a stable phase with no gouty arthritis, and the leucocytosis would have another cause.

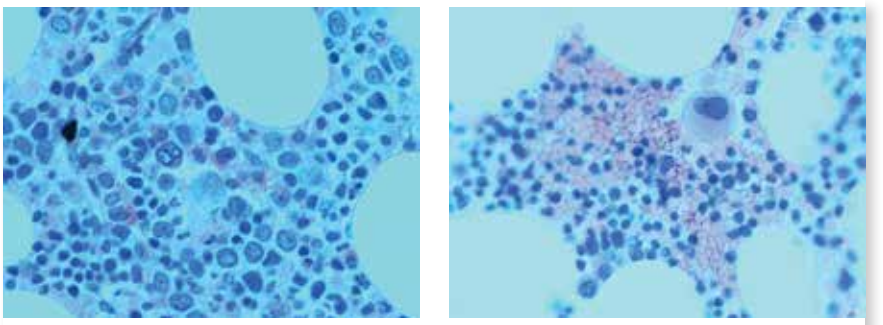
Blood film examination in a patient with myelodysplasia in the early stages may show immature granulocytes such as band-form and other immature neutrophils (Figures 1a and b). Bone marrow aspirate and trephine samples showed moderate hypercellularity and changes in red cell, granulocyte and platelet precursors consistent with a myelodysplastic syndrome or possibly an early myeloproliferative disorder (Figures 2a and b). The population of abnormal precursor cells was confirmed by surface marker studies documenting a limited population of myeloid blast cells. The absence of any chromosomal abnormality in this patient, as indicated by his cytogenetic profile 46XY being normal, was a finding of favourable prognostic significance. Taken together, these findings confirm the original impression of a presentation at an early stage of a significant bone marrow disorder.

The patient and his GP are informed of the nature of the condition and the serious implications. Ongoing observation and monitoring of the patient's blood count and physical state are mandatory to detect as early as possible the development of more definitive markers such as anaemia, advancing thrombocytopenia or physical changes such as splenomegaly, any or all of which would warrant repeat full assessment. It is usual for the GP and consultant to collaborate during this monitoring period.

On the basis of current findings, it is more likely that evolution will be towards a myelodysplasia, a relatively uncommon but serious group of haematological disorders with a poor long-term prognosis.



Figures 1a and b. Blood films. a (left). Myelodysplasia, showing macrocytic anaemia and a band neutrophil (an immature neutrophil with a non-segmented nucleus). b (right). Normal, showing normal red blood cells and a polymorphonuclear neutrophil (with the typical segmented – or multilobular – nucleus).



Figures 2a and b. Bone marrow trephine biopsy. a (left). Myelodysplasia, showing increased density of immature cells and overall celllularity. b (right). Normal, showing more sparse cellularity and predominance of mature forms.

As the condition evolves, intervention will be with supportive blood transfusion and general care. There are some chemotherapeutic interventions available that can have a temporary limited benefit. Stem cell grafting has a place in the right circumstances of recipient suitability (including age usually less than 60 years), donor availability and clear evidence of evolution towards an otherwise fatal outcome.

Myelodysplasia and myeloproliferative disorders have some features in common but are two quite different disorders, the former being disorders of the myeloid stem cells that result in ineffective production of myeloid blood cells (i.e. red cells, platelets and nonlymphocyte white cells) and the latter diseases in which there is excess production of myeloid blood cells. There are more effective therapeutic interventions available for myeloproliferative disorders, and the long-term outlook for these disorders is generally more favourable. The labels should not be treated as interchangeable.

CONCLUSION

Even relatively minor changes in the blood count if consistent on repeated testing should be treated with concern and further examination and testing arranged. Gout of recent onset in an otherwise healthy person, if associated with leucocytosis and/or thrombocytopenia, is a further signal for intervention. A diagnosis of a myelodysplasia or myeloproliferative disorder, while serious, may still be a prelude to slow evolution, and short- or long-term advantage is possible with a variety of treatments. MT

COMPETING INTERESTS: None.