

Slide session, British Society for Haematology, 45th Annual Scientific Meeting, Manchester, 2005

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Summary Each year at the Annual Scientific Meeting of the British Society for Haematology, there is a slide session in which microscopic slides of six patients with haematological disorders are discussed by two experts. Further data and the final diagnosis are then provided. The slide session is presented here, as it occurred at the meeting.

Keywords Morphology, red cells, white cells, leukaemia, eosinophilia, osteopetrosis

Each year at the Annual Scientific Meeting of the British Society for Haematology (BSH), there is a slide session. Microscopic slides of peripheral blood (PB), bone marrow (BM) or trephine biopsy sections are sent in advance to two experts and to other society members who request them. At the meeting the experts discuss their findings and conclusions before the discussion is thrown open to the meeting. Further investigations and the final diagnosis are then presented. The cases are presented here in the same format as at the meeting so that others may participate in this educational exercise.

Case 1 (with thanks to Dr S. Chakravorty and Dr P. Ancliff)

A PB film was provided on a baby girl, the daughter of nonconsanguineous northern European parents, who presented at 10 days of age with epistaxis. Her full blood count (FBC) showed white cell count (WBC) $36 \times 10^9/l$,

Hb 13.3 g/dl and platelet count $74 \times 10^9/l$. PB karyotype was stated to be normal but BM karyotype was not.

The first discussant (JM) noted abnormal red cell features including basophilic stippling and the presence of stomatocytes and nucleated red cells. There were also giant platelets (Figure 1) and blast cells with budding cytoplasm (Figure 2). He suspected transient abnormal myelopoiesis (TAM) or acute megakaryoblastic leukaemia in a baby with Down's syndrome. The normal PB cytogenetic analysis was puzzling and led him to postulate mosaic Down's syndrome or trisomy 21 confined to haemopoietic cells. The second discussant (KP) had observed the same features and also suspected mosaic Down's syndrome.

Case 2 (with thanks to Dr Chi Wong and Professor I. Hann)

A PB film and an electronic image of a trephine biopsy section were provided on a 4-month-old girl born to nonconsanguineous northern European parents. She presented with hepatosplenomegaly and an abnormal FBC; the WBC was $44 \times 10^9/l$. A week later, when the film was made the FBC was: WBC $24.8 \times 10^9/l$, Hb 13.3 g/dl and platelet count $74 \times 10^9/l$.

Accepted for publication 25 August 2005

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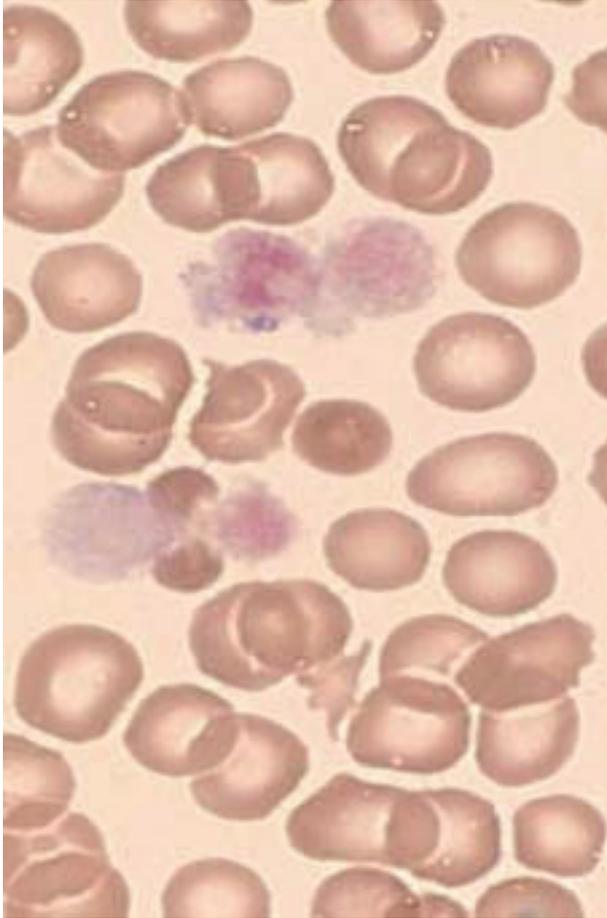


Figure 1. Peripheral blood film of case 1 showing giant platelets, May Grünwald-Giemsa (MGG).

The first discussant (KP) found the film to be leucoerythroblastic with occasional blast cells (Figure 3), basophilic stippling, target cells and teardrop poikilocytes. He thought the trephine biopsy showed solid bone and some remnants of crushed tissue that might have been BM (Figure 4). Overall he thought the features were those of osteopetrosis. The second discussant (JM) was in complete agreement.

Case 3 (with thanks to Dr Chi Wong and Professor I. Hann)

Peripheral blood and BM films were provided on a 5-month-old boy presenting with anaemia from birth and subsequent failure to thrive. The blood film had been prepared 3 months after the most recent transfusion. FBC was: WBC $12.2 \times 10^9/l$, Hb 8.9 g/dl, platelet count $617 \times 10^9/l$ and reticulocyte count $86 \times 10^9/l$. Haemoglobin F was 8.6%, haemoglobin A₂ 2.4% and serum ferritin 55 µg/l.

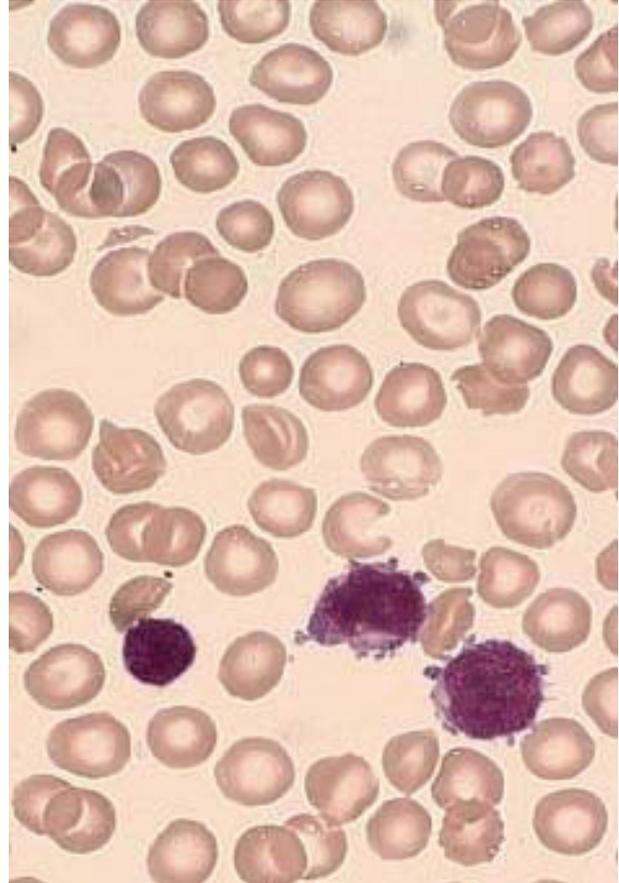


Figure 2. Peripheral blood film of case 1 showing blast cells with budding cytoplasm, MGG.

The first discussant (JM) noted teardrops, elliptocytes and basophilic stippling (Figure 5) and in the BM noted inclusions in erythroblasts, dyserythropoiesis and perhaps an increase in blast cells. He thought the differential diagnosis was very wide but he wondered if this could be a monosomy seven syndrome. He did not find any vacuolation such as might have been expected if this were Pearson's syndrome. The second discussant (KP) noted target cells and hypochromic microcytes in addition to the aforementioned features and he thought the film was probably dimorphic (Figure 6). He thought the differential diagnosis was between $(\epsilon)\gamma\delta\beta$ thalassaemia and congenital sideroblastic anaemia. He favoured the former diagnosis because the history given suggested that perhaps the condition was becoming milder as the baby became older.

Case 4 (with thanks to Dr Chieh Wong and Dr N. Philpott)

A PB film was provided from a 24-year-old man of Pakistani ethnic origin who had last visited Pakistan for

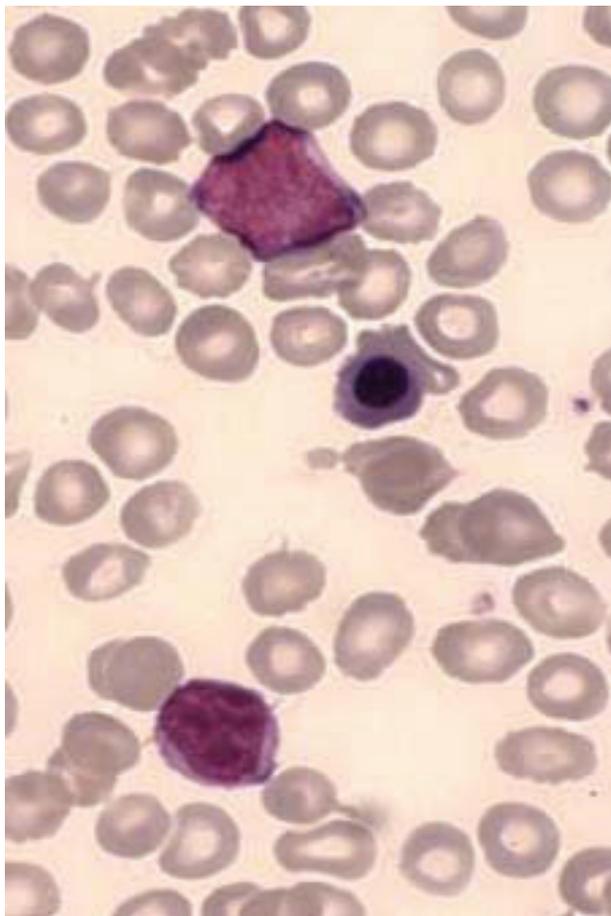


Figure 3. Peripheral blood film of case 2, MGG.

3 weeks about a year before presentation. He presented with intermittent cough and dyspnoea of several months duration, relieved by a steroid inhaler. Negative or normal tests included echocardiography, a computerized tomography (CT) scan of chest, serum IgE and a serological test for *Aspergillus fumigatus*. An antineutrophil cytoplasmic antibody (ANCA) test had previously been weakly positive but was negative on repeat testing. FBC was: WBC $36.8 \times 10^9/l$, Hb 12.9 g/dl and platelet count $194 \times 10^9/l$.

The first discussant (KP) noted striking eosinophilia with some hypogranular eosinophils. He thought the differential diagnosis was wide and included parasitic infection and eosinophilic leukaemia with either a *FIP1L1-PDGFRB* or an *ETV6-PDGFRB* fusion gene. The second discussant (JM) noted hypogranular, vacuolated and hypolobated eosinophils (Figure 7). He agreed the differential diagnosis was wide and commented that reactive eosinophilia occurred not only in Hodgkin's disease, T-cell lymphoma and drug allergies but even in some myeloid neoplasms. He did not favour *t(5;12)/ETV6-*

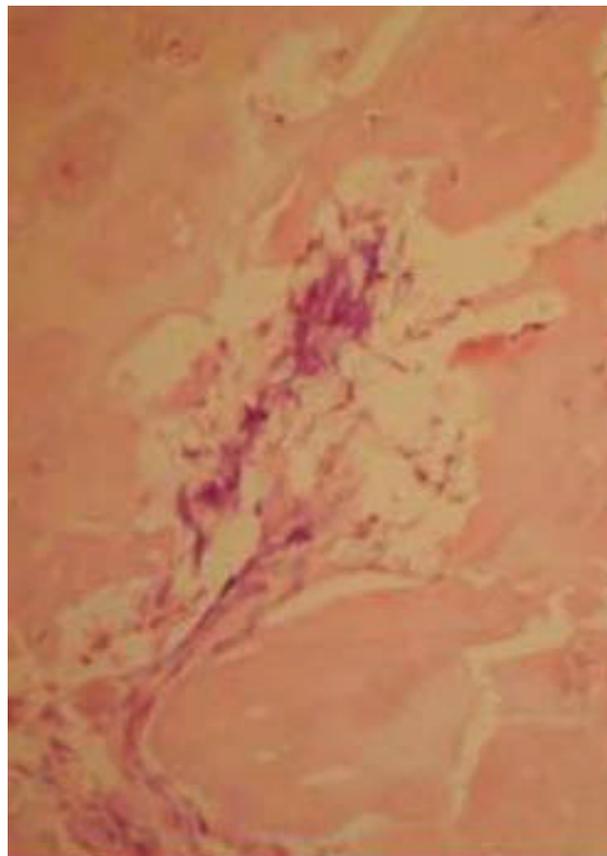


Figure 4. Bone marrow film of case 2, MGG.

PDGFRB as there was no monocytosis but favoured a diagnosis of *FIP1L1-PDGFRB* fusion syndrome or the 8p11 syndrome.

Case 5 (with thanks to Dr S. Bolam)

A PB film was provided on a 60-year-old woman who presented with generalized aches and pains, fatigue and shortness of breath on exertion following return from a holiday in Peru. She posed a diagnostic problem. Her FBC was: WBC $36.7 \times 10^9/l$, Hb 7.7 g/dl and platelet count $92 \times 10^9/l$. Immunophenotyping on PB cells was: CD2 9%, cCD3 11%, CD7 9%, CD10 4%, CD11c 8%, CD13 10%, CD14 14%, CD19 62%, CD33 67%, CD34 62%, CD38 83%, CD61 6%, CD79a 52%, CD117 1%, HLA-DR 63%, MPO 25%, terminal deoxynucleotidyl transferase 20%, glycoprotein A 19% kappa 4% and lambda 3%.

The first discussant (JM) thought that there were two populations of abnormal cells, differing in size, nuclear characteristics and nucleocytoplasmic ratio; possibly these were lymphoblasts and myeloblasts (some had granules; Figure 8). He suggested biphenotypic leukaemia. The

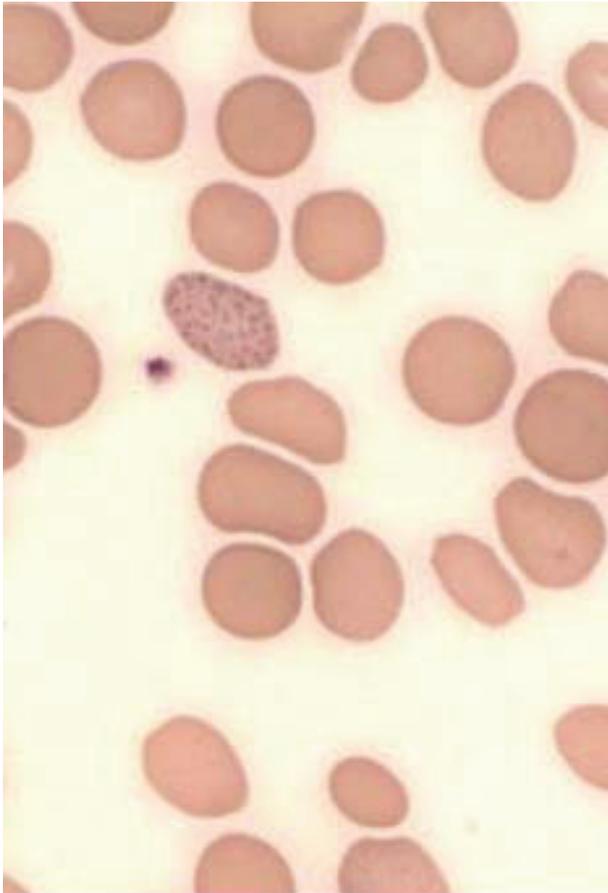


Figure 5. Bone marrow film of case 3 showing inclusions in erythroblasts and erythrocytes, MGG.

second discussant thought that this might represent a mixed lineage transformation of chronic myeloid leukaemia or possibly a transformation of B-lineage chronic lymphocytic leukaemia as some of the abnormal cells were small with rather condensed chromatin; perhaps there had been prior chemotherapy and there was also dysplasia.

Case 6 (with thanks to Dr W Thomas)

Trephine biopsy sections were provided on a 53-year-old man who present with dyspepsia, chest discomfort, dry cough, lethargy, sweats (day and night) and marked weight loss. Earlier in the year he had holidayed in Zante. There were no abnormal physical findings but abdominal CT scan showed a 14-cm spleen.

The first discussant (KP) thought the sections showed leishmaniasis (Figure 9) and that HIV infection should be excluded. The second discussant (JM) agreed that the patient was suffering the regrettable consequences of a holiday. He had discovered that Zante was a Greek island.

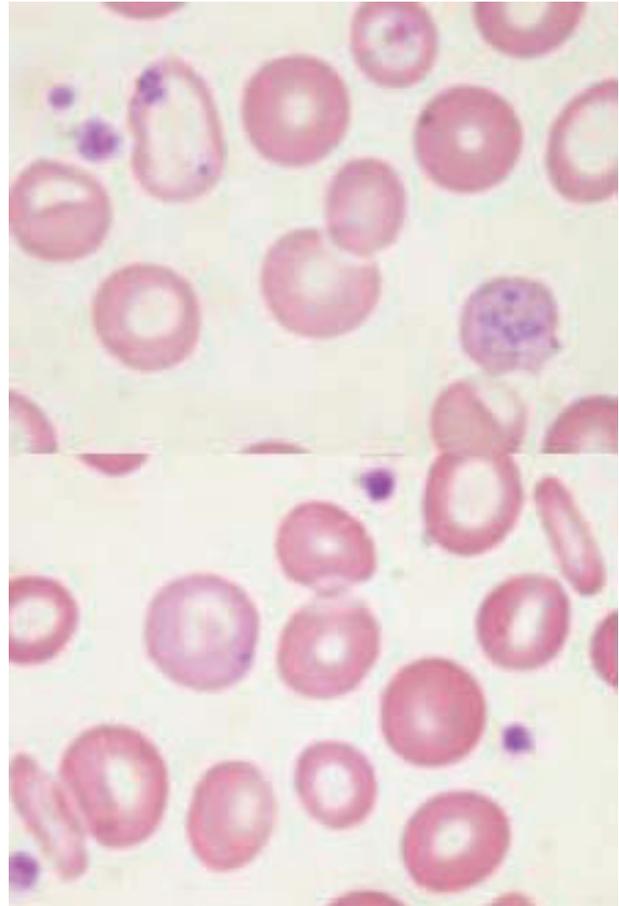


Figure 6. Peripheral blood film of case 3, MGG.

Three entomological investigations had been carried out during the summers of 1979, 1980 and 1982 in the Ionian islands of Corfu, Cephalonia and Zante and in the Aegean islands of Andros, Tinos, Samos and Ikaria. Systematic sampling with oiled paper traps produced 24 184 sandflies (Pesson, Leger & Madulo-Leblond 1984). Sandflies on beaches can spread leishmaniasis, particularly if visitors sleep on the beach.

Discussion and final diagnoses

Case 1

The chairman (BB) commented that she thought that mosaic Down's syndrome was a most ingenious explanation although it was not actually correct. The baby had been found to have $t(1;22)(p13;q13)$, a translocation known to be associated with acute megakaryoblastic leukaemia in infants. This type of leukaemia may be of intrauterine origin since concordance has been observed in identical twins (Ng *et al.*, 2002) and a

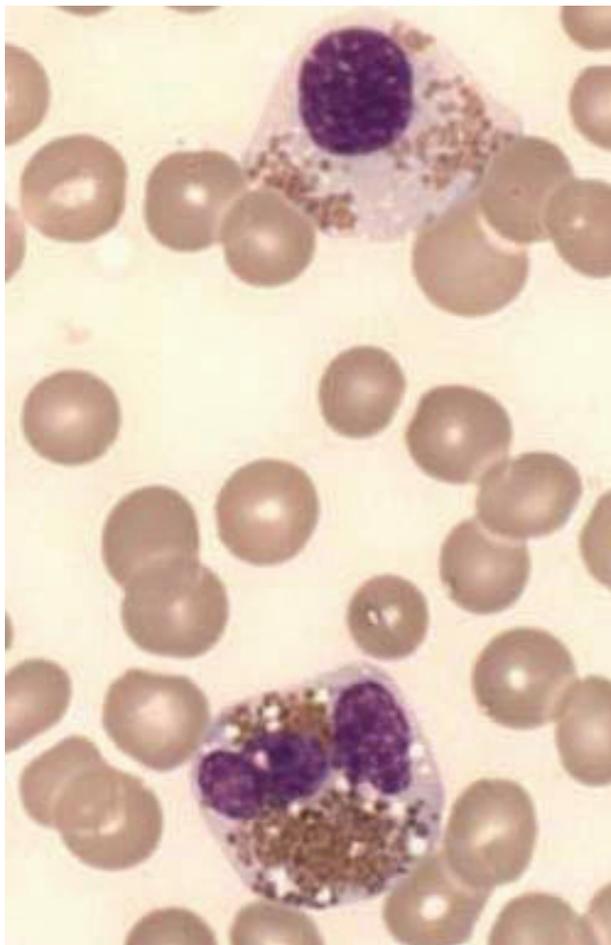


Figure 7. Peripheral blood film of case 4, MGG.

previous congenital case has been described (Bresters *et al.*, 2002).

Both discussants expressed themselves puzzled by the normal PB karyotype as there were significant numbers of blast cells in the PB. The chairman wondered whether this cytogenetic analysis might have been performed on PHA-stimulated lymphocytes in order to exclude a constitutional trisomy 21 but subsequent to the meeting further enquiries disclosed that the PB cytogenetic analysis had not actually been normal; it had yielded poor metaphases which were not analysed further once the relevant abnormality had been detected in the BM aspirate taken a day later.

Case 2

The chairman confirmed that this was a leukaemoid reaction resulting from osteopetrosis. The abnormality of bone is shown on chest radiology (Figure 10). A discussant from the audience (Dr D. Swirsky) thought that there

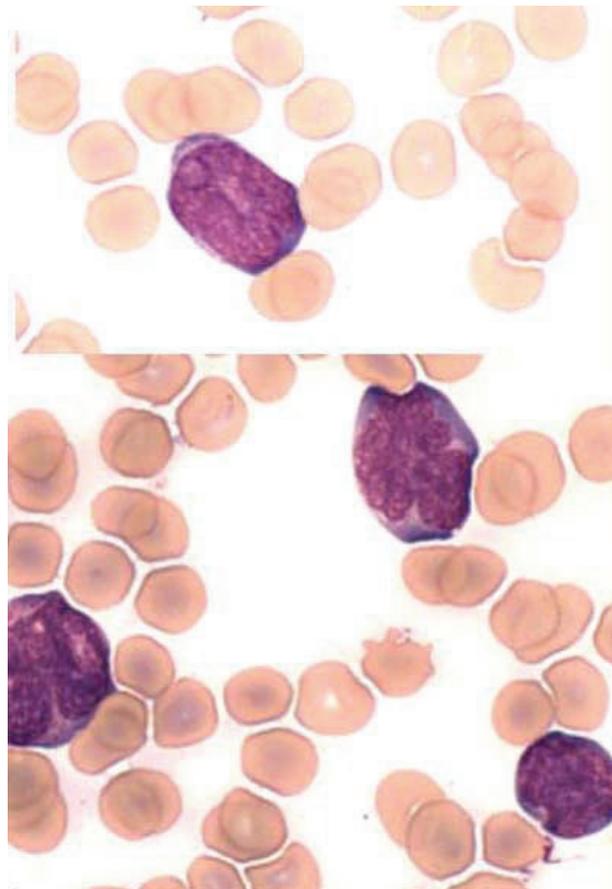


Figure 8. Peripheral blood film of case 5, MGG.

were some dysplastic features; BB agreed and thought this might be due to the abnormal environment of the haemopoietic cells. She also reported that the child was deaf.

Case 3

The diagnosis was congenital sideroblastic anaemia. Ring sideroblasts in a Perls' stain of the BM were demonstrated. Red cell indices at the age of 9 months were: RBC $5.3 \times 10^{12}/l$, Hb 10.2 g/dl, MCV 61 fl, MCH 19 pg and MCHC 31 g/dl.

Case 4

The chairman reported that the patient had been investigated by Professor Nicholas Cross, who had found PCR for *FIP1L1-PDGFR*A to be negative but nested PCR to be positive; this was confirmed by FISH analysis. The diagnosis was therefore eosinophilic leukaemia. More specifically, the patient was suffering from the *FIP1L1-PDGFR*A fusion syndrome or, if this designation is

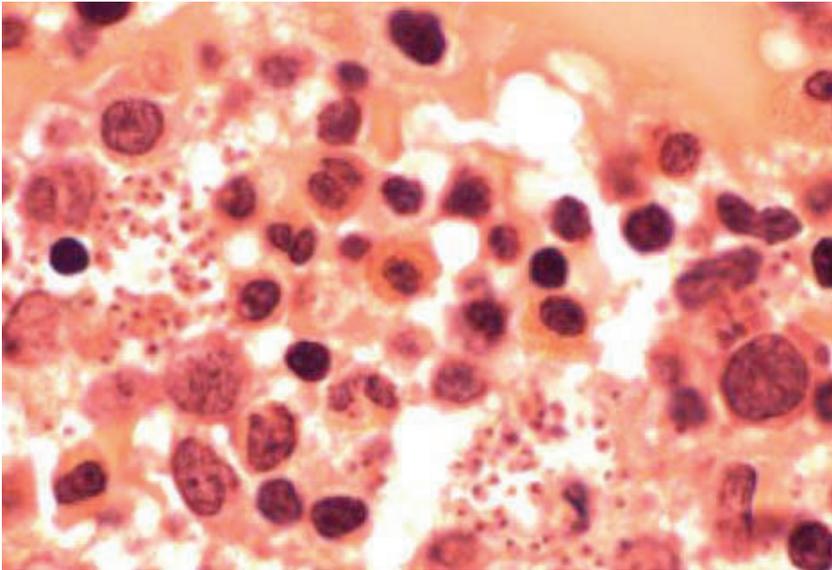


Figure 9. Trephine biopsy section, case 6, haematoxylin and eosin.



Figure 10. Chest radiograph, case 2, showing osteopetrosis.

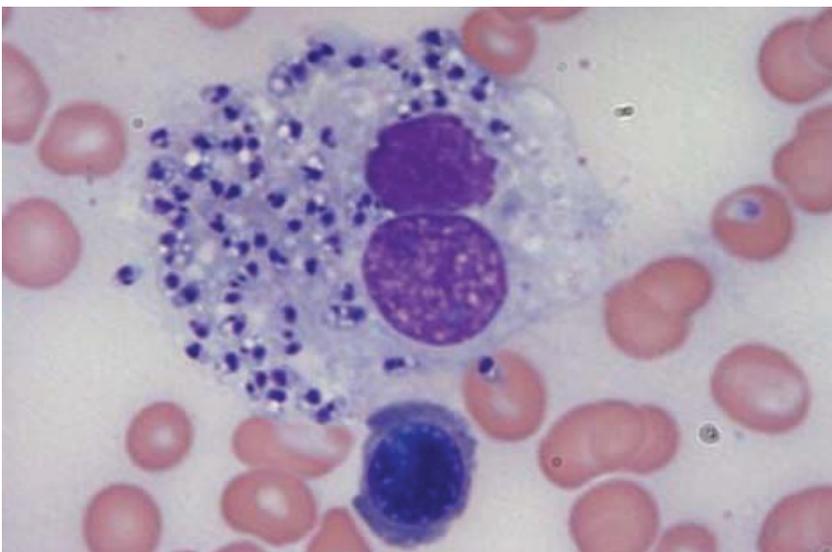


Figure 11. Bone marrow aspirate, case 6, MGG.

considered too cumbersome, from what might be designated the '4q12 syndrome'. The patient was started on imatinib immediately the diagnosis was made and had an excellent response.

Case 5

The chairman reported that there had been no previous haematological diagnosis or treatment. Although on the PB film there appeared to be two populations of cells with some cells looking very like mature lymphocytes, the immunophenotyping showed a single population of cells and the case met the WHO criteria for acute biphenotypic B lymphoid/myeloid leukaemia. There was a complex cytogenetic abnormality and the patient had relapsed after an initial remission.

Case 6

Dr Cynthia Beatty reported, on behalf of the case contributor, that the diagnosis was leishmaniasis

(Figure 11) and that the patient was HIV negative. Following an initial response to treatment he had relapsed and was undergoing further treatment.

The chairman thanked the discussants for their informative and entertaining presentations and closed the meeting.

References

- Breesters D., Reus A.C.W., Veerman A.J.P., van Wering E.R., van der Does-van den Berg A. & Kaspers G.J.L. (2002) Congenital leukaemia: the Dutch experience and review of the literature. *British Journal of Haematology*, **117**, 513–524.
- Ng K.C., Tan A.M., Chong Y.Y., Lau L.C. & Lu J. (2002) Congenital acute megakaryoblastic leukaemia (M7) with chromosomal t(1;22)(p13;q13) translocation in a set of identical twins. *Journal of Pediatric Hematology Oncology*, **21**, 428–430.
- Pesson B., Leger N. & Madulo-Leblond G. (1984) Leishmaniasis in Greece: the sandflies of the Ionian islands and Aegean sea. *Annales de Parasitologie Humaine et Comparee*, **59**, 277–295. (article in French, English abstract in PubMed, PMID: 6465795).