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A case of acute megakaryoblastic leukaemia following a mediastinal germ cell tumour

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A 22-year-old man presented with nausea and fever. His medical history reports a mediastinal germ cell tumour 1 year prior, treated with chemotherapy (cisplatin, bleomycin, ifosfamide) and pneumonectomy, and is now in remission. The blood count revealed anaemia (haemoglobin concentration 114 g/L) and severe thrombocytopenia (platelet count 15×10^9/L). The white blood cell count was within the normal range (WBC 4.75×10^9/L) without neutropenia (3.2×10^9/L). Microscopic examination of the blood film revealed 23% atypical cells of small size, with high nuclear-cytoplasmic ratio, round regular nucleus, condensed chromatin and basophilic cytoplasm sometimes with round expansions that may suggest unusual micromegakaryocytes or megakaryoblasts (figure 1A). These observations led to a bone marrow aspiration which revealed 45% of megakaryoblasts (figure 1B) of medium size, with high nuclear-cytoplasmic ratio, round regular nucleus, intermediate chromatin and basophilic cytoplasm with cytoplasmic granules and blebs similar to platelet expansions suggestive of megakaryocytic lineage. Flow cytometry immunophenotyping showed 26% atypical cells in blood and 44% in bone marrow with low expression of CD45 and intermediate Side Scatter (SS). They did not express B (CD19, CD79a), T (CD3c) or myeloid (CD13, CD33, CD117, MPOc, CD11b, CD14, CD64) lineage markers. Immature markers CD34 and HLA-DR were also negative. This population only expressed the platelet glycoprotein CD41, confirming acute megakaryoblastic leukaemia. Cytogenetic analysis revealed a hyperdiploid and complex karyotype but none of the recurrent genetic abnormalities recognized by WHO and ICC acute myeloid leukaemia classifications. Molecular analysis detected a high level (VAF 0.55) mutation of *TP53* (c.581T > C, p.Leu194Pro) and a *KIT* mutation (c.1679_1681del, p.Val560del) at an intermediate level (VAF 0.26). A cytogenetic reanalysis on the DNA extract of the tumour found the same mutations of *TP53* and *KIT* (VAF: 0.94 and 0.63, respectively). Following these results, Li–Fraumeni syndrome was suspected, but further analysis excluded germline involvement. The patient received an allogeneic haematopoietic stem cell transplant and is now in complete haematological response on imatinib + azacytidine.

This observation highlights the difficulty in identifying atypical megakaryocytic cells in peripheral blood and their importance for the diagnosis of acute megakaryoblastic leukaemia, especially in this specific condition. The succession of non-seminomatous mediastinal germ cell tumour followed by acute megakaryoblastic leukaemia in a young man is a rare phenomenon but well described in the literature [1]. Although in our case, the temporality between the two diseases could incriminate the chemotherapy of the germ cell tumour, the literature shows that this acute myeloid leukaemia should not be considered therapy-related [2] but nevertheless retains a poor prognosis.

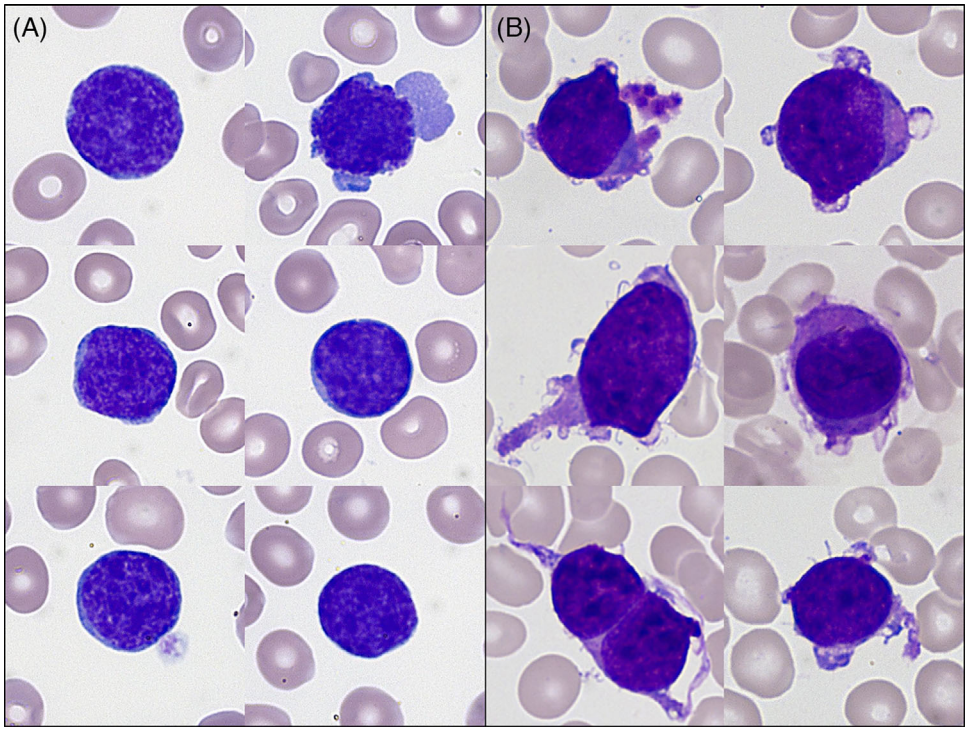

FIGURE 1 (A) Blood film examination, May–Grünwald–Giemsa, ×100 objective. Atypical cells that may suggest unusual micromegakaryocytes or megakaryoblasts. (B) Bone marrow aspiration, May–Grünwald–Giemsa, ×100 objective. Megakaryoblasts.

AUTHOR CONTRIBUTIONS

PLM and AC wrote the paper. PLM and JBR performed the blood smear examination. AC performed the bone marrow examination. JBR performed flow cytometric studies. AC took the pictures. LR performed molecular studies. SB and ST followed the patient. All authors contributed to the final manuscript.

CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest.

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PATIENT CONSENT STATEMENT

The authors did not obtain written informed consent from the patient but the patient did not object to his data being used for research purposes (as required by the ethic policy of CHU Toulouse).

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CLINICAL TRIAL REGISTRATION

The authors have confirmed clinical trial registration is not needed for this submission.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analysed in this study.

ETHICS APPROVAL STATEMENT

This manuscript respect the ethic policy of CHU Toulouse for the treatment of human research participants.

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