Acute megakaryoblastic leukemia AML FAB-M7 in a patient 15 years after kidney transplantation

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Abstract: Letter to the Editor

Acute megakaryoblastic leukaemia AML FAB-M7 in a patient 15 years after kidney transplantation

Response to Reviewers: Arnold Ganser, M.D.
Editor-in-Chief
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Dear Editor

please find enclosed the revised version of our manuscript AOHE-D-10-00398

"Acute megakaryoblastic leukaemia AML FAB-M7 in a patient 15 years after kidney transplantation "

by Alexandra Scholze, Igor W. Blau, Martin Tepel

for publication in Annals of Hematology as a Letter to the Editor.

The Answers to the Reviewer's comments are given below.

"All authors have read and approved the submission of the manuscript; the manuscript has not been published and is not being considered for publication elsewhere, in whole or in part, in any language, except as an abstract."

Enclosed you find the manuscript, uploaded online, including all figures.

Competing interests statement: The authors declare that they have no competing financial interests.

Yours sincerely

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Answers to Reviewer's comments

1. Molecular changes were not determined.

2. Because the patient presented severely disabled (Karnofsky score 30), the therapy was limited.

3. The immunosuppressive regimen consisted of cyclosporine A and prednisolone. The antihypertensive treatment comprised furosemide, a beta blocker and an ACE inhibitor. No episodes of acute rejection had occurred in the post-transplant course.

4. The typographical errors were corrected

***Conflict of interest**

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Letter to the Editor

Acute megakaryoblastic leukaemia AML FAB-M7 in a patient 15 years after kidney transplantation

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Dear Editor

we report a case of acute megakaryoblastic leukaemia French-American-British classification M7 (AML FAB-M7), a rare form of leukaemia in the late post-transplantation period, which occurred in a patient 15 years after kidney transplantation. A 42-year-old man presented severely disabled (Karnofsky score 30) with fever of unknown origin and pancytopenia. He complained of weakness, loss of appetite and elevated temperature for several days, ranging from 38°C to 40°C. The patient had been transplanted with a cadaveric kidney 15 years earlier. The cause of end stage renal disease was unknown. No episodes of acute rejection had occurred in the post-transplant period. There was a slow progressive loss of renal function, a renal transplant biopsy obtained 1 year earlier showed a pronounced chronic allograft nephropathy with a severe arteriolohyalinosis but no signs of acute rejection or calcineurin inhibitor toxicity. The immunosuppressive regimen consisted of prednisolone (10 mg/day) and cyclosporine A (200 mg/day) throughout. The antihypertensive treatment comprised furosemide, beta blockers and angiotensin converting enzyme inhibitor. White blood count was reduced to 1.83/nL consisting of 76% neutrophilic granulocytes, 11% lymphocytes 13 % monocytes 0% eosinophilic granulocytes and 0% basophilic granulocytes. Platelet count was reduced to 70/nL and hemoglobin was reduced to 7.0g/dL. The clinical evaluation of the skin, head and neck, heart and lung, abdomen including the side of transplantation, and the neurological status showed no pathological findings. Kidney function was stable with creatinine values of 400µmol/L. Urinanalysis did not show urinary tract infection. Blood cultures were negative. Ultrasound of the transplanted kidney showed no pathologic findings. A computed tomography of thorax and abdomen did not show pathological findings except enlargement of the spleen with 15 cm. Lymph node enlargement was not observed. Transoesophageal echocardiography did not show signs of endocarditis. A broncho-alveolar lavage excluded pneumocystis carinii, mycobacteria or legionellae, and the patient was tested negative for human immunodeficiency virus and hepatitis. Screening for cytomegalovirus was negative, whereas polymerase chain reaction for Epstein-Barr virus was slightly positive. A bone marrow aspirate showed mainly myeloid cells with enhanced expression of cluster of differentiation 13 (CD 13), representing an early granulocytic antigen. On the other hand, CD 33, an antigen of myeloid progenitor cells, was observed in only 3%. The stemcell factor receptor c-kit, a marker of immature blast cells, was enhanced and could be detected in 4% of cells. A cytogenetic analysis showed no structural or clonal numerical chromosomal aberrations. The cytological picture showed an extensive megakaryopoiesis with a shift to

early cell stages and partially atypical nuclei (**Figure 1**). Staining showed an excess of stored iron. The erythropoiesis/granulopoiesis (E/G) ratio was markedly shifted in favor of granulopoiesis. All specimens showed a population of megakaryocytic blast cells. Cytology of the bone marrow aspirate showed acute AML FAB-M7. Because the patient was severely disabled, a therapy with low dose cytarabine was started. However, the patient developed severe aplasia and septicemia. The patient died 3 weeks after diagnosis.

A wide variety of causes are considered when fever occurs in a patient after renal transplantation. The most common causes are viral, bacterial or opportunistic infections, transplantat rejection, side effects of new medications or malignancies [1]. It appears that AML does develop more frequently after transplantation than in the normal population [2-4]. The incidence of AML after solid organ transplantations is about 0.2 to 2.5%. Post-transplant-AML seems to develop after a median interval of 5 years (range 1-17 years). It is heterogeneous with respect to FAB classification and may show chromosomal and molecular changes [4]. However, the present case shows that AML FAB-M7 may develop as treatment related without carrying multiple chromosomal aberrations.

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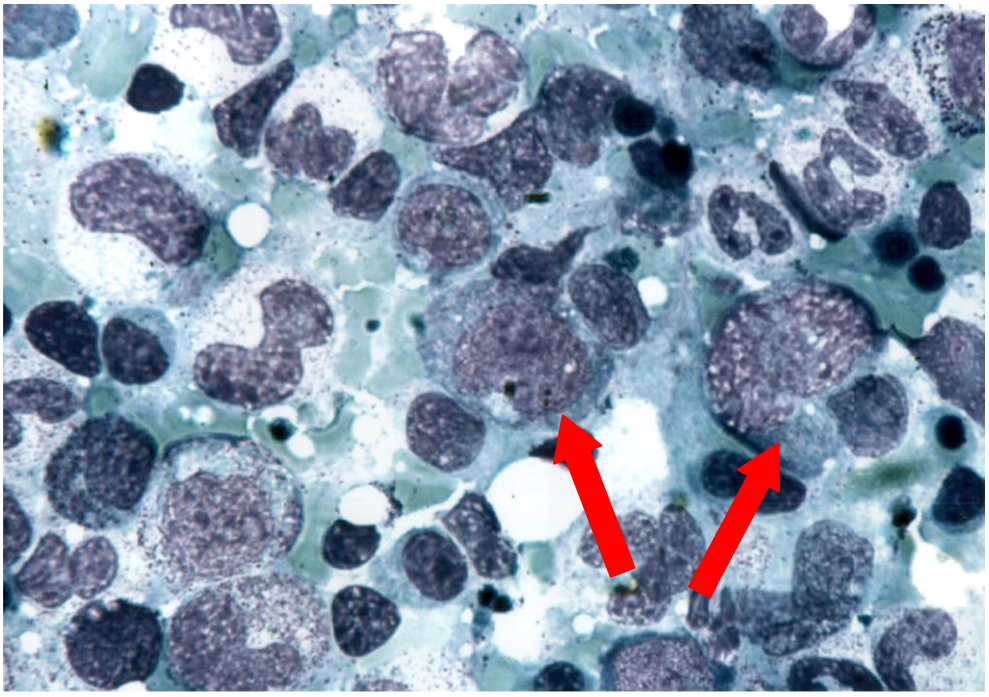
Figure legend

Figure 1. Bone marrow aspirate in a patient with recurrent fever of unknown origin and pancytopenia 15 years after renal transplantation. Cells of the hematopoiesis are shown. Arrows indicate megakaryoblasts, i.e. large cells with basophilic cytoplasm and loose chromatin in their eccentric and noncircular nucleus. Cytological picture of the cellrich, leukaemic bone marrow led to the final diagnosis of acute megakaryoblastic leukaemia French-American-British M7 (AML FAB-M7).



Scholze et al., Figure 1.