Granulocytic sarcoma of the brain in a patient with acute myeloid leukemia

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Granulocytic sarcoma is extramedullary tumor composed of immature leukemic cells most frequently located in close proximity to bone, but it also can be found in the skin, breast, gastrointestinal tract, ovaries and brain. Granulocytic sarcoma may arise during the course of leukemia or precede its development in the bone marrow. The majority of reported cases of granulocytic sarcomas in acute myeloid leukemia have chromosome translocation t(8;21). We report a 46-year-old man with acute myeloid leukemia, type M2 involving the marrow and peripheral blood and chromosome t(8;21) who developed granulocytic sarcoma in the brain, as a first manifestation of relapse 6 months after complete remission was achieved. During a neurosurgical operation a cortically located tumour (3.5x5 cm) in the brain was partially removed. Histology showed tumor consisted of homogenous infiltrate of blasts, admixed with more mature haematopoietic cells. The blasts have large round to oval nuclei, delicate chromatin, one or more small well-defined nucleoli and scant basophilic cytoplasm. Immunohistochemistry showed that blast cells were myeloperoxidase positive, confirming the diagnosis of myeloblastic sarcoma in the brain. The patient died two days after surgery.

Key words: granulocytic sarcoma, brain

INTRODUCTION

Granulocytic sarcoma is a localized extramedullary tumor of poorly differentiated cells of the myelogenous series. It may develop simultaneously with an acute myeloid leukemia, and can be also the first evidence of a relapse after acute myeloid leukemia treatment, or precede the diagnosis of a myeloid leukemia by months or years. The most common sites for this tumors are the skull, paranasal sinuses, sternum, ribs, vertebrae and pelvis. Granulocytic sarcomas in the brain in patients with acute myeloid leukemia (AML) and t(8;21) have been reported very rarely.

Granulocytic sarcomas occur most commonly in patients with two types of leukemia, AML with t(8;21) and chronic myeloid leukemia (CML). However the pathogenesis of extramedullary tumor formation in AML with t(8;21) and CML is unclear. These patients have a less favourable prognosis than others with t(8;21), who, in general have favourable outcome with chemotherapy. The treatment of granulocytic sarcomas include chemotherapy, local radiotherapy and surgical excision, if possible.

CASE REPORT

A 46-year-old man presented in September 2001, with malaise and fever. On physical examination palor and bleeding was found. Liver was palpable 2 cm below the right costal margin. Blood counts showed hemoglobin 42 g/l, white blood cells(WBC) 21.1x10⁹/l, platelets 3x10⁹/l, differential count: myeloblasts 46%, myelocytes 2%, metamyelocytes 1%, neutrophils 21%, eosinophils 2%, lymphocytes 23%, monocytes 5%, Erythrocyte sedimentation rate was 120/1⁰ hour. Biochemical analyses of the blood were within normal limits. Bone marrow aspirate showed hypercellularity with 94% of blasts which were myeloperoxidase positive. Cytogenetic analysis showed abnormal clone 46XY, t(8;21)(q22;q22) in six of twelve analyzed metaphases. Induction chemotherapy was performed with daunorubicin and cytosine-arabinoside. A complete remission was achieved and consolidation therapy according to MRC AML 10 protocol was administered. Six months later, the patient developed speech difficulties and lost concience. The difficulties in talking remained. His laboratory data were as follows: Hb 111 g/l, WBC 2.3x10⁹/l, (differential count was normal), platelets 50x10⁹/l, bone marrow aspirate showed relapse with normocellularity and 36% of myeloblasts. CT scan of brain showed a tumor in left frontotemporal region (Fig. 1). The neurosur-
gical operation was performed and a cortically located poorly demarcated tumour (3.5x5 cm) diameters within the brain was partially removed. The patient died two days after surgery. Histology showed granulocytic sarcoma infiltrating the brain (Fig. 2).

**DISCUSSION**

Granulocytic sarcomaa is a localized tumor consisting of myeloblasts or immature myeloid cells occurring in the bone or an extramedullary site in patients with acute leukaemias or different myeloproliferative disorders e.g. chronic myeloid leukemia, polycythaemia rubra vera, agnogenic myeloid metaplasia. Granulocytic sarcomas were initially described in 1823. The association with acute leukemia was not recognised until 1893. Granulocytic sarcoma is composed of myeloblasts or neutrophil precursors. The myeloid tumor may be the initial manifestation of relapse in a previously treated AML in remission. The most frequent sites of occurrence are subperiosteal bone structures of the skull, sternum, paranasal sinuses and pelvis. Lymph nodes and skin are also commonly affected sites. The diagnosis is often difficult in these cases, the most common problem being distinction from malignant lymphoma. Immunohistochemical and enzyme histochemical staining are useful in establishing the diagnosis.

A less common is monoblastic sarcoma which may precede or occur simultaneously with acute monoblastic leukemia. Staining of sections with antibody to myeloperoxidase, lysozyme and chloroacetate esterase are of critical importance for the diagnosis. The myeloblasts in the granulocytic sarcomas have profiles similar to the blasts and precursor cells in AML, expressing myeloid-associated antigens: CD13, CD33, CD117, MPO.

In adults granulocytic sarcomas are most frequently associated with FAB M2 morphology, although they occasionally occur in other morphologic subtypes of acute leukemia including myelomonocytic leukemia (M4, M5) and acute megakaryocytic leukemia. These tumors are found in only 3-7% of all other types of AML (5-9).

Karyotype analyses were not performed in the majority of reported cases with granulocytic sarcoma, but the vast majority of reported abnormal karyotypes involved either t(8;21) or t(9;22)15,16. Swirsky et al. reported 33 patients with t(8;21), seven of which (21%) developed granulocytic sarcomas either at the time of diagnosis or at the time of relapse. Abe et al. reported granulocytic sarcomas associated with t(8;21) in 17% of patients (16). In the same series among 117 patients with either a normal karyotype or other chromosome abnormalities, only one patient had a granulocytic sarcoma. According to these data association of granulocytic sarcoma and t(8;21) is more common than generally recognized. Patients with t(8;21) should be observed closely for signs and symptoms of granulocytic sarcoma, because they may have a less favourable prognosis than other patients with t(8;21). In these patients aggressive therapy such as bone marrow transplantation may be warranted early in the therapeutic strategy.

**REZIME**

**GRANULOCITNI SARKOM MOZGA KOD BOLENIKA SA AKUTNOM MJUELIDNOM LUEKEMIJOM**

Granulocitni sarkom je ekstramedularni tumor sastavljen od nezrelih leukemijskih čelija naješe lokalizovan u blizini kosti, redje u koži, dojka, gastrointestinalnom traktu, ovarijsnjima i mozgu. Granulocitni sarkom može nastati u toku lekemije ili predhoditi njoj pojavi u

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**Figure 1**

CT SCAN SHOWING A CORTICAL TUMOR MASS IN FRONTOTEMPORAL REGION OF THE BRAIN.

**Figure 2**

SHOWING THE BRAIN PARENCHYMA INFILTRATED WITH DENSE HOMOGENOUS INFILTRATE OF BLASTS ADMIXED WITH MORE MATURE HAEMATOPOIETHIC CELLS. SOME EOSINOPHILS ARE SCATTERED AMONG THE BLASTS. BLASTS HAVE LARGE ROUND TO OVAL NUCLEI, DELICATE CHROMATIN, ONE OR MORE SMALL WELL-DEFINED NUCLEOII AND SCANT BASOPHILIC CYTOPLASM. H&E X400.
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kostnoj srži. Većina prikazanih granulocitnih sarkoma u akutnoj miješodnom leukemiji imala je hromosomsku translokacij (t(8;21). Autori prikazuju 46 godina starog muškarca sa akutnom miješodnom leukemijom tipa M2 sa hromosomskom translokacijom (t(8;21) koja je zahvalila perifernu krv i kostnu srž, u toku koje se razvio granulo
citni sarkom mozga kao prva manifestacija recidiva bolesti, šest meseci nakon što je postignuta kompletan re
misija. Tokom neurohirurške operacije kortikalni tumor promera 3.5x5 cm delimično je odstranjen. Histološki tu
mor je sadržavao homogene infiltrate blaste pomešane sa hematopoetskim celijama u sazrevanju. Blasti su imali
kruna ovalna jedra, nezna hromatin, jedan ili više malih
nukleolusa i oskudnu bazofilnu citoplazmu. Imunohisto
ehemski blasti su bili mijeloperoksidaza pozitivni. Boles
nik je umro 2 dana nakon operacije.

Ključne reći: granulocitni sarkom, mozak, akutna
miješodna leukemija

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