

Acute Myeloid Leukemia Presenting as Subcutaneous and Epidural Granulocytic Sarcoma Inside and Outside of the Frontal Bone

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Abstract

An 18 year-old male was admitted to our hospital suffering from a large tumor which was located at the right frontal bone. He was diagnosed to have acute myeloid leukemia (AML) with granulocytic sarcoma (GS). A chromosomal analysis showed t (8 ; 21), and a flow cytometric analysis demonstrated the leukemic cells to be positive for CD56.

Systemic chemotherapy and radiation therapy to the GS, but the patient experienced a relapse in the lumbar vertebrae. He underwent an umbilical-cord blood stem cell transplantation, however, he died 7 months thereafter. GS is a localized tumor consisting of leukemic myeloblasts, which is generally observed as a complication of either AML, myelodysplastic syndrome, or myeloproliferative disorders. We herein report this case due to its rarity, even though various sites of GS have been reported. (Kitakanto Med J 2007 ; 57 : 183~185)

Key Words : Acute myeloid leukemia (AML), granulocytic sarcoma, CD56, t (8 ; 21), Frontal bone

Introduction

Granulocytic sarcoma (GS) is a localized tumor consisting of leukemic myeloblasts, and a form of extramedullary leukemia. GS is generally observed as a complication of either acute myeloid leukemia (AML), myelodysplastic syndrome, or myeloproliferative disorders, with an incidence of from 3 ~ 5 %.¹ GS may occur in any part of the body, including the skin, lymph nodes, spine, small intestines, orbit, bone, breast, cervix paranasal sinus, meninges, menialastinal mass, brain, and tends to occur in young persons.² When occurring in the head and neck area, GS has been reported to occur in the maxilla, soft palate, nasopharynx, lip, salivary glands and mandible. In children, it tends to occur in the orbit³ and temporal bone, and it is only very rarely observed in the frontal bone. We herein describe a rare case of GS which occurred on the inside and outside of the frontal bone

which presented as the first sign of AML (M2), which also expressed CD56 and demonstrated a chromosomal abnormality of t (8 : 21).

Case report

An 18 year-old male was admitted to another hospital in May 2003 suffering from 5×5×4 cm tumor located in the right frontal bone. Blast cells appeared in the peripheral blood. His past, familial and life medical history was unremarkable. Physical examination demonstrated no anemia, no surface lymph nodes swelling or hepatosplenomegaly. Although he has choked disks and quadrant hemianoptics in both eyes, he did not show any other neurological abnormalities. Laboratory tests were as follows : Hb 14.1 g/dl, platelet count 308×10⁹/l, WBC 5.0×10⁹/l with 47.0% of blasts.

Biochemical tests showed serum LDH 514 U/l (< 229 U/l), ALP 285 U/l, AST 22 U/l, ALT 36 U/l. A

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bone marrow examination showed 63.4% of myeloblasts to be positive for myeloperoxidase and ASD chloroacetate esterase staining and negative for α -naphthyl butyrate esterase. He was thus diagnosed to have having acute myeloid leukemia (FAB: M2). A flow cytometric analysis demonstrated the leukemic cells to be positive for CD13, CD33, CD34, CD56, CD117, and HLA-DR. A chromosomal analysis of the bone marrow cells showed t (8; 21) in 10 of 20 cells, and multiplex quantitative RT-PCR showed the presence of the AML1/MTG8 chimeric gene. CT scans showed a markedly high density tumor both inside and outside of the right frontal bone with hypodense peritumoral edema and a slight midline shift. The hyperdense mass was homogeneously enhanced with iodinated contrast medium. The tumor inside of the skull was an epidural tumor while the outside one was a subcutaneous tumor. There was no lytic or sclerotic destruction of the bone except for a slight periosteal reaction (fig. 1). Gallium scintigraphy demonstrated an abnormal uptake in the same region. A pathological examination of the tumor revealed a diffuse proliferation of atypical cells which appeared to be similar myeloblast. A flow cytometric analysis showed the same phenotype as bone marrow blasts except for the fact that CD19 was positive. This tumor was thus diagnosed to be GS.

Induction chemotherapy consisting of idarubicin 12 mg/m² for 3 days and cytarabine 100 mg/m² for 7 days was initiated and a CT scan showed a remarkable reduction of the tumor size on day 26. A bone marrow examination on day 40 revealed a complete remission (CR) with 2.4 % of myeloblasts, while both a chromosomal analysis and a FISH analysis of a bone marrow specimen demonstrated no abnormal karyotype. Three courses of consolidation chemotherapy, consisting of high dose cytarabine 2 g/m² × 2 for 5 days, was initiated. After first performing consolidation therapy, a lumbar puncture examination revealed a few atypical cells in the cerebrospinal fluid. He was administered intrathecal methotrexate 15 mg/body, cytarabine 40 mg/body and prednisolone 10 mg/body each consolidation chemotherapies. After these procedures, the atypical cells disappeared. The tumor thereafter significantly decreased and a CT scan showed a slight subcutaneous high density area after the last consolidation chemotherapy. In addition, the choked disks and quadrant hemianoptics also improved. After the consolidation chemotherapy, he received radiation therapy to the right frontal bone with total 10 Gy and to the whole brain with a total 10 Gy.

In May 2004, he felt pain in his right leg. MRI demonstrated a tumor mass at the L5/S1, and a bone



Fig. 1 A computed tomography (CT) image showing a subcutaneous and epidural mass in the right frontal bone.

marrow examination revealed a relapse. A flow cytometric analysis of the bone marrow specimen demonstrated the blasts to be positive for both CD56 and CD19. It was also the same phenotype as the first presence of GS. Re-induction chemotherapy was not effective and he thus underwent an umbilical-cord blood stem cell transplantation with conditioning regimen of 12 Gy of total body irradiation (TBI)+60 mg/kg of cyclophosphamide under a non-CR status in March 2005. However, at 7 months after transplantation, he relapsed again, and died due to a progression of the disease.

Discussion

GS occurring in the head and neck is not very rare, however, there have only been two previously reported cases occurring in the frontal bone based on our search.^{4,5} Our case demonstrated intracranial GS which arose from the hematopoietic tissues of the skull bones and then transverse the haversian canals to reach the subperiosteum and the dura mater. It then penetrated through the perivenous adventitial tissue and reached the subarachnoid space. The characteristics of GS in this case were very similar to those of the previously reported cases.⁴

It is interesting to note that there were two different phenotypes of blasts in the bone marrow and GS according to the expression of CD56/CD19. Most of the blasts in the bone marrow were CD56+/CD19- but the blasts in the GS were CD56+/CD19+. Recent reports have noted that CD56 expression tends to be seen at a higher rate in patients with GS than in those without it⁶ and an expression of the CD56 was

also significantly more frequent among the 8 ; 21 translocation cases than in other translocation cases.^{6,7}

When our patient relapsed, bone marrow blasts became positive for CD56 and CD19. The association between the co-expression of CD56/CD19 in AML (M2) and the t (8 ; 21) karyotype remains to be elucidated, and the role of CD19 antigen in GS is also unknown.^{6, 7} This phenomenon may be because a very small population of the CD56+/CD19+ blasts in the bone marrow formed the GS, and this minor population was chemo-resistant, thus resulting in a relapse.

GS is very often misdiagnosed as a malignant lymphoma, and it is generally treated with the chemotherapy regimen for lymphoma. As a result, the appropriate treatment is delayed, thus leading to a poor outcome. Therefore an early and accurate diagnosis is important in such cases.

Our patient had the unique presentation of AML with a large subcutaneous and epidural granulocytic sarcoma both inside and outside of the frontal bone, thus leading to an unfortunately outcome. In the future, AML with t (8 ; 21) and having such unfavorable characteristic as GS, and CD56 expression should be more thoroughly characterized.

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