Abstract

A 30-year-old female presented with a rare case of isolated recurrence of granulocytic sarcoma manifesting as extra- and intracranial masses 16 months after successful treatment of acute myeloblastic leukemia (M-2). She presented with a swelling located on her forehead that had appeared just after hitting her forehead, and never diminished in size. The mass was elastic hard and not freely mobile. Computed tomography and magnetic resonance imaging demonstrated enhanced masses in the right frontal extra- and intracranial region with no bone destruction. There was no evidence of relapse in the bone marrow. Needle aspiration biopsy of the subscalpal mass was performed. Fluorescence in situ hybridization revealed AML1/MTG8 fusion gene associated with t(8; 21). Two courses of systemic chemotherapy with high-dose cytarabine and total neural axis irradiation resulted in complete remission.

Key words: acute myeloblastic leukemia, granulocytic sarcoma, subcutaneous tumor, intracranial tumor, head trauma

Introduction

Granulocytic sarcoma, also known as chloroma, myeloblastoma, and extramedullary leukemia, is a localized tumor consisting of leukemic myeloblast and myeloid precursors. Granulocytic sarcoma may occur in any part of the body, such as bone, orbit, paranasal sinus, para- and intraspine, skin, stomach, colon, kidney, breast, cervix, and vagina. Granulocytic sarcoma is generally observed as a complication of acute myeloblastic leukemia, myelodysplastic syndromes, or myeloproliferative disorders, with an incidence of 3.1–4.7%. Isolated recurrence is uncommon, especially as an intracranial mass.

We describe a rare case of isolated recurrence of granulocytic sarcoma manifesting as extra- and intracranial masses which went into complete remission after intensive treatment.

Case Report

A 30-year-old female presented with purpura of the extremities and palpitations in April 2001. She was admitted to another hospital. The diagnosis was acute myeloblastic leukemia M-2 in the French-American-British classification. Peripheral blood examination showed hemoglobin level of 5.5 g/dl, platelet count of 130,000/mm³, and white blood cell count of 10,500 cells/mm³ with 56% myeloblasts. The bone marrow was markedly hypercellular with myeloblasts. Surface marker analysis of the bone marrow mononuclear cells revealed positive reaction for CD19 (50.9%), CD13 (37.9%), CD33 (35.2%), CD34 (75.1%), CD56 (57.3%), and human leukocyte...
antigen-DR (75.6%). Chromosomal analysis of the bone marrow cells showed 46, XX, add(3)(q27) (arrowhead), t(8; 21)(q22, q22) (arrows). Fig. 1 G-banded metaphase from bone marrow biopsy material. Karyotype showing 46, XX, add(3)(q27) (arrowhead), t(8; 21)(q22, q22) (arrows).

She underwent one course of systemic chemotherapy with cytarabine and idarubicin hydrochloride, which did not achieve complete remission. She then received two courses of chemotherapy with cytarabine, etoposide, and mitoxantrone hydrochloride, which resulted in complete remission.

She was admitted to our hospital for allogeneic peripheral blood stem cell transfusion (PBSCT) in October 2001. After administration of thiotepa and cyclophosphamide, and total body irradiation (12.5 Gy), she received PBSCT from her human leukocyte antigen-identical sister. Engraftment was prompt and confirmed by the variable number of tandem repeats. She was discharged in January 2002.

She hit her forehead and developed a swelling in September 2002. As the swelling never diminished in size, she was referred to our clinic. Physical examination found a 3-cm swelling over the right frontal region, which was elastic hard with no signs of inflammation and not freely mobile. Neurological examination was unremarkable with no meningeal signs and no focal neurological deficits. Computed tomography (CT) demonstrated a subcutaneous extracranial irregular high density mass and an intracranial diffuse slightly high density mass with perifocal brain edema. There was little skull destruction between the masses (Fig. 2). At this time we could not establish definitely whether the masses were hematoma/contusion or tumor.

T1-weighted magnetic resonance (MR) imaging demonstrated the extracranial mass as an irregular high intensity area and the intracranial mass as a relatively low intensity area with peritumoral edema. T1-weighted imaging showed that the masses were slightly low intensity. T1-weighted imaging with contrast medium showed the extracranial mass with irregular enhancement and the intracranial mass with strong homogeneous enhancement. The sagittal images clearly showed that the lesion spread dorsally along the superior sagittal sinus (Fig. 3). Right external carotid angiography showed marked vascular staining at the region of the masses. Right internal carotid angiography showed only a scant...
blood supply from the anterior falcial artery, and almost no flow near the mass in the superior sagittal sinus in the venous phase (Fig. 4). These CT, MR imaging, and angiography findings were compatible with granulocytic sarcoma.28,37)

We concluded that the masses were tumors and aspiration biopsy of the extracranial mass by needle was carried out. Cytological study revealed high nuclear cytoplasmic ratios, fine chromatin, nucleoli, and immature atypical cells classified as class V. Fluorescence in situ hybridization showed the AML1/MTG8 fusion gene which is associated with t(8; 21). There was no evidence of leukemic relapse in the bone marrow or peripheral blood. The final diagnosis of the masses was isolated recurrence of granulocytic sarcoma of the skull.

Surgical resection was avoided because of the possibility of infection during the following consecutive chemotherapy, the definitive diagnosis, and mass reduction would offer no advantage in the absence of progressive neurological disorders.36,38) Two courses of systemic chemotherapy with high-dose cytarabine were given followed by whole neural axis irradiation (whole brain 16 Gy, total spinal 24 Gy). She is now free from symptoms and both the bone marrow and extra- and intracranial lesions have remained in complete remission (Fig. 5).

**Discussion**

Only 24 cases of isolated recurrence of granulocytic sarcoma after prior acute myeloblastic leukemia have been described since 1973.8) The onset of granulocytic sarcoma was almost always followed by bone marrow relapse after 1–19 months (mean 7 months) and the outcomes were poor.28)

Subscalpal tumors can be difficult to identify without a surgical procedure. Fine needle aspiration biopsy can be performed to minimize the trauma to the patient. Eighteen cases of subscalpal masses were found among 1772 cases of subcutaneous masses, of which six were myeloma, 10 were metastatic tumors, one was malignant lymphoma, and two were benign masses.4) In our case, aspiration biopsy established the diagnosis based on pathological and cytogenetic evidence.

Tumors growing both extra- and intracranially are generally primary neuroepithelial tumors, primary bone lesions, and metastases.11) Such tumors are usually associated with osteolytic or sclerotic lesions. In our case, there was little destruction of the skull bone. Granulocytic sarcoma has been reported in extra- and intracranial locations.8,33) Intracranial granulocytic sarcoma arises from the hematopoietic tissue of the skull bones and transverses the haversian canals to reach the subperioste-
um and the dura mater, then penetrate through the periventricular adventitial tissue to the subarachnoid space.2,11,15,27) Any disruption of the pia-glial membrane results in intracerebral granulocytic sarcoma, which may infiltrate through the subarachnoid space into brain parenchyma and eventually form an intracerebral tumor.29) Other common sites are the orbits and the paranasal sinuses,12,17) Paraspinal12) and intraspinal20) granulocytic sarcomas are also common. Multifocal granulocytic sarcoma is known but is relatively rare.20)

Malignant lymphoma may occur as a subscalpal mass at the site of a previous head trauma.18,22,24,34,35,39) Prolonged or repeated inflammation caused by trauma may induce cellular atypia leading to neoplasm, as in a case of post-traumatic intracranial meningioma.5) Review of eight cases of malignant lymphoma of the scalp suggested that circulating lymphoma cells may lodge and accumulate at the locus minoris resistantiae.24) No similar case of granulocytic sarcoma has been reported, but one patient presented with chronic subdural hematoma and 3 months later a meningeal tumor was discovered adjacent to the previous hematoma and was found to be granulocytic sarcoma.1) Although the link between trauma and granulocytic sarcoma in our case remains obscure, we suppose that the trauma could have induced extra- and intracranial granulocytic sarcoma.

The translocation t(8; 21) is present in 7% of all patients with acute myeloblastic leukemia and in 18% of patients with the M-2 subtype of acute myeloblastic leukemia.14) The prognosis is usually rather good, but the presence of granulocytic sarcoma unfavorably affects the remission rate and overall survival in patients with acute myeloblastic leukemia and t(8; 21).9) Co-expression of CD56 may be involved in the predisposition of t(8; 21) acute myeloblastic leukemia to develop granulocytic sarcoma.21) CD56 was expressed in 63% of acute myeloblastic leukemia cases with t(8; 21) but in only 14% of other M-2 leukemias.16) CD56 is known to identify an isoform of the neural cell-adhesion molecule (NCAM), a member of the immunoglobulin superfamily of cell-adhesion molecules. Adhesion molecules like NCAM represent homing receptors which tend to target neoplasia in particular types of tissue and to determine patterns of metastasis.32) NCAM is found in cells of the brain, nerve, and muscle, and natural killer cells.10) We speculate that a patient with t(8; 21) and CD56-positive leukemic blasts may develop granulocytic sarcoma involving unusual sites such as the central nervous system, as in our case.

Patients who did not receive systemic chemotherapy expired after bone marrow relapse.13) Review of eight reported cases concluded that immediate prophylactic systemic chemotherapy for granulocytic sarcoma during bone marrow remission would lead to favorable outcomes.38) Our patient received systemic chemotherapy and whole neural axis irradiation, and achieved complete remission. Although surgical excision remains controversial,26,33,36,38) we think there is no advantage following chemotherapy and irradiation, except in the presence of progressive neurological deficits such as increasing intracranial pressure or disturbance of consciousness which are uncontrollable by the conservative treatment. Surgery would increase the risk of infection and central nervous system dissemination. Therefore, we suggest that the important factors for the favorable outcome of isolated granulocytic sarcoma are immediate pathological and cytogenetic diagnosis, and intensive treatment with chemotherapy.

References

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Yuki K, Kodama Y, Onda J, Emoto K, Kirimoto K,

Address reprint requests to: S. Nishimura, M.D., Department of Neurosurgery, Hiratsuka Kyosai Hospital, 9–11 Oiwake, Hiratsuka, Kanagawa 254–8502, Japan.
E-mail: nishimura-s@kkr.hiratsuka.kanagawa.jp