CASE REPORT

Solitary Preleukemic Granulocytic Sarcoma as a Cause of Small Bowel Obstruction

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Granulocytic sarcoma is an extramedullary tumor composed of immature granulocytic cells. These tumors usually occur simultaneously with or follow after the onset of acute myeloid leukemia (AML) or other myeloproliferative disorders. Rarely, it is the first manifestation of AML which appears several months before the onset of leukemia. We report a case of a 48-year-old man presenting with symptoms of small bowel obstruction. Laparotomy and open biopsy were performed. Immunohistochemical studies showed that the neoplastic cells were of myeloid lineage positive for myeloperoxidase and leukocyte common antigen, but negative for CD3, 20, 56, 79a, and cytokeratin. Initially, there was no evidence of blood or bone marrow involvement suggesting acute leukemia or other myeloproliferative disorders. The findings were consistent with the diagnostic findings of solitary granulocytic sarcoma (preleukemic). However, one month later, bone marrow biopsy revealed 57% myeloblasts. Sequentially, the patient developed FAB M2 acute myeloid leukemia. Induction chemotherapy including cytarabine and idarubicine was done which led to complete remission. Allograft bone marrow transplantation was performed later, and there is no evidence of recurrence till present. (*Gut and Liver* 2007;1:82-86)

Key Words: Granulocytic sarcoma; Acute myeloid leukemia; Small bowel obstruction

INTRODUCTION

Granulocytic sarcoma is a rare disease which is characterized by immature myeloid cells that originate from the bone marrow.¹ It forms a mass in organs located outside

the bone marrow. Granulocytic sarcoma develops primarily with acute myeloid leukemia or chronic myeloid leukemia as well as with myelodysplastic syndrome.¹ Granulocytic sarcoma was first reported in 1811, and in 1853, it was referred as a chloroma because when tumor surface was exposed to air, the tissue turned to a green color due to the myeloperoxidase within the leukemic cells.²⁻⁴ However, the term granulocytic sarcoma is used today because this distinct color change was not identified in all cases.⁴

Granulocytic sarcomas are usually diagnosed simultaneously with acute or chronic myelocytic leukemia or during their treatment course in most cases.¹ However, it can be detected as a mass in patients without a history of leukemia or in patients with normal bone marrow findings. Because it is clinically rare, it may be misdiagnosed as malignant lymphoma or other diseases.⁵⁻⁷ Although it may develop at any age, it is most frequently detected before the age of 40 year-old. The preferential sites include bone, periosteum, lymph node, and skin. However, it may develop in any part of the body such as small intestine, central nervous system, and pleura.^{1,8}

In Korea, 41 cases of granulocytic sarcoma have been reported. In this report, it seems that granulocytic sarcoma develop in patients prior to the age of 40 in most cases.⁹ In regard to the lesion sites, the central nervous system was affected in approximately 30 cases being the most common site of involvement. In addition, approximately 10 cases were affected at sites including the eyelid, the bone and the heart. The finding of a granulocytic sarcoma in the abdominal cavity including the small intestine has not been previously reported in Korea. Granulocytic sarcoma in small intestine is very rare that

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only 10 cases have been reported to date.^{8,10-14} We treated a patient with small intestinal granulocytic sarcoma diagnosed during the evaluation of intestinal obstruction prior to the diagnosis of acute myelocytic leukemia.

CASE REPORT

A 48-year-old man with abdominal discomfort which started approximately 9 months ago visited our hospital. He was admitted to another hospital for intermittent lower abdominal pain about one month ago. The patient consumed small amounts of porridge because of intermittent postprandial abdominal pain. On the standard abdomen X-ray and small bowel series which were performed in another hospital revealed a lesion near to the ileum. Positron emission tomography-computed tomography (PET-CT) revealed a small bowel obstruction caused by a suspicious lymphoma like lesion. The patient was transferred to our hospital. The patient lost approximately 6.5 kg over the past few months due to abdominal discomfort after eating. The only past medical history was appendectomy which was performed 15 years ago. Social history revealed 2-3 times per week of alcohol drinking and one

pack per day for 15 years of cigarette smoking. On admission, blood pressure was 100/60 mmHg, temperature was 36.0°C, pulse rate was 62 times/minute, and respiration rate was 20 times/minute. Neither cervical nor inguinal lymph nodes were palpated. Bowel sound was slightly increased with mild abdominal distension.

The result of complete blood count revealed as follow; white blood cell 3,400/mm³, hemoglobin 12.3 g/dL, and platelet 364,000/mm³. The leukocyte differential count revealed that the neutrophils were 44.7%, lymphocytes were 41.8%, monocytes were 13%, eosinophils were detected to be 1.2%, and the reticulocyte count was 0.9%. The biochemical analysis showed that total protein was 6.7 g/dL, albumin was 3.7 g/dL, AST was 69 IU/L, ALT was 35 IU/L, alkaline phosphatase was 45 IU/L, and the total bilirubin was 0.7 mg/dL, and LDH was 437 IU/L. Tumor markers are as follow; CEA 1.3 ng/ml, CA 19-9 8.1 u/mL, and CA 71-4 2.5 u/mL all within normal ranges.

The standard abdominal X-ray imaging revealed a bowel obstruction. Small bowel series demonstrated several strictures due to submucosal lesions in the ileum (Fig. 1). On the abdominal CT scan, the ileum diameter was dilated partially and the small bowel wall was thickened. The

Fig. 1. Small bowel series. It shows stenotic lesions and luminal dilatation of the ileum.

Fig. 2. Positron emission tomography-CT scan of the abdomen. Multiple hypermetabolic lesions are noted in the ileum.

Fig. 3. Microscopic findings. (A) Tumor cells with medium to large sized hyperchromatic pleomorphic cells are noted. Eosinophils are scattered in the background (H&E stain, $\times 400$). (B) Tumor cells show a positive reaction to myeloperoxidase (Immunohistochemical stain $\times 400$).

PET-CT scan showed multiple nodules with increased metabolic activity (Fig. 2). A bone marrow biopsy at the left iliac crest prior to surgery, showed a cell density of 60%; myeloblasts 0.8%, myelocytes 5.0%, and neoplastic lymphocytes 0%. There was no infiltration of other malignant cells. Abdominal laparotomy was performed for the diagnosis and treatment of the bowel obstruction.

Surgical findings along the ileal mesentery revealed peritoneal metastases and multiple nodules of different patterns and size ranging from 0.5 cm to 2 cm. Due to the presence of the nodules, strictures of the ileum were observed; particularly at two sites of severe bowel obstruction. For the diagnosis, a frozen biopsy was performed from samples taken at the two sites. As a result, an undifferentiated carcinoma of unknown origin was suspected. There was no other abnormal finding in other organs or lymph nodes. An internal bypass was performed. On post surgical microscopic examination, granulocytic cells with hyperchromatic nuclei of diverse sizes were noted (Fig. 3). Immunohistochemical stain showed a positive leukocyte common antigen with a positive myeloperoxidase test (Fig. 3). In contrast, CD 3, 5, 15, 20, 30, 56, 79a, Bcl-6, and cytokeratin, were all negative. Therefore, final diagnosis was a solitary granulocytic sarcoma that developed in the small intestine. Another bone marrow biopsy which was performed 4 weeks later revealed leukemic cells and myeloblasts increased up to 57.6%. The patient was diagnosed with M2 according to the French-American-British (FAB) classification for leukemia. The final diagnosis of this patient was acute granulocytic leukemia. After induction chemotherapy using cytarabine and daunorubicin, complete remission was achieved. Six months later, an allogeneic bone marrow transplant was performed.

DISCUSSION

The underlying mechanism for the development of a granulocytic sarcoma is unknown. However, it is usually identified under the following conditions; (i) as a concomitant manifestation of acute myelocytic leukemia, (ii) as leukemic transformation of chronic myelogenous leukemia, myelodysplastic disorder, or recurrent acute myelocytic leukemia, and (iii) as a solitary lesion prior to the diagnosis of acute myelocytic leukemia. In most cases, it manifests in conjunction with acute myelogenous leukemia and chronic myelogenous leukemia, although it may develop in other allogeneic bone marrow syndromes.¹ Patients usually do not present with distinct symptoms, and thus, its accurate incidence is difficult to assess. Nevertheless, in autopsy cases, granulocytic sarcoma with clinical symp-

toms has been reported in about 2.5-4.5% of the cases.¹⁵ However, at the time of diagnosis, the presence of a solitary granulocytic sarcoma with normal bone marrow findings has been reported in only 30% of granulocytic sarcoma cases. In most cases, acute myelocytic leukemia is ultimately diagnosed after 1-49 months. Therefore, when regarding the time of diagnosis of granulocytic sarcoma, the incidence and clinical course of the hematopoietic disorder are different.^{1,6,7}

Granulocytic sarcomas can manifest in any part of the body. However, granulocytic sarcoma originating from gastrointestinal tract is very rare. Granulocytic sarcomas have been reported in the stomach, small intestine, large intestine, liver, pancreas, other digestive organs.^{1,7} The most common reported originating site for solitary granulocytic sarcoma include skin, soft tissues, and lymph nodes which is not that different from the general distribution of granulocytic sarcoma.^{7,8} The identified sites for granulocytic sarcoma are associated with the onset of myeloproliferative disorder. For granulocytic sarcomas in organs other than the small intestine, diagnosis is generally simultaneously made with the diagnosis of acute myelocytic leukemia. However, in a small intestine granulocytic sarcoma like our case, solitary myelocytic sarcoma is a more common diagnosis.⁷ It is uncertain why a granulocytic sarcoma in the small intestine manifested alone prior to the onset of acute myelocytic leukemia. Nevertheless, as in our case, the presence of a granulocytic sarcoma in the bowel requires diagnostic laparoscopy due to bowel obstruction.

Generally, the incidence of hematopoietic diseases such as acute myelocytic leukemia or chronic myelocytic leukemia increases with age. The age of patients with simultaneous granulocytic sarcoma and hematopoietic diseases ranges from 32 to 82 years with a median value of 56 years. However, for patients with a solitary granulocytic sarcoma, the age of the patient range from 2 to 84 years with a median value 31 years, which is relatively a younger range of age. In addition, granulocytic sarcomas develop prior to the age of 45 in most cases, which is different from the present case.^{1,7,8}

The histopathological diagnosis of a granulocytic sarcoma could be difficult. Cases which do not occur simultaneously with bone marrow proliferative disorders, it can be misdiagnosed such as malignant lymphoma in 45-75% cases.^{1,16} For the histopathological diagnosis of granulocytic sarcoma, immunohistochemical staining with naphthol-ASD-chloroacetate esterase is the most common method for identification. However, more recently, immunohistochemical staining with myeloperoxidase (MPO), lysozyme or CD34 antigens has been carried out since

Naphthol-ASD-chloroacetate esterase reveals negative in immature tumor cells.^{6,14} Therefore, for the diagnosis of granulocytic sarcoma, immunohistochemical staining with myeloperoxidase might be more sensitive and helpful.

For granulocytic sarcoma of the small intestine, abdominal laparotomy is required because of small bowel obstruction despite in a relatively young age. Diagnosis of solitary granulocytic sarcoma is made via surgery in most of the cases, although some misdiagnosis is made with H&E staining and immunohistochemical staining. Diagnosis is usually made with a positive myeloperoxidase and leukocyte common antigen, and negative T-cell markers (CD3,4,5,8), B-cell markers (CD20, 79a), and cytokeratin.

Identification of a solitary granulocytic sarcoma is usually followed by the manifestation of acute myelocytic leukemia within approximately 10 months (1 week-49 months) in most cases. In cases treated with local treatment, such as surgery or radiation without systemic chemotherapy, acute myelocytic leukemia manifests in approximately 80-90% cases.¹ Therefore, patients are diagnosed as a solitary granulocytic sarcoma, and treated with cytarabine and daunorubicin chemotherapy which are used primarily for patients with acute myelocytic leukemia. Complete remission rate is around 65% and the 3-year survival rate is approximately 30%.⁶ For solitary granulocytic sarcoma treated with chemotherapy, interval to the development of acute myelocytic leukemia is approximately 12 months. The manifestation of disease is prolonged for 3-6 months in patients that do not receive chemotherapy. In some patients, there is a long interval, 4-16 years, between the diagnosis of a solitary granulocytic leukemia and the development of acute myelocytic leukemia.^{1,6-8}

The prognosis of cases with an abnormal chromosome 8 has been reported to be poor, and thus aggressive systemic chemotherapy should be considered in such cases.⁶ However, in our case, there was no chromosomal abnormality. Aggressive chemotherapy for solitary granulocytic sarcoma may not only delay the onset of acute myelocytic leukemia, but may also lower its incidence. Therefore, long-term survival can be anticipated. However, the overall prognosis is not favorable that some investigators have recommended bone marrow transplantation when complete remission is achieved after the chemotherapy.¹⁰ Five months after complete remission with chemotherapy, our patient underwent allogeneic bone marrow transplant. There is no evidence for 12 months.

Although granulocytic sarcoma has been previously reported in Korea, a solitary granulocytic sarcoma of the small bowel has not been reported yet. There are only 10 cases of solitary granulocytic sarcoma of the small bowel

reported previously. Most small bowel granulocytic sarcomas manifest as solitary lesions without the diagnosis of acute myelocytic leukemia. Therefore, tissue biopsy from an abdominal laparotomy specimen evaluated by immunohistochemical staining is required to differentiate granulocytic sarcomas from other diseases. The prognosis of a solitary granulocytic sarcoma is poor because most cases usually progress to acute myelocytic leukemia. Therefore, aggressive chemotherapy with or without bone marrow transplantation are required for a better survival.

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