Spinal Granulocytic Sarcoma Manifesting as Radiculopathy in a Nonleukemic Patient

—Case Report—

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Abstract

A 26-year-old nonleukemic woman presented with lumbosacral granulocytic sarcoma manifesting as progressive low back pain and numbness of her left lower leg persisting for 3 months. Physical examination revealed hypesthesia within the left S1 area of the sensory dermatome, decreased Achilles tendon reflex in the left lower extremity, and walking impairment due to severe pain in her left hip and leg. Magnetic resonance imaging confirmed an extradural mass in the spinal canal at the L5–S2 levels with invasion to the pelvis from the left sacral foramen. Positron emission tomography with [^{18}F]fluorodeoxyglucose (FDG-PET) showed hyperaccumulation indicating malignant tumor. Baseline laboratory data were normal. Decompressive laminectomy and tumor removal were performed. Histological examination identified granulocytic sarcoma. Bone marrow involvement was absent. She underwent adjuvant chemotherapy and radiotherapy, resulting in reduced residual lesion and neurological improvement. Immediate diagnosis and adequate systematic treatment are recommended for spinal granulocytic sarcoma in nonleukemic patients to prevent or delay progression to leukemia. The importance of immunohistochemical staining in the differential diagnosis from other types of spinal tumor, and the efficacy of FDG-PET for evaluation of the treatment are also emphasized.

Key words: granulocytic sarcoma, leukemia, immunohistochemistry, positron emission tomography, spine

Introduction

Granulocytic sarcoma originates from myeloid precursor cells and occurs in 0.7–9.0% of patients with acute or chronic myelogenous leukemia, myelodysplasia, and myeloproliferative disorders.¹⁾ Granulocytic sarcoma was initially reported in 1811,³⁾ and described as chloroma in 1853 due to the typical greenish-yellow appearance (from the Greek chloros, green).¹³⁾ Granulocytic sarcoma most commonly occurs in the soft tissues of the head and neck, bone, and skin,⁹⁾ and less often in the central nervous system and spinal cord.^{2,5–7,9–12,14–28,30)}

Granulocytic sarcoma seldom manifests before the identification of leukemia in the peripheral

blood or bone marrow.^{2,5–7,9–12,14–28,30)} The finding of granulocytic sarcoma in patients with leukemia may predict the first presentation of blast crisis.¹⁾ On the other hand, granulocytic sarcoma may occur in the absence of leukemia.^{2,6,21)} The correct diagnosis of granulocytic sarcoma is obtained only in about 50% of nonleukemic patients due to its rareness and the histological and radiological similarities to malignant lymphoma or Ewing sarcoma.²⁹⁾ Spinal granulocytic sarcoma in aleukemic patients is rare but important because late bone marrow involvement may be related to blast crisis and cause death.^{6,14,16,18,20,24,26)}

We treated a nonleukemic patient with radiculopathy caused by spinal extradural granulocytic sarcoma. This case indicates the importance of immunohistochemistry in the differential diagnosis, and the efficacy of positron emission tomography

with [^{18}F]fluorodeoxyglucose (FDG-PET) for evaluation of the treatment.

Case Report

A 26-year-old previously healthy woman presented with progressive low back pain and numbness of her left lower leg persisting for 3 months. She denied motor weakness and bowel or bladder incontinence.

Physical examination revealed hypesthesia within the left S1 area of the sensory dermatome, decreased Achilles tendon reflex in the left lower extremity, and walking impairment due to severe pain in her left hip and leg. Laboratory examinations were normal. Magnetic resonance (MR) imaging confirmed an extradural mass in the spinal canal at the L5–S2 levels with invasion to the pelvis from the left sacral foramen (Fig. 1A). FDG-PET indicated the lesion had a maximum standardized uptake value (SUV) of 7.8 (Fig. 2A). SUV indicates the tissue activity of FDG per unit body weight, calculated as (mean concentration of radioactivity in the region of interest)/(injected radioisotope activity/body weight) $\times$ calibration factor.

The patient underwent tumor removal for dural sac decompression through S1–2 laminectomy. A rubbery and grayish tumor was found in the epidural space, compressing the dural sac and left S1 root. The tumor in the intracanal space was totally removed. Histological examination demonstrated fibroadipose connective tissue including diffuse cellular infiltrates. Neoplastic cells with small round and hyperchromatic nuclei proliferated in a diffuse pattern (Fig. 3A). Intraoperative pathological assessment by frozen section suggested malignant lymphoma or Ewing sarcoma/primitive neuroectodermal tumor (PNET). Immunohistochemical staining showed the tumor cells were positive for myeloperoxidase (Fig. 3B), CD15 (Fig. 3C), neutrophil elastase (Fig. 3D), CD45 (Fig. 3E), and lysosome (Fig. 3F), but negative for CD3, CD79 α , CD56, synaptophysin, neurofilament protein, CD1a, S-100 protein, cytokeratin, and CD99. The final histological diagnosis was granulocytic sarcoma.

Postoperative examination found no indications of bone marrow involvement on bone marrow aspiration. The patient underwent adjuvant chemotherapy for acute myeloid leukemia using cytarabine, idarubicin, and leuporelin, followed by irradiation of the craniospinal deposits and bone marrow transplantation. Four months later, MR imaging showed disappearance of the intracanal tumor mass with marked reduction of the intraforaminal and extrasacral tumor (Fig. 1B), and FDG-PET demonstrated decreased maximum SUV of 2.4 (Fig. 2B). She

Fig. 1 A: T₁-weighted magnetic resonance (MR) images with gadolinium enhancement showing a slightly enhanced extradural mass (arrow) in the spinal canal at the L5–S2 levels with invasion to the extrasacrum through the left anterior and posterior sacral foramen (arrowheads). B: T₁-weighted MR images with gadolinium enhancement 4 months after the systemic chemotherapy and radiotherapy revealing disappearance of the intracanal tumor mass with marked reduction of the intraforaminal and extrasacral tumor.

Fig. 2 A: Positron emission tomography with [^{18}F]fluorodeoxyglucose (FDG-PET) scan indicating the lesion had a maximum standardized uptake value (SUV) of 7.8 (arrow). B: FDG-PET scan 4 months after the systemic chemotherapy and radiotherapy showing decreased maximum SUV of 2.4 (arrow).

Fig. 3 A: Photomicrograph showing neoplastic cells with small round and hyperchromatic nuclei proliferating in a diffuse pattern. Hematoxylin and eosin stain, original magnification $\times 40$. B–F: Photomicrographs demonstrating positive immunohistochemical staining for myeloperoxidase (B), CD15 (C), neutrophil elastase (D), CD45 (E), and lysosome (F). Original magnifications $\times 40$.

had achieved neurological improvement without graft versus host disease and MR imaging revealed no recurrence at 12 months after the transplantation.

Discussion

Twenty-six aleukemic patients with spinal granulocytic sarcomas, 23 men and three women aged 2 to 74 years (median, 33 years), have been reported to date (Table 1).^{2,5-7,9-12,14,16-28,30} The male predominance could be associated with the higher incidence of acute myeloid leukemia in men.⁴⁾ The affected sites included two cases at cervical, 17 at thoracic, 10 at lumbar, and three at sacral spinal levels. The chief clinical findings were related to the affected sites and included pain in 17 patients, paresis or weakness in 21, bowel or bladder incontinence in 13, and sensory impairment such as hypesthesia or numbness in 16.

The treatment strategy will individually vary for nonleukemic patients with spinal granulocytic sarcoma. Surgical decompression was performed in 22 of 26 patients, and 21 of these received additional acute myeloid leukemia type therapies consisting of chemotherapy, radiotherapy, or bone marrow transplantation. The follow-up period varied, but the outcome was generally poor, especially in patients showing progression to leukemia. Eight patients developed acute leukemia,^{6,14,16,18,20,25,26,30)} and six patients died following leukemic relapse or graft versus host disease.^{6,14,16,18,20,26)} On the other hand, 13

of the 26 patients showed no bone involvement,^{2,5-7,9,11,12,17,27,28)} and only four patients died of chemotherapy or radiotherapy related clinical disorders.^{6,7,17,24)} This finding possibly reflects the aggressive initial treatment and prevention of progression to leukemia. Therefore, prompt diagnosis and adequate treatment are essential to achieve good outcome.

The histological diagnosis of granulocytic sarcoma is difficult in the absence of evidence of acute myeloid leukemia. The differential diagnosis includes malignant lymphoma, Ewing sarcoma/PNET, Langerhans histiocytosis X, and metastatic tumors.^{1,3)} Granulocytic sarcoma consists of histologically uniform immature cells, but often includes mature neutrophils and immature eosinophils.^{12,19,22)} Therefore, immunohistochemistry is effective and should be performed to confirm the diagnosis of granulocytic sarcoma. Table 2 summarizes the differences in the immunohistochemical staining of tumors resembling granulocytic sarcomas. Myeloperoxidase, CD15 (granulocyte associate antigen), and neutrophil elastase are especially effective to differentiate granulocytic sarcoma from other tumors. CD99 (MIC2), synaptophysin, and neurofilament protein are positive for Ewing sarcoma/PNET, but negative for granulocytic sarcoma. CD3, CD56, and CD79 α are useful for differentiating granulocytic sarcoma from malignant lymphoma. CD1a and S-100 protein are positive for Langerhans histiocytosis X, and cytokeratin for metastatic tumor, but all are negative for granulocytic sarcoma.

In the present case, we used FDG-PET to estimate the malignancy of the tumor and the efficacy of the treatment. MR imaging with gadolinium enhancement is considered to consistently slight enhance the tumor mass, but cannot evaluate the metabolism. On the other hand, PET can estimate the metabolism of tumors in vivo using various positron tracers.⁸⁾ Increased uptake and consumption of deoxyglucose is related to aerobic glycolysis in tumors. FDG-PET is considered to be sensitive to detect this process because malignant tumors have increased glucose metabolism.⁸⁾ In our case, FDG-PET successfully identified the metabolically active lesion and suggested the high malignancy, and demonstrated decreased uptake after chemotherapy and radiotherapy. This follow-up FDG-PET may indicate that there was reduction in tumor cellularity due to the treatment. However, it is difficult to regard the findings as complete remission because, to the best of our knowledge, any previous reports about spinal granulocytic sarcoma did not evaluate the lesions by FDG-PET.

The malignancy cannot be investigated by

Table 1 Summary of clinical findings in patients with non-leukemic spinal granulocytic sarcoma

Author (Year)	Age (yrs)/ Sex	Locations	Symptoms (disorders)			Treatment	Bone marrow involvement (months from diagnosis)	Outcome (months from diagnosis, cause of death)
			Pain	Motor	Sphincter	Sensory		
Ragins and Tinsley (1950) ²³⁾	22/M	T3-T10	back	+	-	+	SD, Rad	not described
Mason et al. (1973) ¹⁸⁾	20/M	T8	back	+	+	+	SD, Che, Rad	AML (2)
McCarty et al. (1980) ¹⁹⁾	33/M	T9-T12	back	-	+	-	SD, Che, Rad	not described
Chan et al. (1986) ²⁾	13/M	T12-L1	-	+	-	+	SD, Rad	no (72)
Meis et al. (1986) ²⁰⁾	29/F	T9-T12	-	+	-	-	SD, Che, Rad, BT	AML (7)
Zuible et al. (1989) ³⁰⁾	31/M	T12-L4	leg	-	-	-	SD, Che, Rad, BT	AML M3 (1)
Ripp et al. (1989) ²⁴⁾	58/M	T5-T8	back	+	+	+	Che, Rad	refractory anemia (1.5)
Kim et al. (1990) ¹²⁾	70/M	L2-L3	leg	+	-	+	SD, Che, Rad	no (3)
Doshi et al. (1991) ⁷⁾	74/M	T9-T10	-	+	+	+	SD, Che	no (6 days)
Kook et al. (1992) ¹⁴⁾	10/M	T5	-	+	+	+	SD, Che, Rad	AML (14)
Lagrange et al. (1992) ¹⁶⁾	22/M	T4	-	+	-	-	SD, Che, BT	AML M2 (11)
Sajjad et al. (1997) ²⁵⁾	22/M	L4-S1	-	-	+	+	not described	AML M4 (1)
Deme et al. (1997) ⁶⁾	47/M	C6-C7	neck, arm	+	-	-	SD, Che, Rad	no
	49/M	L3-L4	back	+	+	+	SD, Che	no
	15/M	L2	-	+	-	-	SD, Che, PBST	AML (10)
Sandhu et al. (1998) ²⁶⁾	22/M	L3-S1	leg	-	+	-	Che, Rad	AML M5 (1.5)
Mostafavi et al. (2000) ²¹⁾	29/M	T2-T4	back	+	+	+	SD, Che, Rad	not described
Machii et al. (2000) ¹⁷⁾	73/M	T4-T6	back	+	+	-	SD, Che, Rad	no (2)
Niedermayer et al. (2000) ²²⁾	58/M	T3-T7	back	+	-	+	SD, Che	not described
Ugras et al. (2001) ²⁸⁾	13/M	T11-L1	back	+	-	+	SD	no (6)
Buckland et al. (2001) ²⁾	35/F	C4-C5	neck	+	+	-	SD, Che, Rad	no (3)
Hamadani et al. (2005) ⁹⁾	33/M	T6-T8	back	+	-	+	SD, Che, Rad, BT	no (7)
Shiozawa et al. (2005) ²⁷⁾	2/M	below L3	-	+	+	+	Che, Rad	no (12)
Kalayci et al. (2005) ¹¹⁾	24/M	T3-T5	-	+	+	+	SD, Che, Rad, BT	no (8)
Howell and Abramowsky (2005) ¹⁰⁾	11/M	T1-T5	back	+	-	-	SD, Che	not described
Present case	26/F	L5-S2	back	-	-	+	SD, Che, Rad, BT	no (12)

AML: acute myeloid leukemia, BT: bone marrow transplantation, C: cervical, Che: chemotherapy, DIC: disseminated intravascular coagulation disorder, GVHD: graft versus host disease, ICH: intracranial hemorrhage, L: lumbar, MTX: methotrexate, PBST: peripheral blood stem cell transplantation, Rad: radiotherapy, S: sacral, SD: surgical decompression, T: thoracic.

Table 2 Characteristics of immunohistochemical staining in tumors resembling granulocytic sarcoma

	Granulocytic sarcoma	Malignant lymphoma	Ewing sarcoma/PNET	Langerhans histiocytosis X	Carcinoma metastasis
Myeloperoxidase	+	—	—	—	—
CD15	+	—	—	—	—
Neutrophil elastase	+	—	—	—	—
CD45	+	+	—	+	—
Lysosome	+	—	—	+	—
CD3	—	+	—	—	—
CD79 α	—	+	—	—	—
CD56	—	+	—	—	±
Synaptophysin	—	—	+	—	±
Neurofilament protein	—	—	+	—	±
CD1a	—	—	—	+	—
S-100 protein	—	—	—	+	—
Cytokeratin	—	—	±	—	+
CD99	—	±	+	—	—

PNET: primitive neuroectodermal tumor.

peripheral blood examination or cerebrospinal fluid cytology in aleukemic patients, but PET can provide useful independent and complementary metabolic information. The present case indicates that the combination of MR imaging and FDG-PET allows detection of primary spinal malignant tumor and comprehensive evaluation of treatment response.

Granulocytic sarcoma is rare, and clinical diagnosis is especially difficult without bone marrow involvement. Spinal granulocytic sarcoma should be included in the differential diagnosis of spinal lesion. Adequate systemic therapy should be initiated to prevent blast crisis. Immunohistochemistry can establish the final diagnosis of granulocytic sarcoma.

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