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CASE REPORT

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Anaplastic large cell Ki-1 lymphoma with bone involvement: Report of two cases

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Abstract Two cases of anaplastic large cell Ki-1 lymphoma involving bone as the most prominent and initial manifestation are reported. The first patient was a 20-year-old male who had back pain and incomplete paraparesis due to vertebral involvement. The second was a 14-year-old girl, whose first clinical signs were fever of unknown origin and sternal bone pain. Radiologically, skeletal lesions were lytic and destructive. Histopathologically, the tumour cells had pleomorphic bizarre nuclei and abundant basophilic cytoplasm. Immunohistochemically, Ki-1(CD30) reactivity was strongly positive in both cases. Tumour cells were also CD3, CD4, epithelial membrane antigen and interleukin-2 receptor positive in the first case, and CD10, HLA-DR positive in the second case. The former tumour was considered to be of T-cell lineage and the latter of lymphoid progenitor cell origin. Radiation and chemotherapy were temporarily effective. However, both patients died 14 and 7 months after diagnosis, respectively, due to systemic lymph node involvement. These observations suggest that the prognosis for Ki-1 lymphoma involving bone is poorer than indicated in previous reports.

Key words Lymphoma · Large cell · Ki-1 · Bone neoplasms · Prognosis

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Introduction

Anaplastic large cell Ki-1 lymphoma is a recently recognized disease entity [10, 17]. The Ki-1 antibody was raised against the Hodgkin's disease cell line L428 [4]. The sites predominantly involved, described in previous reports, are the lymph nodes and the skin [2]. Bone is so rarely involved that only thirteen cases have been reported [3, 4, 7, 12, 15]. Two additional cases of anaplastic large cell Ki-1 lymphoma which were manifest initially and prominently in bone are described in this report.

The prognosis for anaplastic large cell Ki-1 lymphoma has been considered to be relatively favourable even in cases with skeletal involvement. The outcome of our two cases however, indicate that the prognosis is not as good as previous reports have suggested.

Case reports

Case 1

A 20-year-old male student was admitted to the hospital with low back pain and incomplete paraparesis. Physical examination disclosed swelling of the lymph nodes in bilateral inguinal and axillary and in the left supraclavicular regions. A deep subcutaneous mass in the middle of the back was also noted. Neurological examination revealed muscular weakness of both lower extremities and superficial sensory disturbance below the level of D_7. The patella tendon reflex was weakened and ankle reflexes were bush. Babinski reflex was not demonstrated. Urinary incontinence appeared 2 days after admission. Laboratory examinations showed leucocytosis (13000×10^6/l), and increased serum C-reactive protein (CRP; 1.7 mg/dl) and lactate dehydrogenase (LDH; 407 IU/l). Human T-cell leukaemia virus-1 serology was negative. Radiographs revealed destructive changes in the L_4 vertebral body and the disappearance of the pedicle shadow at D_7. A myelogram and computed tomography (CT) myelogram revealed compression of the cauda equina by the tumour at the level of L_4. Magnetic resonance imaging elucidated a neoplastic lesion enhanced by gadrinium at the level of L_4 (Fig. 1) and a similar lesion in the paravertebral muscle at the level of D_7. Malignant lymphoma and metastatic cancer were suspected. Because of increasing paraparesis, posterior decompression and instrumental fixation of the lumbar lesion was performed. An intraoperative histopathological di-

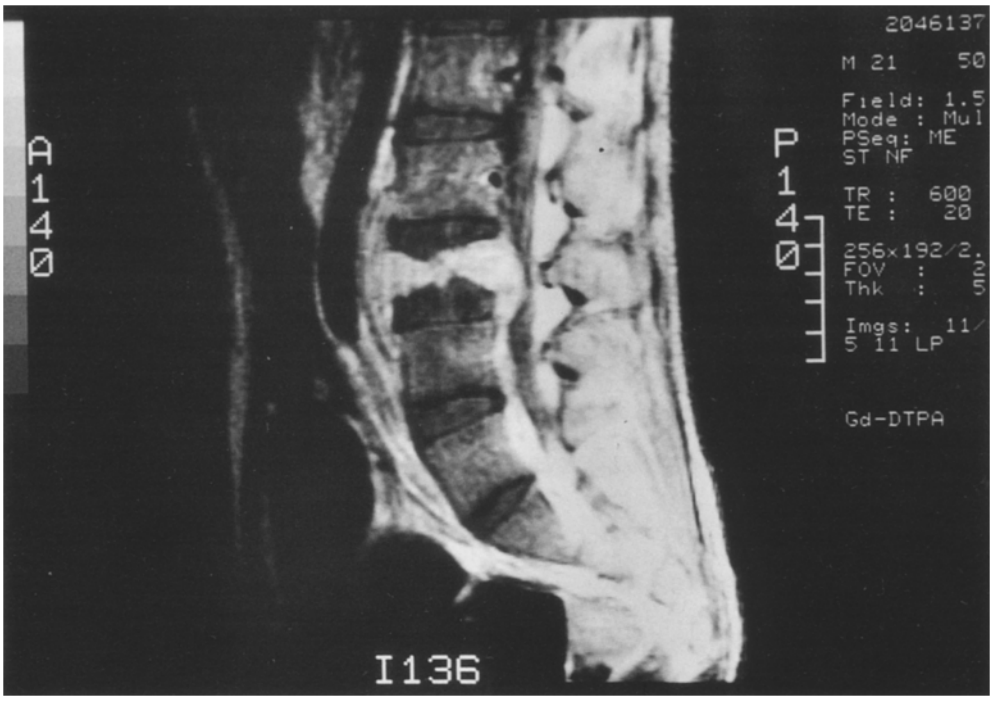

Fig. 1 Magnetic resonance imaging findings (case 1). Tumorous lesion was enhanced with gadrinium

agnosis of malignant lymphoma was made. Postoperative radiation therapy and chemotherapy were performed. Temporarily, both lesions decreased in size and the patient improved neurologically. After several courses of chemotherapy (CHOP: cyclophosphamide, vincristine, adriamycin, predonisone, COP-BLAM III: cyclophosphamide, prednisone, bleomycin, adriamycin, methotrexate) however, recurrence was seen in the paravertebral muscle and cervical lymphadenopathy increased. The patient died 14 months after the initial diagnosis with systemic lymph node involvement.

Case 2

A 14-year-old girl was admitted to the hospital because of low grade fever of unknown origin lasting for 2 months. Frequent nasal bleeding, general malaise and anterior chest wall pain appeared subsequently. Her past and family history were uneventful. On physical examination, her body temperature was 38.2° C, but no superficial lymph node swelling was detectable. Tenderness in the skull and sternum was revealed. Laboratory tests showed increased white cell count (20400), units ESR (77 mm; 1 h/101 mm; 2 h), CRP (8.4 mg/dl) and LDH (1082 IU/l). Bone marrow aspiration of the ilium revealed normal findings. Increased uptake of radioisotope was noted in the skull sternum and pelvis, and tomography showed multiple destructive lesions in the sternum (Fig. 2). Cranial CT revealed erosion of the temporal bone. An open biopsy of the sternum revealed malignant lymphoma. After chemotherapy and irradiation, the fever and osteopaenia subsided for a while. However, a recurrence occurred with subsequent progression to systemic lymph nodes, and the patient died 7 months after diagnosis.

Materials and methods

The biopsy material was fixed in buffered formalin and processed for paraffin embedding. Paraffin sections were stained with haematoxylin and eosin. Immunohistochemical staining was done using the avidin-biotin-peroxidase complex method. Monoclonal an-

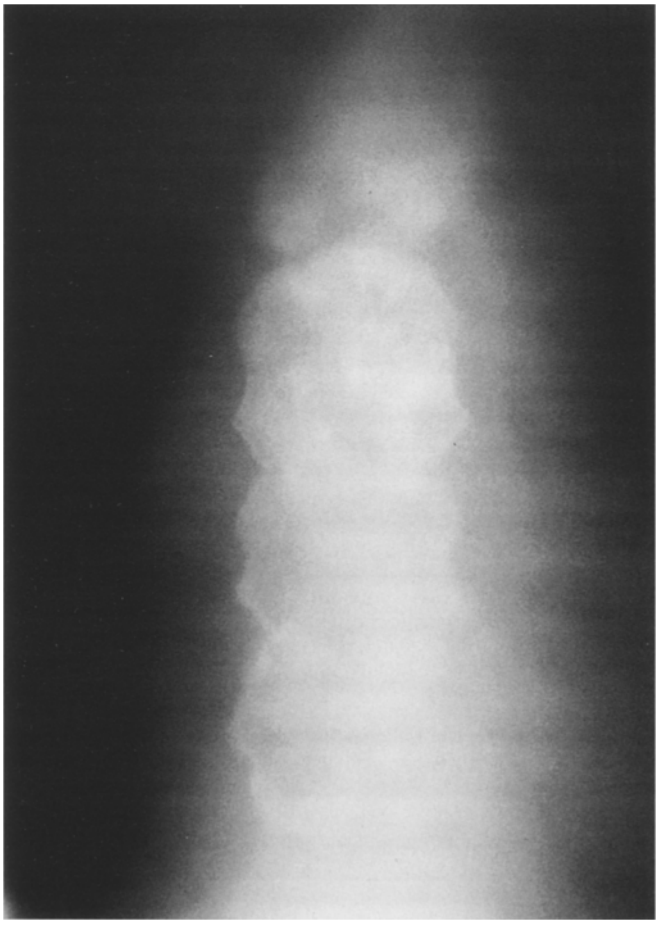

Fig. 2 Roentgen tomography (case 2). Multiple osteolytic lesions of the sternum were notable

Table 1 Monoclonal antiodies applied on sections: their specificities and results (*CALLA* common acute lymphoblastic leukaemia antigen, *IL-2R* interleukin-2 receptor)

Antibody	Source	Specificities	Results of staining	
			case 1	case 2
LCA (CD45)	DAKO	Leukocyte common antigen	+	+
BerH2 (Ki-1, CD30)	DAKO	Reed-Sternberg cell associated antigen	+	+
Leu3a (CD4)	Becton	Helper/inducer T cell	+	−
Leu4 (CD3)	Becton	Pan T cell	+	−
CALLA (CD10)	Becton	Lymphoid progenitor cell	/	+
EMA	DAKO	Epitherial membrane antigen	+	−
HLA-DR	DAKO	HLA-class II antigen	/	+
IL-2R (CD25)	Becton	Activated T, B cell	+	/

tibodies applied to the paraffin embedded sections and to the frozen sections are listed in Table 1.

Results

Histopathologic findings

In case 1, sections showed that most of the tumour cells were of the anaplastic large cell type (Fig. 3A). The nuclei were either round or convoluted. The cytoplasm was abundant and basophilic. Mitoses were frequent. Some tumour cells resembled Hodgkin's cells (Fig. 3B). Malignant cells were not observed in the biopsied inguinal lymph nodes, which exhibited reactive proliferation. In case 2, large anaplastic cells with irregularly shaped nuclei were seen, around which fibrosis was prominent (Fig. 4A). Smaller lymphoid cells were also noted.

Immunohistochemical findings (Table 1)

In case 1 Ki-1 (CD30; BerH2) reactivity was demonstrated in most of the tumour cells (Fig. 3C). The tumour cells were also positive for CD3 and CD4 antigens, therefore this neoplasm was considered to be of T cell lineage. Tests for epithelial membrane antigen (EMA) and (IL-2R) interleukin-2 receptor were similarly positive (see Table 1).

In case 2 expression of Ki-1 was observed in most of the tumour cells (Fig. 4B). CD10 (common acute lymphoblastic leukaemia antigen; CALLA) reactivity was also found, but CD19 and CD20 were not detected. The cells lacked reactivity to CD15 and myeloperoxidase, and therefore a lymphoid progenitor cell origin was considered. Tumour cells were also positive for the activation antigen, HLA-DR.

Discussion

Recently, Stein and Kadin have introduced the term anaplastic large cell Ki-1 lymphoma, as a distinct entity among non-Hodgkins lymphomas (NHL) showing reactivity with Ki-1 antibody; subsequently these investigators reported their histopathological and clinical findings [10, 17]. In the last few years, the number of reported cases has increased [1, 4, 9, 15].

Table 2 Ki-1 lymphoma of bone (*NED* no evidence of disease, *AWD* alive with disease, *CR* complete remission, *DOD* dead of disease, *M* male, *F* female, *m* months)

Author/Reference/Year	Number of patients	Age	Sex	Location	T or B	Initially involved sites		Prognosis
						Lymph node	skin	
Koike [12] 1989	1	4	F	Skull, scapula	T	+	+	DOD (3m)
Chott [4] 1990	3	70	M	?	T	?	?	?
		?						
		?						
Fujimoto [7] 1990	2	10	F	Pelvis	?	+	?	DOD (8m)
		14	M	Femur	?	+	?	Alive (8m)
Penny [15] 1991	4	21	M	Rib, spine	?	+	−	DOD (6m)
		18	M	Spine	?	+	−	AWD
		22	M	Shoulder	?	+	−	AWD (11m)
		57	M	?	?	+	−	NED (37m)
Chan [3] 1991	3	22	M	Spine	T	−	−	NED (42m)
		8	F	Spine, skull	Uncertain	−	−	CR (30m)
		22	M	Pelvis, femur	B	−	−	NED (34m)
Present report	2	20	M	Spine	T	−	−	DOD (14m)
		14	F	Skull, pelvis, sternum	Lymphoid progenitor cell	−	−	DOD (7m)

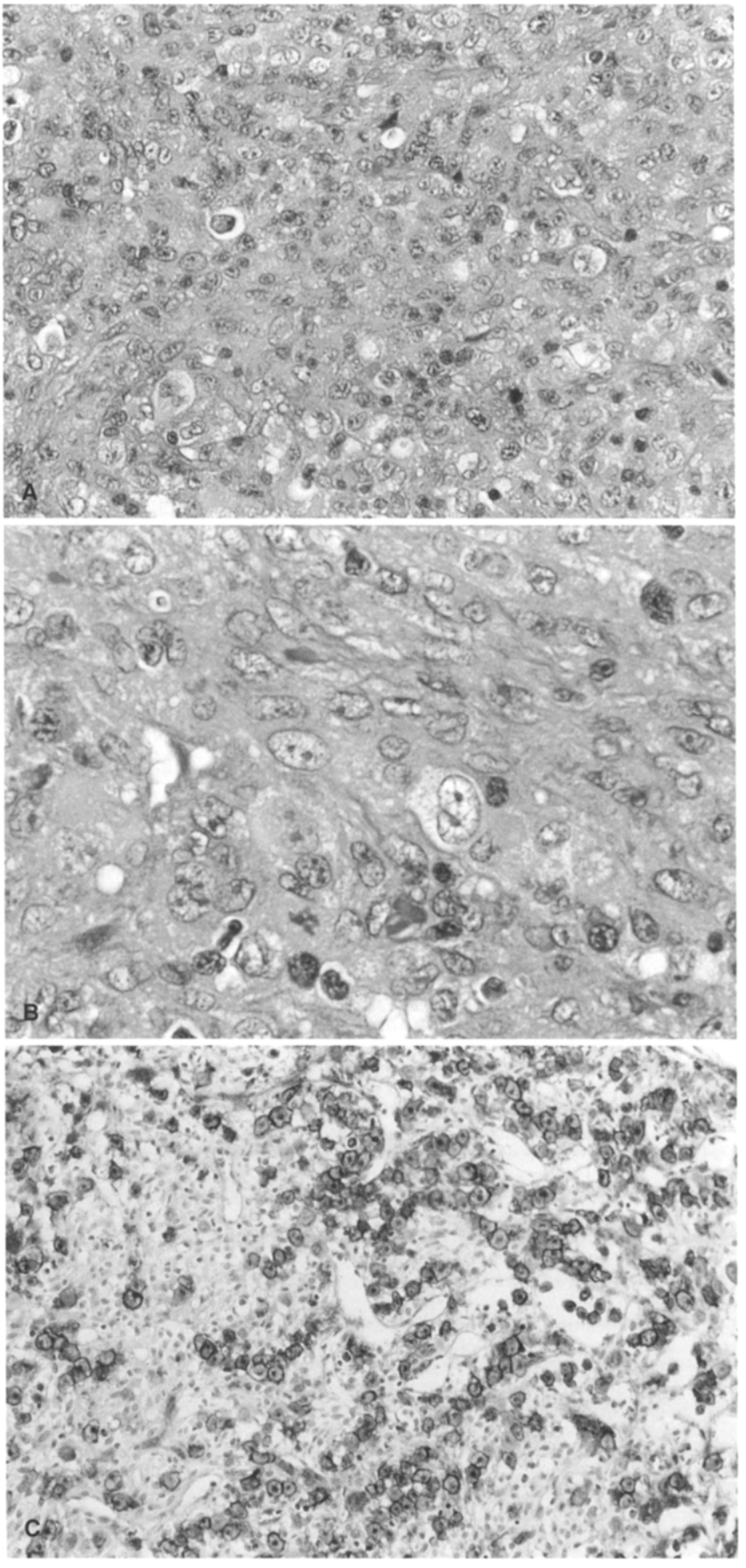

Fig. 3 **A** Histopathological findings [Haematoxylin and eosin (H & E), case 1]. **B** Some tumour cells resemble Hodgkin's cells. (H & E, case 1). **C** Most of the large neoplastic cells were Ki-1 positive (case 1)

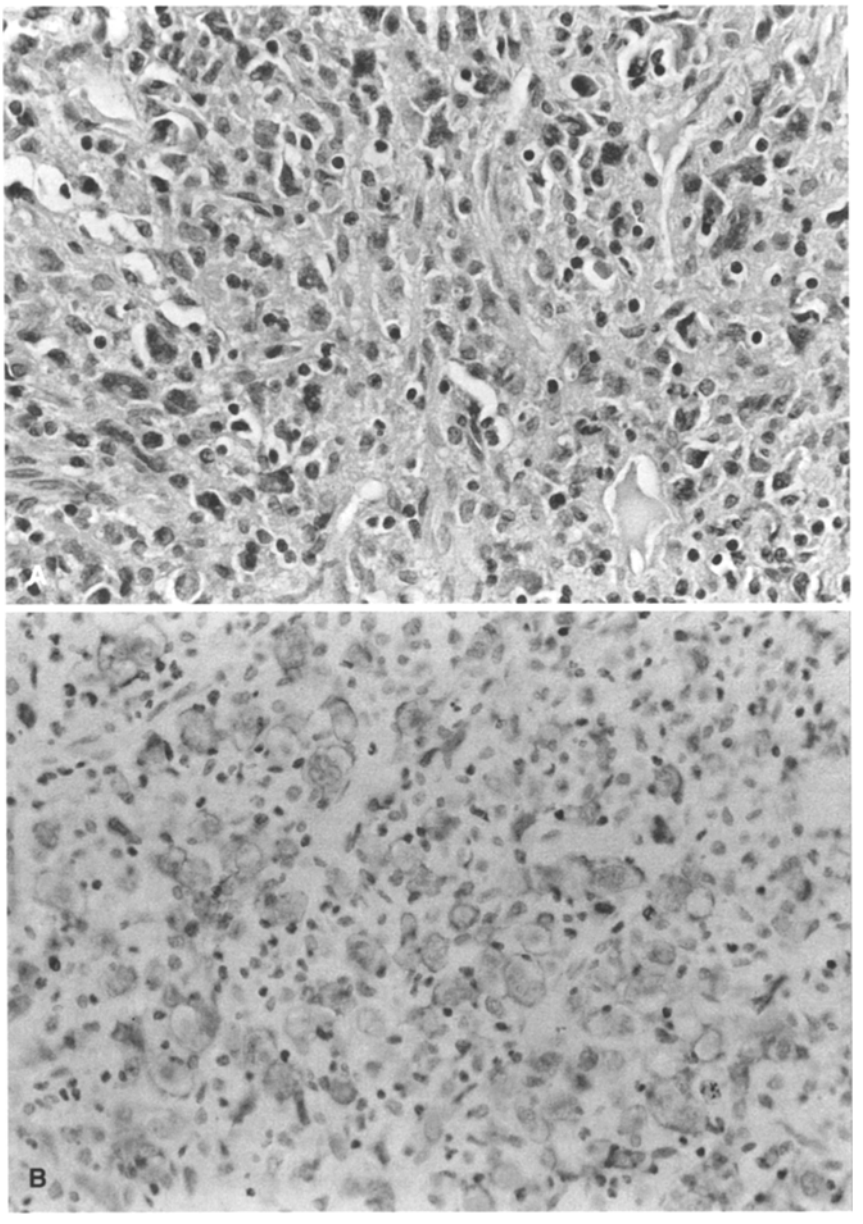

Fig. 4 **A** Histopathological findings, (H & E, case 2). **B** Expression of Ki-1 was observed in most of the tumour cells (case 2)

The initial manifestation in most of these cases has been lymphadenopathy. Half of the previous cases incorporated skin lesions. The age of the patients was lower than the usual for NHL, and the prognosis was reported to be relatively good [2, 11, 16]. Most tumours were of T-cell lineage. Our first case presented with lymphadenopathy in the early stages of the disease; however, no malignant cells were found in the biopsied lymph nodes. In the second case, lymphadenopathy appeared only in the later stages of the disease. Skin involvement was not seen in either case. However, the primary site could not be determined in either case.

Reports of anaplastic large cell Ki-1 lymphoma with bone involvement are very rare, so that only another 3 cases have been reported up to date. Chott [4] described 3 cases out of total of 41 lymphomas involving bone, and Chan [3] reported three cases considered to manifest primarily in bone. Penny [15] described 4 cases out of total of 24 lymphomas involving bone. In the Japanese literature, Koike and Fujimoto reported one and two cases, respectively [7, 12]. Of the 13 reported cases, 9 occurred in patients younger than 25-years-old. Most of the lesions were located in the axial skeleton, notably the skull, pelvic bone and spine (Table 2). Most lymphomas originating in bone are of B-cell origin [6, 13, 14]. However, the incidence of T-cell type is relatively high among Ki-1 positive bone lymphomas, though B-cell lesions have also been reported. Stein speculated that Ki-1 lymphomas are the neoplastic counterpart of activated T or B lymphocytes, since both T and B lymphocytes express Ki-1 antigen when activated by various methods [1, 17]. The fact that Ki-1 lymphomas express several antigens related to cell activation, notably, EMA, HLA-DR, and/or IL-2R, supports this hypoth-

esis [5, 8, 17]. Both of our cases expressed these antigens.

T-cell Ki-1 positive lymphomas with bone involvement outside Japan show no serological correlation with HTLV-1infection. In contrast, Tashiro [18] reported the presence of antibodies to the adult HTLV-1 in 5 of 12 Ki-1 positive Japanese lymphomas. However, case 1 was HTLV-1 negative.

According to Chan, the prognosis of Ki-1 lymphoma involving bone is relatively good because of its good response to chemotherapy and radiation. Our two cases however, as well as the three other reported tumours had such poor prognosis that the patients died within approximately 1 year of diagnosis, despite intensive therapy (Table 2). These cases suggest that the prognosis is not as favourably as has been previously suggested.

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