Title

Therapeutic modalities for central nervous system involvement by granulocytic sarcoma (chloroma) in children with acute nonlymphocytic leukemia

Journal

Journal of Neuro-Oncology, 4(4)

ISSN

0167-594X

Authors

Takaue, Yoichi
Culbert, Steven J
Baram, Tallie
et al.

Publication Date

1987-12-01

DOI

10.1007/bf00195608

Journal of Neuro-Oncology 4: 371–381 (1987)

Therapeutic modalities for central nervous system involvement by granulocytic sarcoma (chloroma) in children with acute nonlymphocytic leukemia

Yoichi Takaue[1], Steven J Culbert[2], Tallie Baram[3], Ann Cork[4], and Jose M Trujillo[5]
[1,2,3] *Departments of Pediatrics,* [4,5] *Laboratory Medicine, The University of Texas M.D. Anderson Hospital and Tumor Institute at Houston, 6723 Bertner Avenue, Houston TX 77030, Texas USA ([2]addres for offprints)*

Keywords: acute myelocytic leukemia, granulocytic sarcoma (chloroma), central nervous system, chromosome

Abstract

Four cases of central nervous system involvement by granulocytic sarcoma (three intracranial and one paraspinal) in children with acute nonlymphocytic leukemia (FAB M1 or M2 subtype) are presented, and therapeutic modalities are discussed. All tumors were noted at initial presentation with diagnosis being made on clinical and radiological findings without biopsy. All patients had karyotypic abnormalities: three had translocation of chromosomes 8 and 21, and one had an unspecified hypodiploid clone. The three patients who developed intracranial tumors responded well to triple agent (cytosine arabinoside, hydrocortisone, and methotrexate) intrathecal chemotherapy and systemic chemotherapy, with or without local irradiation, as evidenced by rapid disappearance of the tumors. Two children are disease-free after 17 and 57 months. One patient with paraspinal tumor failed to achieve a systemic remission but had no evidence of granulocytic sarcoma at autopsy. Thus, the prognosis of CNS granulocytic sarcoma is not uniformly gloomy if treated aggressively by combined modalities. The value of surgical intervention in terms of primary management, however, is limited.

Introduction

Granulocytic sarcoma (chloroma) is an extramedullary accumulation of predominantly primitive cells of the myeloid series that tends to occur in younger patients with acute nonlymphocytic leukemia (ANLL) [1 – 3]. This tumor type can develop at any body site but most commonly occurs in the tissues of the orbital region, bone, soft tissue, skin, and sinuses. Involvement of the central nervous system (CNS) by granulocytic sarcoma has been considered to be unusual. However, the frequency is expected to increase because of therapeutic advances in systemic therapy. The optimal management of this tumor remains to be established; experience has thus far been limited because of small patient numbers. We present four cases of CNS granulocytic sarcoma that were present at diagnosis in childhood ANLL. Other case reports are reviewed to better elucidate the biological and clinical significance of this complication of leukemia.

Materials and methods

The medical records of all patients, aged 15 years or younger, who were treated for ANLL in the

Department of Pediatrics, The University of Texas M.D. Anderson Hospital and Tumor Institute at Houston between 1970 and 1985, were reviewed to document intracranial or paraspinal granulocytic sarcoma (chloroma), defined as CNS granulocytic sarcoma. The diagnosis of ANLL was based on morphological, cytogenetic, and cytochemical examinations that included periodic acid-Schiff (PAS), myeloperoxidase, naphthol AS-D chloroacetate esterase, and nonspecific esterase staining of initial bone marrow smears. Clot sections of bone marrow aspirates were studied with light and electron microscopy. The French-American-British (FAB) classification system of ANLL [4] was performed on all patients registered after 1977. Specimens were submitted for cytogenetic studies on the majority of the patients registered after 1975. Chromosome analyses were performed on bone marrow aspirates obtained at the time of diagnosis. The techniques employed have been previously reported [5]. The bone marrow cells were cultured overnight in Ham's F10 medium supplemented with 20% fetal bovine serum. No mitotic stimulants were used. G-banding procedures were utilized on the chromosome preparations following a trypsin pretreatment. A maximum of twenty-five metaphases were analyzed and the results were reported according to the International System of Human Cytogenetic Nomenclature.

The diagnosis of granulocytic sarcoma was based on clinical findings and radiologic examinations, including computed tomography (CT) scanning and myelography. Lumbar puncture was routinely performed at presentation of the disease and thereafter at regular intervals. Cerebrospinal fluid was evaluated for malignant cells by cytocentrifugation followed by Wright-Giemsa staining.

Results

A review of the records of 108 children admitted to M.D. Anderson Hospital between 1970 and 1985 with acute nonlymphocytic leukemia showed that 17 of the children (15.7%) developed granulocytic sarcoma (chloroma) in the orbital area, soft tissue, lymph node, mediastinum, brain, paraspinal region, skin, or bone. Karyotypic abnormalities were observed in 9 of the 10 patients evaluated; 6 had a translocation involving chromosomes 8 and 21.

Four of 108 children that were treated for ANLL had CNS granulocytic sarcoma (three intracranial and one paraspinal). All tumors were present at diagnosis. All patients had cytogenetic abnormalities in bone marrow karyotypes: three had translocation of chromosomes 8 and 21 and one had an unspecified hypodiploid clone. All 8;21 translocations were also associated with missing sex chromosomes. Three patients were classified as having FAB M2 subtype ANLL and one had M1 subtype.

Three children received combined therapy including local irradiation, intrathecal chemotherapy, and systemic induction chemotherapy. Intrathecal chemotherapy consisted of methotrexate (MTX, 12 mg/m^2), hydrocortisone (HDC, 15 mg/m^2), and cytosine arabinoside (Ara-C, 30 mg/m^2). One child received intrathecal chemotherapy and systemic induction chemotherapy without irradiation. No surgical intervention, either for diagnosis or decompression, was performed.

Two of four patients are disease-free after 17 and 57 months. One child with a lower paraspinal tumor died without having achieved a marrow remission, but autopsy revealed complete resolution of the tumor; the other child died six months after the diagnosis. In two patients with intracranial granulocytic sarcoma, the tumor had regressed completely following primary intrathecal chemotherapy and systemic induction therapy and before cranial radiation therapy. In one case, regression of the tumor was observed by CT scan within two weeks of initiation of systemic therapy and one course of IT medication. The presenting features of these four patients are summarized in Table 1, and illustrative case reports are presented.

Case reports

Case One

A 14-year-old boy developed cellulitis of the leg. Laboratory examination disclosed the following:

Table 1. Presenting features of patients with CNS granulocytic sarcoma: 1970 and 1985.

Case No.	Age/Sex (yr)	Peripheral blood		Bone marrow blasts (%)	FAB	Karyotype
		WBC ($\times 10^3$/)l)	Platelet ($\times 10^3$/)l)			
1	14/M	27.8	58	86	M2	(45,X, − Y,t[8q − ;21q +])
2	15/M	10.9	12	81	M2	Hypodiploid (Not specified)
3	4/M	5.3	239	87	M1	(45,X, − Y,t[8q − ;21q +])
4	11/F	4.8	28	44	M2	(45,X, − X,t[8q − ;21q +])

yr, year; M, male; F, female; WBC, white blood cell; FAB, French-American-British classification for acute leukemia.

WBC count, 27800/ml with 83% blasts; platelet count, 58000/ml, and hemoglobin, 9.7 g/dl. Bone marrow aspiration biopsy revealed peroxidase and chloroacetate esterase positive, but nonspecific esterase and PAS-negative leukemic blasts. Acute nonlymphocytic leukemia (FAB M2 subtype) was diagnosed. Cytogenetic study of bone marrow cells revealed an abnormal karyotype, (45,X,–Y,t[8q−;21q+]). Cerebrospinal fluid was negative for leukemic cells. A routine CT scan of the brain was normal.

Within 24 hours of admission, the patient developed signs of lower spinal cord compression with bilateral paresis of the lower legs. Admission neurological examination had been normal. He then developed acute neurogenic bladder and loss of bowel function. An emergency myelogram revealed complete spinal block at the inferior level of T6. Radiation therapy was begun with 3000 rad to the spine from T1 to T9, followed by craniospinal irradiation using 2400 rad and systemic chemotherapy, including Ara-C and 6-thioguanine. The patient regained some spontaneous movement of the lower extremities but was unable to stand or walk unassisted. Although his general status improved with these therapies, no systemic remission could be induced. He died 11 weeks after diagnosis. Results of autopsy demonstrated subdural and subarachnoid hemorrhage of the brain and spinal cord; however, no evidence of local, residual leukemic infiltration was found.

Case Three

A four-year-old boy who was in good health until April 1982, when he developed a left otitis media, which was treated by oral antibiotics. One week later he began complaining of headache and was noted to have drooping of the left side of the face. A maxillary tumor was found. A biopsy was interpreted as malignant lymphoma and he was referred to M.D. Anderson Hospital. Physical examination revealed marked swelling of the left side of the face associated with left facial nerve palsy. Bilateral papilledema was also noted. The liver and spleen were not palpable. Laboratory evaluation revealed the following; WBC count, 5300/ml with 39% blasts; hemoglobin, 8.7 g/dl; and platelet count, 239000/ml. Bone marrow was infiltrated with blast cells strongly positive for peroxidase and esterase stains. Numerous Auer bodies were also noted. Periodic acid-Schiff and nonspecific esterase stains were negative. A cytogenetic study revealed the presence of (45,X,–Y,t[8q−;21q+]). A diagnosis of ANLL (FAB M1 subtype) was made. Pathological review of the maxillary tumor was consistent with granulocytic sarcoma. A skull X ray revealed marked spitting of the cranial sutures, presumably secondary to increased intracranial pressure. Complete opacification of the left maxillary sinus was also noted. A CT scan of the head disclosed a mass in the left maxillary sinus extending into the left nasal cavity with destruction of the medial wall. Furthermore, lobulated intracranial masses were also noted in the left temporal, frontal, and parietal regions, all of which markedly enhanced with con-

trast medium (Fig. 1). Although no histopathological documentation of intracranial tumor was available, a myeloblastic origin was assumed in view of the clinical course. The patient was started on systemic chemotherapy, including vincristine, Ara-C, and dexamethasone, and radiation therapy using 3000 rad to the skull and maxilla. Prompt response to these measures was evidenced by complete disappearance of the tumors in the maxillary sinus and brain (Fig. 2). The finding of increased intracranial pressure precluded a lumbar puncture at the initial work-up; it was performed four weeks later for the first time, and the results were normal. After a hematologic remission was obtained, the patient was treated on cyclic maintenance chemotherapy for 18 months. He remains in initial complete remission 57 months after the diagnosis. A follow-up CT scan is shown in Fig. 3. This child has learning disabilities. He is currently in special education classes and required two years to complete kindergarten.

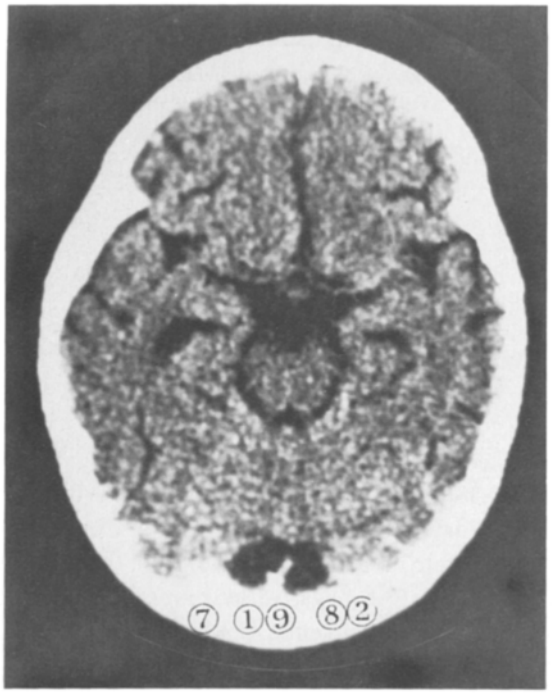

Fig. 2. Complete disappearance of the tumors in the maxillary sinus and brain occurred following skull irradiation therapy and systemic chemotherapy (July 19, 1982).

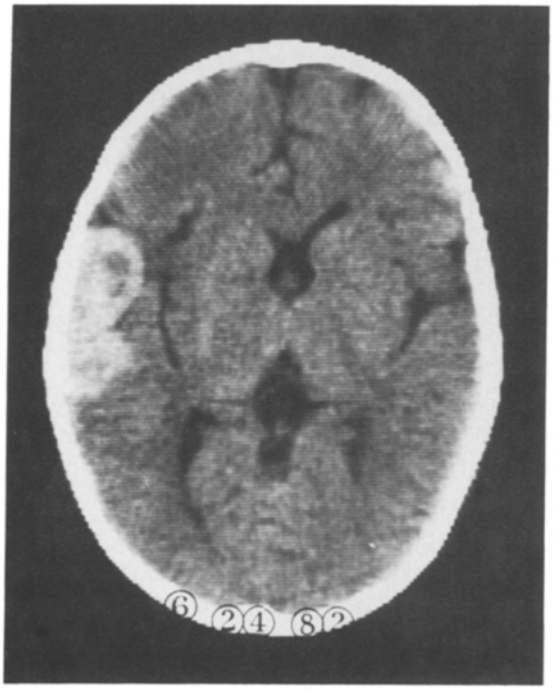

Fig. 1. Multiple, lobulated intracranial tumors were observed in the left temporal and frontal lobes with marked enhancement by injected contrast medium (June 24, 1982).

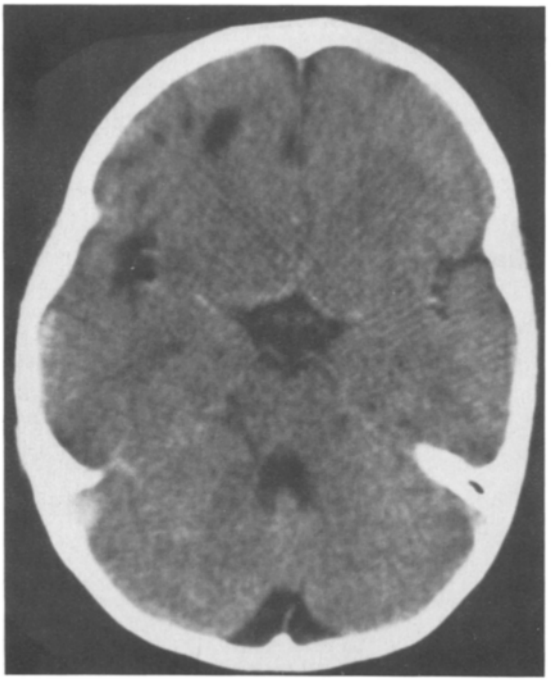

Fig. 3. Follow-up CT scan of the brain showed marked dilatation of the cortical sulci and focal area of atrophy of the brain (June 13, 1985).

Case Four

An eleven year old girl developed headaches, chest pain and progressive pallor. A complete blood count showed hemoglobin 3.2 gm%, white blood count 4800/ml with 36% blasts, and platelets 28000/ml. Symptoms resolved with a transfusion of packed red cells. A bone marrow aspirate showed FABM2 Auer rod positive blasts which were perioxidase, PAS, choroacetate esterase and Tdt positive. A cytogenetic analysis showed the presence of 45, X, −X, t[8q;21q+] blasts. She was begun on systemic induction with daunorubicin, Ara C and 6TG; a single intrathecal injection of methotrexate, Ara C and hydrocortisone was administered. Cerebrospinal fluid cytology was negative. A routine CT scan showed a modular contrast enhanced tumor adjacent to the lateral ventricle. A follow up CT scan done 3 weeks later showed marked resolution of the mass. Her induction regimen was repeated; intrathecal chemotherapy was also administered. A follow up CT scan showed complete resolution. More intensive intrathecal chemotherapy along with cranial irradiation was then given. Follow up CT scan done 6 months from diagnosis showed no evidence for recurrence. She remains in CNS and marrow remission. She has not received further therapy directed at the CNS.

Discussion

Granulocytic sarcomas usually develop in patients with a known diagnosis of nonlymphocytic leukemia, although development of tumors may precede the diagnosis of leukemia [6–10]. Routine morphological methods are limited for making a definitive pathologic diagnosis of these tumors. Naphthol AS-D chloroacetate esterase staining seems to be the most conclusive yet simplest method for differential diagnosis [10], especially when applied on freshly prepared slides [11], and should be included in the diagnostic work-up. Although reported survival rates of patients who developed granulocytic sarcoma appear to be similar to survival rates of patients without those tumors [6, 9], the ultimate prognosis has been invariably poor in pediatric patients [2, 3, 8]. The tumor develops at various stages of nonlymphocytic leukemia with a reported frequency ranging from 2.9 to 6.8% [2,9,12]. Major progress in the treatment of ANLL has occured during the past decade; more than 25% of children with ANLL have been in initial complete remission for two years with intensive therapy [13–16]. Thus, the actual frequency of granulocytic sarcoma is probably higher than reports suggest. We have observed development of granulocytic sarcoma in 17 of 108 children (15.7%) with ANLL in a 16-year period of time (Unpublished data).

The reported frequency of CNS involvement in ANLL ranges from 25 to 38% [17–18], but most cases involve diffuse meningeal infiltration. The actual occurrence of CNS granulocytic sarcoma is unusual. None of 323 patients with ANLL reported by Muss and Moloney [12] developed intracranial tumors, although two of them developed paraspinal tumors. Liu et al. [2] reported that five of 338 patients with myelogenous leukemia developed intracranial tumors. Neiman et al. [10] reported that among 61 biopsy-proven granulocytic sarcomas, seven developed in the vertebral and paravertebral regions, and only one tumor developed in the brain. A recent report by Pui et al. [19] from St. Jude Children's Research Hospital documented that two of 184 children with ANLL developed intracerebral mass. They also reported the development of paraspinal granulocytic sarcoma in one of 309 children with ANLL at presentation [20] and two of 297 children throughout their course of ANLL [21]. In 1981, Petursson and Boggs [22] reviewed 67 previously published cases of spinal cord involvement in leukemia patients and found that 31 had acute myeloid leukemia. Clinical features and therapeutic modalities in well-documented recent reports of CNS granulocytic sarcoma are summarized in Table 2 [2, 6, 7, 20, 22–32]. Most of the previously published cases of CNS granulocytic sarcoma developed in older patients; the clinical and biological significance of this complication of leukemia in pediatric patients is obscure. In our series, CNS involvement by granulocytic sarcoma was found at diagnosis in

Table 2. Clinical features of reported CNS granulocytic sarcoma (GS).

Age (yrs)/ Sex	Onset of GS after Dx. of ANLL	Signs and symptoms	Laboratory findings			Therapy	GS Response	Follow-up after GS	Outcome	Ref.
			CSF cytology	BM	Presentation of GS (Diagnostic tests)					
44/F	−17 mo	Headache, Convulsion, Blurred vision	Neg	N1	Fronto & fronto-occipital tumors (Brain scan)	1) Systemic BCNU, 20 mg/m^2 × 3/wk for 21 doses	NR			7
						2) XRT (1950 rad)	CR	18 Mo	DOD	
26/F[a]	7 mo	Headache, Vomiting, Cranial nerve palsy	Pos	Active ANLL	Cerebellar hemisphere mass (Initial Dx. of hematoma by CT scan, Angiography)	Craniotomy + IT MTX & XRT (1600 rad)	CR	–	–	23
24/F[a]	1) 22 mo	Headache, Convulsion	Neg	N1	Large avascular fronto-parietal tumor (Angiography	Dexamethasone, 20 mg	CR			24
	2) 31 mo	Convulsion, Hemiparesis	?	N1	Parietal tumor	Prednisone + IT Ara-C (35 mg) + XRT (2500 rad)	CR			
	3) 36 mo	Low back pain	Pos	N1	Extradural defect at L5-S1 (Myelography)	1) IT Ara-C (35 mg) + XRT (1800 rad)	PR			
						2) IT MTX (18 mg/m^2) + XRT (2500 rad)	PR	36 mo	DOD	
60/F[a]	3 mo	Cranial nerve palsy, Convulsion	Neg	N1	Multiple tumors in fronto-parietal lobes (Brain scan, Angiography)	IT MTX (12 mg/m^2) × 3	NR	1 mo	DOD	25
20/F[a]	10 mo	Headache, Vomiting, Cranial nerve palsy, Convulsion	Pos	Relapse	Superior-posterior site of 3rd ventricle (CT scan)	XRT (3000 rad; 250 rad every 4 days) + IT Ara-C	CR	5 mo	NED	26
15/F[a]	19 mo	Headache, Vomiting	Neg	N1	Cystic lesion with contrast enhancement in postero-parietal lobe (CT scan)	Craniotomy + XRT (2400 rad) + IT Ara-C (45 mg q Mo × 3)	CR	6 mo	Alive	27
29/M	0	Swelling of temporo-parietal area	–	Active ANLL	Avascular mass, increased attenuation in temporo-parietal lobe (Angiography, CT scan)	Craniotomy + XRT	CR	16 mo	Died	28
37/M	− 8 mo	Headache, Vomiting, Blurred vision	–	N1	Increased attenuation in frontal lobe (Brain scan CT scan, Angiography)	Craniotomy + Systemic chemotherapy	PR	–	–	28
29/F	2 yr	Headache, Vomiting Staggering gait	Neg	N1	Cerebello-pontine tumor with uniform contrast enhancement (CT scan)	Craniotomy + XRT (2400 rad) + IT MTX	Improved	–	–	29

Table 2. Continued.

Age (yrs)/ Sex	Onset of GS after Dx. of ANLL	Signs and symptoms	Laboratory findings			Therapy	GS Response	Follow-up after GS	Outcome	Ref.
			CSF cytology	BM	Presentation of GS (Diagnostic tests)					
54/M	25 mo	Headache, Neck pain	Pos	Relapse	Parietal lobe tumor (Brain scan)	XRT (3300 rad) + IT Ara-C	CR	34 mo	NED	30
63/M	52 mo	Drowsiness, Ataxia	Neg	N1	Basal ganglia tumor (CT scan)	XRT (2100 rad) + IT Ara-C	CR	22 mo	Alive	30
38/M	29 mo	Headache, Cranial nerve palsy	–	Relapse	Cerebellar & cerebral tumors with contrast enhancement (CT scan)	XRT (900 rad)	PR	3 wk	DOD	30
21/M	?	Weakness of legs	–	?	Complete block at T7 (Myelography)	Laminectomy + Tumor removal	PR	16 mo	DOD (recurrent GS)	10
20/F	16 yr	Lumbar pain	–	N1	Tumor at L4 & L5	Laminectomy + XRT	CR	13 mo	DOD	10
25/M	6 mo	Paraplegia	Neg	N1	Complete block at T5 (Myelography)	Laminectomy + XRT	PR	1 mo	DOD (residual GS)	31
21/M[b]	0	Urinary and fecal retention, Pain, Sensory loss	?	CML in blastic crisis	Lower sacral tumor (Myelography)	XRT (1600 rad) + IV Ara-C & Daunorubicin	CR	4 mo	Died after BMT	22
8/M[c]	0	Back pain, Bilateral leg weakness	Neg	Active ANLL (FAB M2)	Complete spinal block at T5 to T6 (Myelography)	Laminectomy & Tumor removal followed by Systemic & IT chemotherapy	CR	5 mo	NED	32
13.5/F	0	Paraparesis	–	Active ANLL (FAB M2)	Complete spinal block at T5 (Myelography)	XRT (200 rad × 3), Dexamethasone & Systemic chemotherapy	CR	11 mo	DOD	20
PRESENT STUDY										
14/M	0	Bilateral paresis of leggs, Neurogenic bladder	Neg	Active ANLL	Complete spinal block at T6 (Myelography)	XRT: Local (3000 rad) & Craniospinal (2400 rad) + IV Ara-C & 6-thioguanine	CR	11 wk	DOD (No evidence of GS at autopsy	
15/M	0	None	Neg	Active ANLL	Increased attenuation in frontal lobe (CT scan)	IT Ara-C (30 mg/m^2), HDC (15 mg/m^2) & MTX (12 mg/m^2) + systemic chemotherapy[d]	CR	6 mo	DOD	

Table 2. Continued.

Age (yrs)/ Sex	Onset of GS after Dx. of ANLL	Signs and symptoms	Laboratory findings			Therapy	GS Response	Follow-up after GS	Outcome	Ref.
			CSF cytology	BM	Presentation of GS (Diagnostic tests)					
4/M	0	Headache, Cranial nerve palsy	–	Active ANLL	Lobulated multiple tumors with contrast enhancement (CT scan)	XRT (3000 rad) + Systemic chemotherapy	CR	57 mo	NED	
11/F	0	Headache	Neg	Active ANLL	Nodular contrast enhanced tumor adjacent to lateral ventricle	IT Ara-C, HDC & MTX + Systemic chemotherapy[d]	CR	17 mo	NED	

[a] These cases were also reviewed by Infante et al. (27); [b] The authors also reviewed 67 previously reported cases of spinal cord involvement in leukemia patients (22).; [c] A cytogenetic study revealed karyotypic abnormality of (45,X, – Y,t[8q – ;21q +]); [d] Radiation therapy followed after remission was obtained.

F = female; M = male; CSF = cerebrospinal fluid; BM = bone marrow; GS = granulocytic sarcoma; wk = week; mo = month; yr = year; Neg = negative; Pos = positive; Nl = normal; ? = evaluated but could not make any definite statement; IT = intrathecal; IV = intravenous; Ara-C = cytosine arabinoside; MTX = methotrexate; XRT = radiation therapy; NR = no response; PR = partial response; CR = complete response; DOD = died of disease; NED = no evidence of disease; BMT = bone marrow transplantation; CT = computerized tomography; FAB = French-American-British classification of acute leukemia.

four of 108 children with ANLL. In previous publications most of the CNS tumors developed months after the initial diagnosis of ANLL.

Previous reports on patients with intracranial granulocytic sarcoma have indicated that the progress of the disease in the adult population is relatively slow, as shown in Table 2. All intracranial tumors that developed in three patients reported by Pippard et al. [30] were highly sensitive to radiation therapy; two of the patients survived 34+ and 22+ months after the tumor developed. The patients reported by Hurwitz et al. [7] and Ballard et al. [24] survived 18 months and 31 months after the development of intracranial granulocytic sarcoma. In our study, two of three patients with intracranial tumor survived: one has been followed 57 months after the initital diagnosis of leukemia (41 months after discontinuation of all therapy).

Most reports have indicated that patients with intracranial tumors benefit from radiation therapy, with or without intrathecal chemotherapy [6, 7, 30]. Chemosensitivity of granulocytic sarcoma has not been completely evaluated, although it was suggested in some reports [6, 35]. In our study, two patients were treated with intrathecal therapy and systemic chemotherapy without radiation therapy. Notably, Case 4 received only a single course of triple intrathecal therapy in addition to systematic chemotherapy including continuous infusion of Ara-C. Ara-C is known to be effective for prevention and treatment of CNS leukemia. Intrathecal chemotherapy, employing three drugs or Ara-C alone, may have tumoricidal ability, although intrathecal methotrexate alone seems to be ineffective [25]. Considering the high chemosensitivity of the tumors observed in our patients, whole skull irradidation could concievably be excluded from the primary treatment, particularly in younger patients, to avoid adverse effects of the therapy on the immature brain.

Computed tomography scanning plays a major role in the diagnosis of CNS granulocytic sarcoma because of the tumor's relatively consistent appearance. On CT scanning, it is usually seen as a mass with increased attenuation with surrounding edema, which is uniformly enhanced following injection of contrast material [28, 29, 34]. Based on these findings and the clinical information, a preliminary diagnosis can be made and confirmed when there is a dramatic response to therapy. Routine surveillance of the CNS system by CT scanning should be included in the initial diagnostic workup in children with ANLL. Laboratory evaluation of CSF has only limited value in the diagnosis of intracranial granulocytic sarcoma.

Extensive reviews of paraspinal granulocytic sarcoma have been published [22, 35]. The tumor may be the presenting symptom of leukemia and may be confused with primary orthopedic disease. Upon development of paraspinal granulocytic sarcoma, it is important to establish an early diagnosis and administer proper therapy to prevent permanent neurological damage from spinal cord compression by the tumor [36]. Even then, as shown by our Case 1, rapid recognition and treatment may not be successful. Myelography is the primary diagnostic procedure for defining disease extension. However, a lumbar puncture procedure may aggravate the neurological dysfunction and be disadvantageous to the patient. Considering the high chemo- and radiosensitivity of this type of tumor [22], paraspinal granulocytic sarcoma should be primarily treated by high-dose corticosteroids followed by systemic chemotherapy and radiation therapy.

There has been no comprehensive study of the karyotypic abnormalities in patients with CNS granulocytic sarcoma. In our study, all four children who developed CNS granulocytic sarcoma also had abnormalities in the karyotype; three had translocation of chromosomes 8 and 21, and one had an unspecified hypodiploid clone. Leukemia associated with 8;21 translocation is known to have a good prognosis [37, 38] but also is closely related to the development of granulocytic sarcoma [39–41]. The relatively benign course of ANLL observed in patients with CNS granulocytic sarcoma may often be explained by the frequent association of this particular karyotypic change.

References

1. Rappaport H: Tumors of the hematopoietic system. Atlas of Tumor Pathology, Section III, Fascicle 8. Armed Forces Institute of Pathology, Washington DC, 1966, pp 241–243.
2. Liu PI, Ishimaru T, McGregor DH, Okada H, Steer A: Autopsy study of granulocytic sarcoma (chloroma) in patients with myelogenous leukemia, Hiroshima-Nagasaki 1949–1969. Cancer 31:948–955, 1973.
3. Cangir A, George S, Sullivan MP: Unfavorable prognosis of acute leukemia in infancy. Cancer 36:1973–1978, 1975.
4. Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DAG, Gralnick HR, Sultan C (FAB Co-operative Group): Proposals for the classification of the acute leukemia. Br J Haematol 33:451–458, 1976.
5. Trujillo JM, Cork A, Ahearn MJ, Youness EL, McCredie KB: Hematologic and cytologic characterization of 8/21 translocation acute granulocytic leukemia. Blood 53:695–706, 1079.
6. Wiernik PM, Serpich AA: Granulocytic sarcoma (chloroma). Blood 35:361–369, 1970.
7. Hurwitz BS, Sutherland JC, Walker MD: Central nervous system chloromas preceding acute leukemia by one year. Neurology 20:771–775, 1970.
8. Cavdar AO, Acrasoy A, Babacan E, Gozdasoglu S, Topuz U, Fraumeni Jr JF: Ocular granulocytic sarcoma (chloroma) with acute myelomonocytic leukemia in Turkish children. Cancer 41:1606–1609, 1978.
9. Krause JR: Granulocytic sarcoma preceding acute leukemia: a report of six cases. Cancer 44:1017–1021, 1979.
10. Neiman RS, Barcos M, Berard C, Bonner H, Mann R, Rydell RE, Bennett JM: Granulocytic sarcoma: a clinicopathologic study of 61 biopsied cases. Cancer 48:1426–1437, 1981.
11. Banerjee D, Silva E: Mediastinal mass with acute leukemia. Arch Pathol Lab Med 105:126–129, 1981.
12 Muss HB, Moloney WC: Chloroma and other myeloblastic tumors. Blood 42:721–728, 1973.
13. Madanat FF, Sullivan MP: Improved survival in young children with acute granulocytic leukemia treated with combination therapy using cyclophosphamide, oncovin, cytosine arabinoside, and prednisone. Cancer 44:819, 1979.
14. Lampkin BC, Woods W, Strauss R, Feig S, Higgins G, Bernstein I, D'Angio G, Chard R, Bleyer A, Hammond D: Current status of the biology and treatment of acute nonlymphocytic leukemia in children (Report from the ANLL strategy group of the Children's Cancer Study Group). Blood 61:215–228, 1983.
15. Weinstein HJ, Mayer RJ, Rosenthal DS, Coral FS, Camitta BM, Gelber RD: Chemotherapy for acute myelogenous leukemia in children and adults. VAPA Update. Blood 62:315–319, 1983.
16. Creutzig U, Ritter J, Riehm H, Langermann HJ, Herze G, Kabisch H, Niethammer D, Jurgens H, Stollmann B, Lasson U, Kaufmann U, Loffler H, Schellong G: Improved treatment results in childhood acute myelogenous leukemia; a report of the German Cooperative Study AML-BFM-78. Blood 65:298–304, 1985.
17. Evans AE, Gilbert ES, Zandstra R: The increasing incidence of central nervous system leukemia in children. Cancer 26:404–409, 1970.
18. Choi SI, Simone JV: Acute non-lymphocytic leukemia in 171 children. Med Pediatr Oncol 2:119–146, 1976.
19. Pui C-H, Dahl GV, Kalwinsky DK, Look AT, Mirro J, Dodge RK, Simone JV: Central nervous system leukemia in children with acute nonlymphoblastic leukemia. Blood 66:1062–1067, 1985.
20. Pui C-H, Dahl GV, Hustu HO, Murphy SB: Epidural spinal cord compression as the initial finding in childhood acute leukemia and non-Hodgkin lymphoma. J Pediatr 106:788–792, 1985.
21. Ch'ien LT, Kalwinsky DK, Peterson G, Pratt CB, Murphy SB, Hayes FA, Green AA, Hustu HO: Metastatic epidural tumors in children. Med Pediatr Oncol 10:455–462, 1982.
22. Petursson SR, Boggs DR: Spinal cord involvement in leukemia: a review of the literature and a case of Ph'+ acute acute myeloid leukemia presenting with a conus medullaris syndrome. Cancer 47:346–350, 1981.
23. Demaray MJ, Coladonato JP, Parker Jr JC, Rosomoff HL: Intracerebellar chloroma (granulocytic sarcoma): a neurosurgical complication of acute myelocytic leukemia. Surg Neurol 6:353–356, 1976.
24. Ballard JO, Towfighi J, Brennan RW, Saleem S, Eyster ME: Neurologic complications of acute myelomonoblastic leukemia of four years' duration. Neurology 28:174–178, 1978.
25. Krishnamurthy M, Nusbacher N, Elguezabal A, Seligman BR: Granulocytic sarcoma of the brain. Cancer 39:1542–1546, 1977.
26. Shalev O, Siew F, Yaar I, Rachmilewitz EA: Intracerebral tumor and diffuse central nervous system infiltration complicating acute myelogenous leukemia. Cancer 44:1066–1069, 1979.
27. Infante AJ, Miller RH, MacRae MA, Gilchrist GS, Forbes GS: Intracranial granulocytic sarcoma complicating childhood acute myelomonocytic leukemia. Am J Pediatr Hematol Oncol 3:173–176, 1981.
28. Sowers JJ, Moody DM, Naidich TP, Ball MR, Laster DW, Leeds NE: Radiographic features of granulocytic sarcoma (chloroma). J Comput Assist Tomogr 3:226–233, 1979.
29. Wendling LR, Cromwell LD, Latchaw RE: Computed tomography of intracerebral leukemic masses. AJR 132:217–220, 1979.
30. Pippard MJ, Callendar ST, Sheldon PWE: Infiltration of central nervous system in adult acute myeloid leukaemia. Br Med J 1:227–229, 1979.
31. Hildebrand J, Leenaerts L, Nubourgh Y, Verhest A, Flament-Durant J: Epidural spinal cord compression in acute myelogenous leukemia. Arch Neurol 37:319, 1980.
32. Kellie SJ, Waters KD: Extradural chloroma with spinal compression. An unusual presentation of acute myelogenous leukemia. Aust NZ J Med 14:160–162, 1984.

33. Mazur EM, Bertino JR: Myeloblastoma and acute myelogenous leukemia: presentation with a cervical neuropathy and complete response to chemotherapy. Cancer 49:637–639, 1982.
34. Pagani JJ, Libshitz HI, Wallace S, Hayman LA: Central nervous system leukemia and lymphoma: computed tomographic manifestations. AJR 137:1195–1201, 1981.
35. Wilhyde DE, Jane JA, Mullan S: Spinal epidural leukemia. Am J Med 34:281–287, 1963.
36. Murray PK: Functional outcome and survival in spinal cord injury secondary to neoplasia. Cancer 55:197–201, 1985.
37. Second International Workshop on Chromosomes in Leukemia: cytogenetic, morphologic and clinical correlations in acute nonlymphocytic leukemia with t(8q–, 21q+). Cancer Genet Cytogenet 2:99–102, 1979.
38. Fourth International Workshop on Chromosomes in Leukemia: Translocation (8;21)(q22;q22) in acute nonlymphocytic leukemia. Cancer Genet Cytogenet 11:284–287, 1984.
39. Tricot G, Broeckaert-van Orshoven A, Casteels-van Daele M, van den Berghe H: 8/21 translocation in acute myeloid leukemia. Scand J Haematol 26:168–176, 1981.
40. Sakurai M, Kaneko Y, Abe R: Further characterization of acute myelogenous leukemia with t(8;21) chromosome translocation. Cancer Genet Cytogenet 6:143–152, 1982.
41. Swirsky DM, Li YS, Matthews JG, Flemans RJ, Rees JKH, Hayhoe FGJ: 8;21 translocation in acute granulocytic leukaemia: cytological, cytochemical and clinical features. Br J Haematol 56:199–213, 1984.