An Autopsy Case of Acute Myelogenous Leukemia associated with Ascending Transverse Spinal Syndrome and Review of the Literature

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The involvement of the nervous system has been noted in 20 to 60 per cent of leukemias^{32,40,43,71,85,94,101,112}. However, the spinal involvement is less common (5 per cent)^{70,102,106}. There have been about 95 reports of such complication in the Western countries since the report of Burns (1824)¹¹, and 40 of such in Japan.

The purpose of this paper is to report of our recent case of myelogenous leukemia with spinal complication, and to discuss the pathogenesis of such complication, reviewing the literature.

Case Report

A 35-year-old Japanese man entered the 3rd Department of Internal Medicine, Kyushu University Hospital on September 22, 1965 with chief complaints of diplopia and neuralgic pain in the right buttock.

History of the present illness: This patient had been in good health until the middle of March 1965, when he suffered from flu-like symptoms of one week's duration, followed by persistent fever of about 38°C. In addition, he suddenly developed a neuralgic pain of moderate degree in the right thigh, which brought him into Tokyo Senbai Hospital on March 22. Immature white blood cells were detected in the peripheral blood first on this occasion. The blood count, on March 27, revealed Hb 13.5 g/dl, RBC 446×10^4 /cmm, and WBC 6,300/cmm with myeloblasts 10.0 per cent, promyelocytes 0.5 per cent, myelocytes 0, metamyelocytes 1.0 per cent, band. 8.5 per cent, poly. 38.0 per cent, eosin. 1.0 per cent, monocytes 3.5 per cent and lymphocytes 37.5 per cent. As the diagnosis of leukemia was not confirmed, he received a symptomatic treatment in the hospital for one month and was discharged with disappearance of the symptoms and some improvement of the blood picture.

In the middle of July 1965, he again developed a slight fever associated with

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cough and rhinorrhea. As he again noted a neuralgic pain in the right thigh, he was readmitted to the Tokyo Senbai Hospital on July 27. After the admission, the fever of about 38°C was persistent, and neuralgic pain began to be felt also in the right lower leg and buttock. In spite of improvement of the subjective symptoms by Aminopyrin and Penicillin, he suddenly noticed of a diplopia on August 17, which had been present until death. The blood count, on August 26, revealed Hb 12.7 g/dl, RBC 401×10^4 /cmm and WBC 17,600/cmm with myeloblast-like cells 19.0 per cent, metamyelocytes 2.0 per cent, band. 8.0 per cent, poly. 46.0 per cent, monocytes 0.5 per cent and lymphocytes 24.5 per cent. Thus he was placed on 6-Mercaptopurin and transferred to Kyushu University Hospital on Sept. 22.

Family history and past medical history were noncontributory.

On admission the patient appeared a well-developed, well-nourished and well-oriented man; 167 cm high and 52 kg in weight. Pulse was regular with the rate of 68/min. The blood pressure was 124 mmHg systolic, and 78 diastolic. The body temperature was 36.6°C. There was no petechia on the skin. The conjunctivae

Table 1. Laboratory Data on Admission.

ESR 4 mm/lhr., 9 mm/2 hr.	Liver function tests
Serological reaction for syphilis (—)	Total serum protein 6.8 g./dl.
Urinalysis	Icterus index 4 M.G. units
Protein (+)/Sulf. (—)/Boil.	CoCl ₂ R ₂₍₃₎
Sugar (—)	TTT 3.8
Urobilinogen normal	Kunkel 10
Feces	BSP 4.2 %/45 min.
Occult blood (—)	Alkaline phosphatase 4.7
Parasite ova (—)	Serum cholesterol 180 mg./dl.
Bleeding time 5.5 min.	GOT 32
Clotting time (Sahli-Fonio)	GPT 40
Beg. 5.5 min.	Serum protein fraction
End 13.5 min.	Albumin 67.4 % (55–65)
Prothrombin time 23 sec.	Globulin 32.6 % (35–45)
Rumpel-Leede (+2)	α ₁ 6.4 % (3–5)
Chest X-ray normal	α ₂ 9.3 % (5–8)
Bone series X-ray normal	β 7.6 % (9–13)
EKG normal	γ 9.3 % (15–21)
ASLO-titer 12 Todd units	Blood urea nitrogen 19.2 mg./dl.
CRP (+)	Serum electrolytes
RA-T (—)	Na 145 mEq./l.
	K 3.8 mEq./l.
	Ca 5.2 mEq./l.
	Cl 105 mEq./l.

Table 2 A. Change in the Peripheral Blood Picture.

Date 1965	Sept. 22	Sept. 28	Nov. 15	Nov. 22
Hemoglobin (% Sahli)	84	82	73	69
Hematocrit (%)	40	39		
RBC ($\times 10^4$ /cmm.)	398	400	376	328
Reticulocyte ($\%$)	12			
Platelets ($\times 10^4$ /cmm.)	12.3	11.2	0.8	0.36
WBC (/cmm.)	4,500	6,400	4,200	4,900
Myeloblast (%)	0	12.0	17.0	42.5
Promyelocyte	1.0	2.5	2.0	0
Myelocyte	0	0.5	0	0
Metamyelocyte	1.5	1.0	0.5	0
Band.	7.0	12.5	4.5	3.0
Poly.	20.0	11.5	0.5	1.5
Eosinophil.	0	1.0	1.5	1.0
Basophil.	0	0	0	0
Monocyte	3.0	0.5	0.5	0.5
Lymphocyte	65.5	57.5	73.5	49.5
Plasma cell	0.5	0.5	0	2.0
Undetermined	1.5	0.5	0	0
Erythroblast (/100 wbc)	3.5	1.0	0	0

were not anemic, and the sclerae not icteric. The pupils were round, isocoric and responded promptly to light and convergence. The lateral gaze of the right eye was paretic and caused an increase in the degree of double vision. Fundoscopic examination was normal. Tongue and gingivae appeared normal. Pharynx was clear with no tonsillar hypertrophy. Neck was not stiff and no lymphadenopathy was detected. Chest was clear to percussion and auscultation with clear heart sounds. The lung-liver-border was in the 6th intercostal space over the right mid-clavicular line. A few lymph nodes of thumb-tip size were detected in the left axilla. Abdomen was flat and soft with no tenderness and no abnormal mass. Liver was not palpable, and the spleen was not enlarged on percussion. The kidneys were not palpable. Inguinal lymph nodes were not swollen. Back was normal without tenderness on the spines or buttocks. Extremities appeared normal. Neurological examination revealed no abnormality except for the right abducens palsy and hypalgesia of the dorsal and plantar aspects of the right 4th and 5th toes.

The results of laboratory examinations on admission are shown in Tables 1, 2A and 2B. There was no evidence of anemia in the peripheral blood nor in the bone marrow. The sternal marrow was hyperplastic, and the myeloblasts showed

Table 2 B. Myelogram (Sternal Puncture).

Date			Sept. 22, '65		Sept. 28, '65	
Nucleated Cell Count (/cmm.)			34.4 × 14 ⁴		43.6 × 10 ⁴	
Myeloblast (%)			57.8	61.6	92.0	93.0
Neutrophil.	Promyel.		0.6		0	
	Myel.		1.0		0.2	
	Metamyel.		0.6		0.2	
	Band.		0.6		0.6	
	Poly.		0.2		0	
Eosinophil.			0.6		0	
Basophil.			0		0	
Mitosis			0.2		0	
Erythroblast	Macr.	Bas.	0.8	35.2	1.4	4.8
		Poly.	0.4		0	
		Orth.	0		0	
	Norm.	Bas.	6.2		2.2	
		Poly.	26.4		1.0	
		Orth.	0.6		0.2	
	Mitosis		0.8		0.2	
Monocyte			0	0	2.2	
Lymphocyte			3.0	2.2		
Plasma Cell			0	0		
Reticulum Cell			0.2	0		
Histio-Basocyte			0	0		
Megakaryocyte			0	+		

high nuclear-cytoplasm ratios and were considered to be leukemic in nature (Fig. 1). Hemorrhagic tendency of mild degree was also detected.

Hospital course (Fig. 2): Soon after the admission, the patient developed increasing symptoms such as general malaise, headache, dizziness, anorexia and moderate fever. On September 28, the peripheral blood (Tabl 2A) revealed a sudden increase of myeloblasts up to 12.0 per cent of the total white blood cell count of 6,400/cmm, and the sternal puncture (Table 2B) revealed an extensive proliferation of myeloblasts (92.0 per cent). With the diagnosis of acute myelogenous leukemia the patient was placed on Betamethasone 3 mg, Tetracycline hydrochloride 1.0 gm and 6-Mercaptopurin (6-MP) 60 mg daily.

Neuralgic pains increased in their severity and spread rapidly from the right

buttock, then to the right thigh and finally to the left. In addition, the patient noted neuralgic pain in the right side of the chest, anteriorly as well as posteriorly, which was aggravated by flexion or extension of the trunk. On October 19, it was noted that the tongue deviated to the right on protrusion. From October 28, the patient complained of dull aches over the right costal margin, and recurrent attacks of shooting pain in the same region, commonly provoked by changing of posture.

Fig. 1. The leukemic cell.

(A): The peripheral blood picture.

(B): The bone marrow picture.

Fig. 2. Clinical course during the hospitalization.

Fig. 4. Ascending myelography 4 days after the onset of paraplegia, showing a complete block between the Th8 and Th9 spine.

In spite of the presence of complete motor and sensory paralysis, the patient began having an excruciating pain in the toes on November 12, for which no narcotics were effective.

On November 17, decompression laminectomy was attempted at the level of Th7 to Th9 spines, which failed, however, because of uncontrollable hemorrhage from the soft tissues around the spinous processes. The laminae were not removed, to prevent more damage to the spinal cord by the possible extraspinal hematoma. In spite of blood transfusion in order to improve the blood coagulation, the bleeding time was still $9\frac{1}{2}$ minutes at that time (normal 3-5 minutes). Soon after the operation, the toe pains were still present. However, the lower limbs became completely anesthetic to all modalities on the following day, with complete loss of deep tendon reflexes in the lower limbs.

In spite of an increased dose of steroids and blood transfusions, the patient took a down-hill course with remittent fever, generalized petechiae and ecchymosis, retinal hemorrhage, macroscopic hematuria and increasing dyspnea, and expired on November 25.

Summary of clinical findings: A 35-year-old man with acute myelogenous leukemia presented first with neuralgic pains in the lower extremities approximately

revealed diffuse infiltration of the leukemic cell. There were miliary nodules in the kidneys of which histology revealed the leukemic cell infiltration in the cortex. Extensive submucous hemorrhage was seen in the right renal pelvis. The palatine tonsils, pharynx and larynx appeared extensively edematous and hemorrhagic, revealing a pseudomembranous inflammation. The lung was emphysematous. The adrenal cortex was atrophic.

Neuropathological findings:

1. Spinal cord and its meninges (Fig. 6): There was yellowish induration on the anterior aspect of the cord, extending from the Th4 to Th8, and from the Th12 to L2 cord. A large hematoma was noted on the posterior aspect of the Th8 and Th9 cords epidurally. The histological findings are as follows:

1) Cervical segments: No abnormal finding was seen, except for slight swelling of the myelin sheaths in the posterior funiculi of the lower segments by Kultschitzky's stain.

2) Thoracic segments:

1. Th4 (Fig. 7): The bilateral posterior funiculi appeared markedly spongy, being associated with softening and necrosis. Other parts of the section also appeared spongy and edematous. Leukemic cells, however, were detected

Fig. 7. Spinal cord (Th4). Spongy appearance of the posterior funiculi, with softening and necrosis. The arrow shows hemorrhage in the posterior root. (H.E. stain, 8×)

Fig. 6. Spinal cord, showing an epidural hematoma (arrow) on the posterior aspect of the Th8 and Th9 segment.

On November 6, the neuralgic pain appeared on the right forearm. On this day, neurological examination (Fig. 3) revealed increase in muscle tone of the lower limbs, a paresis of the right leg, and markedly hyperactive knee and ankle jerks bilaterally. Ankle clonus was not detected, and no pathological reflexes were noted. Hypesthesia was present to all modalities and paresthesia below the level of umbilicus. Within a few days complete paraplegia developed. The patient suffered from persistent urinary and fecal retention from the beginning of November

Myelography (Fig. 4), on November 11, revealed a partial block on the right between the Th12 and L1 spine, and a complete block between the Th8 and Th9 spine. The lumbar puncture revealed the initial pressure of 170 mmH₂O, positive Queckenstedt's test, xanthochromic fluid, protein concentration of 1170 mg/dl, sugar 51 mg/dl, chlorides 122 mEq/l, +3 Pandy's and Nonne's reactions, but no abnormal cells. On this day, there developed analgesia and hypesthesia for touch below the Th8 spinal level, in association with absent deep reflexes of the lower limbs.

Fig. 3 Progress of motor and sensory disturbances

Note: #, ++, +, ± and - show the degree of deep tendon reflex.
[] denotes weakness; -4 complete paralysis, -1 slight paralysis.
□ Anesthesia ▨ Hypesthesia ▤ Neuralgia

8 months prior to death, and developed the transverse spinal syndrome about 3 weeks prior to death, consisting of paraplegia, sensory disturbances below the chest and urinary as well as fecal retention, showing a partial block between the Th12 and L1 spine and a complete block between the Th8 and 9 spine on myelogram. The paraplegia appeared acutely and was completed within 24 hours. The neuralgic pain was gradually replaced by hypesthesia, and finally anesthesia to all modalities with the level at Th3-4.

Post-mortem Examination:

General autopsy findings: Bone marrows of the vertebral body, sternum, humerus and femur appeared yellow, intermingled with hemorrhagic or necrotic foci. The histology revealed a diffuse proliferation of small round cells which consist of scanty cytoplasm and a little larger and lighter nuclei than those of the lymphocyte. In some of the nuclei nucleoli were seen. Venous sinuses were relatively well-defined and slightly congested. Only a small number of erythroblasts and megakaryocytes were present and the picture of normal hematopoiesis was hardly seen. Fatty marrow was seen to some extent in the middle third of the femur.

There were dark-brownish destructive lesions in the parietal bones and the right sphenoid, which were felt extensively fragile. The histology (Fig. 5) revealed proliferation and infiltration of abundant leukemic cells in association with resorption and destruction of the trabeculae.

The liver weighed 2,240 gm, and its histology revealed the leukemic cell infiltration predominantly in the portal area and somewhat in the sinusoids. The spleen, weighing 330 gm, showed the leukemic cell infiltration of moderate degree in the red pulp and to a high degree in the walls of the trabecular veins. The retroperitoneal lymph nodes were enlarged to the pea-size, and the histology

Fig. 5. Histology of the sphenoid bone, revealing an extensive proliferation and infiltration of the leukemic cell in association with resorption of the trabeculae in the right top. (H.E. stain, 135 $\times$)

only partly in the arachnoid. Hemorrhage was found in the posterior root.

2. Th5 (Fig. 8): Softening and necrosis were seen diffusely, with hemorrhage in the grey matter. There were small hemorrhagic foci in the white matter, consisting of pericapillary hemorrhage (Fig. 9).

3. Th6: Softening and necrosis were seen in most parts of the grey as well as white matter. Hemorrhage, but no leukemic cell infiltration, was present in the anterior as well as posterior root. There was a remarkable infiltration of the leukemic cell in the epidural space, forming a tumor-like mass (Fig. 10).

4. Th7 (Fig. 11): Extensive softening, necrosis and hemorrhage were present. Hemorrhage was seen also in the anterior roots.

Fig. 8. Spinal cord (Th5), Generalized softening and necrosis, with hemorrhage particularly in the grey matter.
(H.E. stain, 8×)

Fig. 9. High-power view of a hemorrhagic focus in the white matter of the spinal cord (Th 5), showing a necrotic capillary vessel in the center.
(H.E. stain, 140×)

Fig. 10. Epidural tumor consisting of the leukemic cell infiltration at the spinal cord (Th6). D indicates dura mater.
(H.E. stain, 27×)

Fig. 11. The spinal cord (Th7). Extensive softening, necrosis and hemorrhage. The arrow shows hemorrhage in the anterior root.
(H.E. stain, 8×)

5. Th10: In addition to the softening, necrosis and hemorrhage in the parenchyma, there was a hemorrhage in the posterior root (Fig. 12).

Fig. 12. High-power view of the hemorrhage in the posterior root of the spinal cord (Th10).
(H.E. stain, 180 $\times$)

3) Lumbosacral segments: There were softening, necrosis and hemorrhage in the white as well as grey matter, and in the posterior roots, particularly in the upper lumbar segments.

2. Brain: No hemorrhage, nor leukemic cell infiltration was detected.

Summary of autopsy findings:

1. Diffuse proliferation of the leukemic cells in association with necrosis and hemorrhage in the bone marrows (Acute myelogenous leukemia).

2. Leukemic cell infiltration in the skull, liver, spleen, retroperitoneal lymph nodes and kidneys.

3. A large hematoma in the epidural space of the mid-thoracic segments, and epidural tumor formation by the leukemic cell, extending from the Th6 to Th10 segment. Softening, necrosis and hemorrhage in the parenchyma of the spinal cord, extending from the Th4 to Th8 segment, and from the L1 to L2 segment. But no leukemic cell infiltration was seen in the parenchyma. Hemorrhage was present in the posterior roots.

Review and Discussion

The incidence of neurological manifestations in leukemias varies according to the literature; 20.5 per cent by Schwab and Weiss,⁸⁵⁾ 25.9 per cent (but 83.5 per cent as far as chloroma is concerned) by Okinaka et al.⁷¹⁾, 52.4 per cent by Wells and Silver¹¹²⁾, 61 per cent by Toyokura¹⁰¹⁾, 56.4 per cent by Ito et al.⁴³⁾, 29.8 per cent by Hagbin and Zuelzer³²⁾, and 26 per cent by Hyman et al.⁴⁰⁾.

In comparison with a frequent occurrence of leukemic involvement of the brain, the spinal cord involvement has been said to be less common. Okinaka

et al.⁷⁰⁾ found 9 cases of spinal cord involvement in 185 leukemias (5 per cent) in 1953. Toyokura¹⁰²⁾, in his study in 1960, reported an incidence of 5.8 per cent of spinal paraplegia in 103 cases of leukemia. Hyman et al.⁴⁰⁾ reported 3 paraplegia in 59 children with the central nervous system involvement by leukemia in 1965.

Our case is characterized by a neuralgic pain in the right thigh as the initial symptom followed by ascending spinal transverse syndrome, and the pathological findings of the spinal cord revealing softening, necrosis and hemorrhage, but no leukemic cell infiltration, in the parenchyma.

According to Critchley and Greenfield¹⁴⁾, the early symptoms in the majority of cases were sensory complaint, usually persistent pain. According to Wilhyde et al.¹¹³⁾, the spinal epidural leukemic lesion showed commonly the spinal syndrome as the initial manifestation (66 per cent), and 20 out of 42 patients (48 per cent) had back and/or leg pain secondary to spinal cord compression as the first evidence of leukemia. Toyokura's review¹⁰¹⁾ showed that the spinal symptoms appeared before establishing the diagnosis of leukemia in 19 per cent of all cases, and that in 6 per cent the leukemia was found first at autopsy.

The transverse spinal syndrome of ascending type in our case might be due to softening, necrosis and hemorrhage in the spinal parenchyma at the middle thoracic level as seen by autopsy. Epidural infiltration of the leukemic cells at this level is considered to have produced a picture of complete obstruction in the myelogram. The parenchymatous necrosis with absence of leukemic cell infiltration, as seen in our case, could well be attributed to an ischemia or some circulatory disturbances. As we could not detect any picture revealing thrombosis of the blood vessels, the parenchymatous change might be due to compression by epidural cellular deposits. However, the direct compression by the epidural deposits of leukemic cells alone might not be extensive enough to produce such marked damages in the spinal cord. Here we suppose that a congestive state caused by disturbed venous return played an important role in producing these parenchymatous changes. Regarding the pathogenesis of these parenchymatous changes in the spinal cord, there have been a controversy. Nonne⁶⁷⁾, in 1897, mentioned that the parenchymatous changes in the spinal cord in leukemia differed from that seen in some anemia by the absence of the direct relationship of the focus with the blood vessels in the former. In 1900, Bloch and Hirschfeld¹⁰⁾ reported the first case of leukemic infiltration in the spinal cord, in which they found a close relationship of the lesion with the blood vessels. In 1930, Critchley and Greenfield¹⁴⁾ attached a great importance to the obstruction of blood vessels causing ischemia rather than the direct compression of the spinal cord by the cellular masses. Tokuihiro and Saito¹⁰⁰⁾, in 1956, proposed two ways leading to the funicular in the course of leukemia; one the anemia itself, and the other epidural hematoma resulting in circulatory disturbances by compression.

To explain the hemorrhage in the central nervous system in leukemia, there

are three hypotheses; 1. increased hemorrhagic tendency through thrombocytopenia, 2. destruction of blood vessel walls by the leukemic cell infiltration, and 3. toxic damage to the blood vessels^{36,65)}. Wintrobe¹¹⁴⁾ inferred that the proliferation of leukemic cells might result in destruction of the vessel wall with the formation of a leukemic nodule, and ultimately hemorrhage might occur about the nodule.

As far as we could collect, there were 40 cases of leukemia manifesting spinal symptoms and signs in Japan, and 95 in the Western countries as shown in Tables 3 and 4. Those 135 cases were reviewed with regard to age, sex, types of leukemias, clinical manifestations, pathological changes and their location as shown in Table 5. The age incidence was highest between 10 and 40 years in both groups. There was male predominance with a male-female ratio of 2.4:1 in Japan, and 3.3:1 in the Western countries, in spite of the approximately same

Table 3. Previously Reported Cases of Spinal Leukemia in Other Countries.

No.	Author	Year	Age	Sex	Nature of Leukemia	Clinical Manifest.	Pathological Findings	Location
1	Burns, A. ¹¹⁾	1824			Chloroma	P		
2	Dittrich ¹⁸⁾	1846			Chloroma		I (meningeal)	
3	Mosler, F. ⁵⁸⁾	1869	35	M	Splenic L	Tabetic P		
4	Olivier, S. ⁷²⁾	1877					Bl(meningeal)	
5	Rosenstein, S. ⁷⁹⁾	1881	7	M	Lympho-sarcoma	W (Rt leg)	I	Th & L
6	Schultze, F. ⁸⁴⁾	1884			L		D(funicular)	C
7	Minnich, W. ⁵⁵⁾	1892					D(combined)	
8	Dock, G. ¹⁹⁾	1893	15	M	Chloroma		T (vertebra)	Whole
9	Muller, W. ⁶⁰⁾	1895				Polyneuritis		
10	Nonne, M. ⁸⁷⁾	1897	59	M	L		D (focal, myelin)	C, Th, L
11	Nonne, M. ⁸⁷⁾	1897	31	M	L		D (focal, white matte)	
12	Eichhorst, H. ²¹⁾	1897	17	M	LL	P	T (epidural)	Th5-7
13	Bloch, E. ¹⁰⁾	1900	8/12	M	L		I (gray matte)	C3-4
14	Spitz, R. ⁹⁰⁾	1901	47	F	CL		I(white matte)	Pons, C
15	Harris, T. ³⁵⁾	1902	14	M		P (partial)	I (subdural)	
16	Rosenblath, W. ⁷⁸⁾	1902	15	M			I (meningeal)	Th-S
17	Gondinier ²⁰⁾	1902			LL		D	
18	Geitlin, F. ²⁸⁾	1903						
19	Gumbel, F. ³¹⁾	1903	19	M	Chloroma		I (meningeal)	L
20	Klein, S. ⁴⁷⁾	1904	38	M	Chloroma	Pain (leg)	I (vertebra)	
21	Dock, G. ²⁰⁾	1904						
22	Weinberger, M. ¹¹¹⁾	1907	15	M	Chloroma (LL)	BR	T (epidural)	Th7-8
23	Saltykow, S. ⁸¹⁾	1909	37	F	Chloroma (ML)	P & BR	T (epidural)	Th5-10

No.	Author	Year	Age	Sex	Nature of Leukemia	Clinical Manifest.	Pathological Findings	Location
24	Baudouin, A. ⁸⁾	1910	64	M	L		S D (hyaline, blood vess)	Th6
25	Poensgen, F. ⁷³⁾	1913			ALL		Myelitis	
26	Stursberg, H. ⁹³⁾	1914	30	M	Chloroma (ML)	P (flaccid) BR	I (dura)	Th6-L5
27	Sauer, C. ⁸³⁾	1914	36	M	Chloroma (Mono ML)	Myelitis	T (dura)	L-S
28	Midremet, C.W.G. ⁵⁴⁾	1914	15	M	Chloroma (ML)		T (dura)	L1-3
29	Rummo, R. ¹⁰¹⁾	1916						
30	Schwab, S.I. ⁸⁶⁾	1917			AL		Myelitis	
31	Gross, K. ¹⁰¹⁾	1917				P (flaccid)	I	Pons, Stem
32	Bassoe, P. ⁷⁾	1918	28	F	Chloroma (CML)		T (epidural)	Th4-6
33	Lewis, E.C. ⁵⁶⁾	1919	10	M	Chloroma (LL)	BR	I (meningeal)	Th5-7
34	v. Dolivo ¹⁰¹⁾	1919						
35	Sturrock, A.C. ⁹²⁾	1925	14	M			I (meningeal)	
36	Burns ¹⁰¹⁾	1925						
37	Heissen, F. ³⁸⁾	1925	34	F	Chloroma		T (epidural)	Th2-5
38	Tromner, E. ¹⁰³⁾	1927	55	M	LL	Rt knee jerk (-)	I (meningel)	
39	Well ¹⁰¹⁾	1929						
40	Blaschy, R. ⁹⁾	1929	54	F	L	Q & S		
41	Critchley, M. ¹⁴⁾	1930	19	M	Chloroma (ML)		T	C7-Th7
42	Critchley, M. ¹⁴⁾	1930	8	M	Chloroma (ML)			C8-Th1 Th6-12
43	Critchley, M. ¹⁴⁾	1930	15	M	Chloroma (ML)			Th2, Th7
44	Critchley, M. ¹⁴⁾	1930	11	M	Chloroma (ML)			Th10-L
45	Hettfleisch, F. ³⁹⁾	1930	48	M	CML	F (tabetic)		
46	Reese, H.H. ⁷⁶⁾	1932	13	M	LL		Compression	Th2-5
47	Reese, H.H. ⁷⁶⁾	1932	51	M			Compression	
48	Reese, H.H. ⁷⁶⁾	1932	29	M			Compression	
49	Cornil, L. ¹³⁾	1932	49	M	ML	Landry		Th2-3
50	Haintz, E. ³³⁾	1933	27	M	AML	BR	I (epidural)	Th-L
51	Bamforth, J. ⁵⁾	1933	19	F	Chloroma (LL)	W&Atr (leg) BR		C-L
52	Bamforth, J. ⁵⁾	1933	39	F	Chloroma (LL)	BR		L-S
53	Diamond, I.B. ¹⁷⁾	1934	8	M	AML			Th6-12
54	Weil, P.E. ¹¹⁰⁾	1935	39	M	CML			Th1-5
55	Gordih, R. ²⁸⁾	1936	19	M	ALL		Cav	C-L
56	Scalori, G. ¹⁰¹⁾	1938						

No.	Author	Year	Age	Sex	Nature of Leukemia	Clinical Manifest.	Pathological Findings	Location
57	Nordenson, N.G. ⁶⁸⁾	1939						
58	Laurie, H.W.S. ⁴⁹⁾	1939	11	M	AML		Cav	C-S
59	Bamforth, J. ⁶⁾	1939				P		
60	Weil, H. ¹⁰⁹⁾	1939	19	F	ML	P & S	S Bl (focal)	Th7-10
61	Murphy, J.P. ⁶¹⁾	1940	39	M	AML	P (flaccid)	I (root)	
62	Cruz ¹⁰¹⁾	1940						
63	Dereymacker, A. ¹⁶⁾	1940	24	M	AML			Th5-8
64	Mouriquand ¹⁷¹⁾	1942						
65	Griffin, L.L. ³⁰⁾	1942	26	F	ML			Th9-L1
66	Shenkin, H.S. ⁸⁷⁾	1946	18	F	AMonoL	Q	Compression (epidural)	C7-Th2
67	Rouques, L. ⁸⁰⁾	1946	52	F	AML			Th1-12
68	Roger, H. ⁷⁷⁾	1947	13	M	AML		I (epidural)	Th10-L2
69	Libansky, J. ¹⁰¹⁾	1947						
70	Wade, O.L. ¹⁰⁸⁾	1947	19	M	AML		I (meningeal)	Th3-8
71	Gauld, O.L. ²⁵⁾	1948	14	M	AML	Pain (leg) BR		
72	Gauld, W.R. ²⁵⁾	1948	45	M	CML	W (leg)		
73	Giraud, G. ²⁷⁾	1950						
74	Ragins, A.B. ⁷⁴⁾	1950	22	M	Chloroma		T	Th7-10
75	Gadermann, E. ²⁴⁾	1951						
76	Thanabalasundaram, R.S. ⁹⁷⁾	1951				Landry		
77	Mosberg, W.H. ⁵⁷⁾	1951	5/12	F	LL			L1-2
78	Kissel, A.G. ⁴⁰⁾	1953			ML		I (epidural)	
79	Anderson, C.D. ²⁾	1954	16	F	Chloroma (Mono ML)		T	Th6-10
80	Cunningham, G.L. ¹⁵⁾	1954	50	M	Chloroma (AML)			Th-L-S
81	Stransky, E. ⁷¹⁾	1955	14	M	MonoML		I (dura & epidural)	Th-L
82	Ford, F.F. ²²⁾	1960	12	M	AleukLL	P (flaccid) BR S (<Th10)	T (epidura)	Th2
83	Rand, R.W. ⁷⁵⁾	1960	6	F	CML		T (intraspin)	Th1-5
84	Rand, R.W. ⁷⁵⁾	1960	14	M	MonoML		T (intraspin)	Th2-7
85	Martin, Ph. ⁵²⁾	1960				P	I (epidural)	
86	Baker, G.P. ⁴⁾	1962	28	M	AML	W (leg)	I (meningeal)	Whole
87	Sullivan, M.P. ⁹⁴⁾	1963	7	F	ALL	W & Pain (leg)	I (meningeal & root)	
88	Sullivan, M.P. ⁹⁴⁾	1993	6	M	Lympho-sar2oma	W (leg)	T (meningeal)	

No.	Author	Year	Age	Sex	Nature of Leukemia	Clinical Manifest	Pathological Findings	Location
89	Sullivan, M.P. ⁹⁴⁾	1963	3	M	ALL	W & Pain (leg)	Meningitis	Th3-8
90	Burns, E.W. ¹²⁾	1963	47	M	Chloroma	P	T (epidural)	
91	Wilngh, A. ¹¹³⁾	1963	12	F	CML		I (epidural)	
92	Singh, A. ⁸⁹⁾	1963	34	M	ALL	Pain (leg) DTR (-)		
93	Singh, A. ⁸⁹⁾	1963	25	M	AML	Pain (leg) BR & S Trans myeli		middle Th
94	Singh, A. ⁸⁹⁾	1963	48	M	CML	W(leg) & BR		
95	MacDougall, R.W.A. ⁶¹⁾	1964	56	M	AML		I	

Note :

Clinical Manifestation

P : Paraplegia

T : Transverse symptoms

S : Sensory disturbances

BR : Bladder & rectal disturbance

Landry : Ascending symptoms

W : Weakness

Q : Quadriplegia

Atr : Atrophy

Pathological Findings

I : Infiltration

T : Tumor formation

S : Softening

Bl : Bleeding

N : Necrosis

H : Hematoma

D : Degeneration

Cav : Cavitation

F : Funicular symptoms

Table 4. Previously Reported Cases of Spinal Leukemia in Japan.

No.	Author	Year	Age	Sex	Nature of Leukemia	Clinical Manifest.	Pathological Findings	Location
1	Hatta, T. ⁸⁷⁾	1926	18	F	CML	P (spastic)	I (dura)	C-upper L
2	Yamada, T. ¹¹⁵⁾	1938			L	Landry	Myelitis	
3	Masuda ¹⁰¹⁾	1938						
4	Akanuma, J. ¹⁾	1939	15	M	ML		T (vertebra)	Th5, L3,4
5	Nakama, M. ⁶²⁾	1949	26	M	AML	T (>Th6) Land		
6	Tasaka, S. ⁹⁸⁾	1952	13	M	Chloroma	P (>5ICS)	T&S(epidural)	Th4-8
7	Okinaka, S. ⁷⁰⁾	1953	14	M	AML	T (>Th8)	Bl & S	Th5-7
8	Okinaka, S. ⁷⁰⁾	1953	38	M	AML	P&S(<Th5)	T (epidural) S & N	Th4 <lower Th
9	Okinaka, S. ⁷⁰⁾	1953	26	M	Chloroma	S (S3-4)	T (epidural)	Th10-12
10	Yamamoto, Y. ¹¹⁶⁾	1954	38	M	CML	T		Th
11	Sano, S. ⁸²⁾	1956	22	F		P (flaccid) S(<Th3-4)	H (epidural) Bl (post. col) S D(parenchym)	Th C3-Th1, 2 Th3 Th, L
12	Miwa, K. ⁶⁶⁾	1956	3	M	Chloroma	P & BR	I (vertebra)	L3 & 5

No.	Author	Year	Age	Sex	Nature of Leukemia	Clinical Manifest.	Pathological Findings	Location
13	Ohmura, T. ⁸⁹⁾	1956	12	M	Chloroma (AML)		T(sub-& epidural) D & N	>Th8, L2-3
14	Tokuhiro, H. ¹⁰⁰⁾	1956	23	F	L		N & S H (epidural) Bl (funicular)	Th3-9 C3-Th1
15	Uchibori, E. ¹⁰⁶⁾	1957	20	M		Passage dist. (myelogram, Th3)	T (vertebra) S T (epidural)	Th4-7 Th4-6 Th7-12
16	Fukuhara, A. ²³⁾	1958	22	M	AML	S (<Th7)	Bl & I (dura)	
17	Komori, ¹⁰¹⁾	1959						
18	Ito, T. ⁴⁴⁾	1959	41	M	AML	T	I (epidural) I (dura)	C6-L5 Th5-6, Th12-L2
19	Toyokura, Y. ¹⁰¹⁾	1959	18	F	AML		T S	Th6 <Th6
20	Toyokura, Y. ¹⁰¹⁾	1959	14	M	AML		Bl & S	<middle Th
21	Toyokura, Y. ¹⁰¹⁾	1959	38	M	AML		T (dura& root) Cav & D Bl (vertebra)	Th4 <Th4
22	Ando, K. ³⁾	1960	10	M	L			
23	Inoue, S. ⁴¹⁾	1960	56	F	CML	P (flaccid)		
24	Nakashima, G. ⁶⁴⁾	1960	23	M	LL	P	Bl, I (subarac)	
25	Tsukada, T. ¹⁰⁴⁾	1960	33	M	AML	T	F, S & N	
26	Iwasaki, I. ⁴⁵⁾	1961	21	F	MonoL	P (flaccid) S (>Th7)		
27	Nakamura, H. ⁶³⁾	1961	43	M	SubacutML	P		
28	Shinya, K. ⁸⁸⁾	1961	27	F	Chloroma	P	T	Th
29	Takagi, S. ⁹⁵⁾	1961	14	M	AL	T		
30	Nishikawa, M. ⁸⁶⁾	1961	33	M	AL	P (flaccid, >Th)	F D & Cav	C-upperTh
31	Hamada, T. ³⁴⁾	1962	20	F	Chloroma	P S (Th10)	I (epidural)	Th1-6
32	Motoi, G. ⁵⁹⁾	1962	13	F	Aleuk. L	P (flaccid)		
33	Tsukada, T. ¹⁰⁵⁾	1962	8	F	Chloroma (AL)	P		
34	Taneda, T. ¹⁰⁵⁾	1962	13	M	Chloroma	P	I (subdural) S & Cav	Th2-3
35	Yoshioka, K. ¹¹⁷⁾	1962	7	M	L	P & BR		
36	Ishikura, H. ⁴²⁾	1963	37	M	AML	Landry (>3ICS)	T & N	Th3-8
37	Matsumoto, M. ⁵³⁾	1963	29	M	AML	P	D (post. col)	
38	Ueda, H. ¹⁰⁷⁾	1965	46	M	AML		I (parenchym, post. root & subdural)	
39	Takita, J. ⁹⁶⁾	1966	44	F	AML	T	I (epidural) S & N	<Th3
40	Kobayashi, Y. ⁴⁸⁾	1966	27	M	AML(Chl)	T	T (epidural)	Th5

The figures stand for the same meanings as in the Table 3.

Table 5. Features of Spinal Cord Involvement in Leukemia form Previously Reported Cases in Japan and the Western Countries.

		Japan	The Western countries	Whole
Age	0- 9 y.o.	3 (8.1%)	9(13.2%)	12(11.4%)
	10-19 y.o.	11(29.7%)	26(38.2%)	37(35.2%)
	20-29 y.o.	12(32.4%)	8(11.8%)	20(19.0%)
	30-39 y.o.	6(16.2%)	11(16.2%)	17(16.2%)
	40-49 y.o.	4(10.8%)	6(8.8%)	10(9.5%)
	50-59 y.o.	1(2.8%)	7(10.3%)	8(7.6%)
	60-69 y.o.	0(0)	1(1.5%)	1(1.1%)
	Total	37 (100%)	68 (100%)	105 (100%)
	Range	3 y.o.-56 y.o.	5 ms.o.-64 y.o.	
Sex Ratio	Male	26(70.3%)	52(76.5%)	78(74.3%)
	Female	11(29.7%)	16(23.5%)	27(25.7%)
	Total	37 (100%)	68 (100%)	105 (100%)
Nature of Leukemia	AML	13(50.0%)	12(23.1%)	25(32.1%)
	Chloroma	9(34.6%)	23(44.2%)	32(41.0%)
	CML	3(11.5%)	6(11.5%)	9(11.5%)
	Lymphatic L	1(3.9%)	11(21.2%)	12(15.4%)
	Total	26 (100%)	52 (100%)	78 (100%)
Pathologic Findings	No. of Cases	28	52	80
	Degeneration Softening Necrosis Cavitation	22(78.6%)	9(17.3%)	31(38.8%)
	Hemorrhage	7(25.0%)	3(5.8%)	10(12.5%)
	Epidural Tumor	7(25.0%)	11(21.2%)	18(22.5%)
	Meningeal Infilt.	5(17.9%)	17(32.7%)	22(27.5%)
	Parenchym Infilt.	0(0)	5(9.6%)	5(6.3%)
Location	No. of Cases	23	50	73
	Cervical Cord	6(26.1%)	10(20.0%)	16(21.9%)
	Thoracic Cord	22(95.7%)	39(78.0%)	61(83.6%)
	Lumbar Cord	11(47.8%)	19(38.0%)	30(41.1%)
	Sacral Cord	0(0)	6(12.0%)	6(8.2%)

Reviewed from 135 cases, consisting of 40 from Japan and 95 from the Western countries.

frequency of leukemia in both sexes.¹¹⁴⁾ Although, among various types of leukemia, acute myelogenous leukemia was the commonest cause of the spinal

symptoms in both Japanese and Western groups, chloroma was observed much more frequently in the Western countries than in Japan. Lymphatic leukemia was also one of the commonest causes in the Western countries. As to the clinical manifestations, paraplegia was the commonest in both Japan and the Western countries. In Japan, the pathological changes of the spinal cord causing clinical manifestations were commonly softening and necrosis of the spinal parenchyma, whereas hemorrhage, epidural tumor formation and meningeal infiltration were much less frequent. In the Western countries, however, infiltration of the spinal meninges with leukemic cells, and epidural tumor formation were the commonest findings in contrast with much lower frequency of softening or necrosis. As for the levels of the spinal cord commonly involved, the thoracic cord was the first, and the lumbar cord the second in both groups, while cervical or sacral cord was rarely involved.

Summary

We reported a case of acute myelogenous leukemia associated with complete spinal transverse syndrome, which suddenly developed 3 weeks prior to death and ascended rapidly to the Th4 level. The serial sections of the spinal cord revealed parenchymatous changes consisting of softening, necrosis and hemorrhage in the Th4 through Th8 cord and the L1 and L2 cord, with no leukemic cell infiltration in the parenchyma. There was an epidural infiltration of leukemic cells, forming tumor-like masses between Th6 and Th10 segment. Hemorrhage was seen in the posterior nerve roots.

The involvement of the spinal cord was reviewed from 40 reported cases in Japan comparing with 95 cases from the Western countries. The spinal cord involvement in leukemia was most frequently seen in young males, and in the course of acute myelogenous leukemia. The commonest clinical manifestation was paraplegia and sphincter disturbance. The commonest pathological change was the parenchymatous changes in the Japanese cases, in comparison with the frequent occurrence of meningeal infiltration or epidural tumor formation in the Western ones. In the spinal involvement the thoracic cord was involved most frequently.

In our case, the parenchymatous change of the spinal cord was most likely to have been caused by a circulatory disturbance, due to epidural compression by the deposits of leukemic cells.

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