Acta Medica et Biologica
Vol. 35, No. 3/4, 89-98, 1988

MONOCYTIC SARCOMA
A CASE REPORT

KEIICHI NEMOTO,* KEIICHI HONMA,* YOSHIHISA OHNISHI,*
HIDENORI KUMANO,** NAOKI OHSAKI,**
AND
ATSUSHI ABE***

**The Second Department of Pathology, Niigata University School of Medicine.*
***Department of Internal Medicine, Niigata Rohsai Hospital.*
****Department of Internal Medicine, Niigatakenritsu Chuhoh Hospital.*

(Received August 28, 1987)

ABSTRACT

Clinical, morphologic, cytochemical, immunologic, and ultrastructural features of a case of monocytic sarcoma which revealed pleural infiltration are described. The proliferating cells in the pleural cavity were not only large, bizarre cells, but also small -to medium-sized lymphoid cells. The large cells had the characteristics of monocyte showing a convoluted nucleus, abundant basophilic cytoplasm, numerous vacuoles, and irregular cytoplasmic projections. The cytochemical examination revealed that these cells had a diffuse, slightly-to-strongly positive reaction with α naphthyl butyrate esterase, acid phosphatase, β-glucuronidase, and aminopeptidase. The peroxidase reaction was completely negative and contained no cytoplasmic immunoglobulins. By surface phenotype, the cells showed positive reactions for Ia-like antigen, Mo 2 and My 4. Moreover, ultrastructurally the cells had phagolysosomes in the cytoplasm. On the other hand, the lymphoid cells expressed a phenotype of T cells (T 11 and Leu 3a positive).

4 months after the initial diagnosis, the patient died of heart failure and lung edema without leukemic manifestation.

The present case was a peculiar type of monocytic proliferative disorder (monocytic sarcoma) limited to the pleura and pleural cavity.

(Key words: monocytic sarcoma, malignant histiocytosis)

Monocyte/macrophage proliferative disorders are heterogenous conditions, including monocytic leukemia, malignant histiocytosis, various infectious diseases, and errors of metabolism. It has been generally accepted that tissue macrophages, also termed histiocytes, are derived from circulating monocytes.[11]

The present report describes an unusual form of monocytic proliferative disorder localized in the pleura and pleural cavity. We are presenting in this report an emphasis on the results of clinical, morphological, cytochemical, immunologic, and ultrastructural studies.

A Case Report

A 69-year-old woman was well until October 1985 when a back pain developed, and she was admitted to the Niigata Rohsai Hospital in November 1985. On admission, she was found to have a right pleural effusion after a chest X-ray examination. Neither lymphadenopathy nor hepatosplenomegaly was noted, and the hematological investigation was not remarkable. The laboratory examinations are seen in Table 1. Although a slight elevation of LDH was recognized, no other abnormality was noticed. A bone marrow examination showed hypoplastic bone marrow without leukemic cell proliferation (Table 2). In the right pleural effusion, a great number of large, bizarre mononuclear cells and small-to medium-sized lymphoid cells were noted. Although malignant lymphoma was suspected, the large mononuclear cells had monocytic characteristics. A biopsy of the right pleura established the diagnosis of monocytic sarcoma. As a result of administration of cyclophosphamide, vincristin, and adriamycin, the pleural effusion almost disappeared. The patient remained well until February 1986 when the pleural and pericardial effusion were recognized again. Finally, lung edema was observed, and

Table 1. Laboratory Findings on Admission

T. Bil.	0.5 mg/dl	T. P.	6.9 g/dl
GOT	23 IU/l	Alb.	60.1 %
GPT	19 IU/l	α_1-Gl.	3.8 %
γ-GTP	20 IU/l	α_2-Gl.	10.3 %
AL-P	213 IU/l	β-Gl.	12.0 %
LDH	760 IU/l	γ-Gl.	13.8 %
LAP	33 IU/l	A/G	1.5
Ch. E	6.56 IU/l		
ICG	9 %	CRP	(+)
T. Chol.	243 mg/dl	RA	(−)
		HBsAg	(−)
BUN	17 mg/dl		
Creat.	0.8 mg/dl		
U. A.	7.0 mg/dl		

Table 2. Hematological Examination of Bone Marrow

NCC	$3.1\times10^4/mm^3$	
MgK.	$15/mm^3$	
Myelogram		
Erythroid		32.8%
Pro.	1.2%	
Baso.	2.0%	
Poly.	8.8%	
Orth.	20.8%	
Myeloid		46.8%
Mbl.	1.2%	
Pro.	2.4%	
Myel.	10.0%	
Meta.	5.2%	
Stab.	7.6%	
Seg.	16.4%	
Eosino.	3.6%	
Baso.	0.4%	
Lymph.		16.0%
Mono.		4.0%
Plasma.		0.4%

Table 3. Hematological Findings of Peripheral Blood

		19/XI	2/XII	18/I	17/II	25/II
RBC	$\times10^4/mm^3$	465	414	333	323	342
Hb	g/dl	13.9	12.8	9.9	10.0	10.0
Ht	%	42	40	31.1	32.0	31.4
Ret.	‰	11	/	/	/	/
Plat.	$\times10^4/mm^3$	35.2	33.4	29.2	/	44.5
WBC	$\times10^3/mm^3$	5.4	6.2	3.4	6.3	7.8
Myel.	%			1	1	
Meta.	%			2	0	
Stab.	%	2	3	15	9	2
Seg.	%	59	63	61	69	81
Lymph.	%	37	25	15	10	10
Mono.	%	2	7	5	9	7
Eosino.	%		2	0	0	
Baso.	%			1	2	

she died on February 25, 1986. The clinical course was 4 months. Summary of peripheral blood analysis during her clinical course is shown in Table 3. Although a slight increase of monocytes was noted, no leukemic manifestation was observed.

MORPHOLOGIC FEATURES

The microscopic findings of the right pleura biopsy specimen showed a diffuse

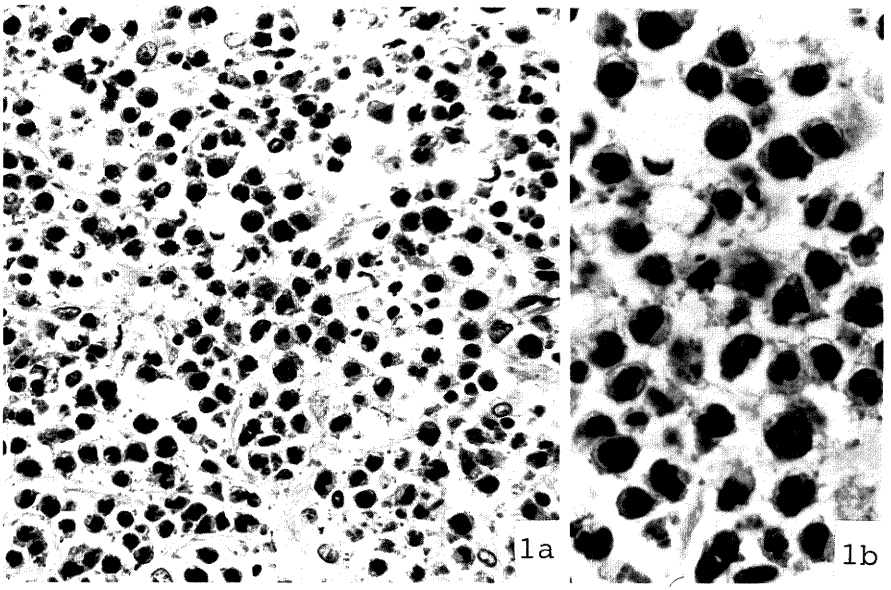

Fig. 1a. Section obtained from right pleura biopsy, showing diffuse proliferation of large cells containing a small number of small lymphoid cells. Hematoxylin and eosin (H. E.), ×600.

Fig. 1b. Same section as in Fig. 1a, demonstrating high-power view of large cells. H. E. ×1,200.

infiltration composed of large cells (Fig. 1a, 1b) and small lymphoid cells. The cytoplasm of the large cells was moderately abundant. Nuclear morphology showed round-to high indentation or lobulation. Mitotic figures were also frequently seen. These large cells were positive in lysozyme, α_1 antitrypsin and α_1 anti-chymotrypsin, but not in S-100 protein.

Cytopathology and Cytochemistry

A May-Giemsa stained pleural effusion smear showed a polymorphic and composite population, consisting of large, bizarre cells and small-to medium-sized lymphoid cells (Fig. 2). The former demonstrated abundant basophilic cytoplasm, often containing a foamy and vacuolated structure. Although irregular cytoplasmic projections were also noted, phagocytosis was not seen. Cytochemical analysis revealed that the cells demonstrated diffuse moderate-to-strong reactions with α naphthyl butyrate esterase (Fig. 3a) and slight-to-marked staining with acid phosphatase (Fig. 3b), β-glucuronidase, and aminopeptidase. Granular PAS-stainable material was noted in the cytoplasm.

On the other hand, a characteristic dot positivity for acid phosphatase and for α naphthyl butyrate esterase was present in the lymphoid cells (Fig. 4).

Immunologic Studies

A summary of the immunologic findings is listed in Table 4. The large cells showed

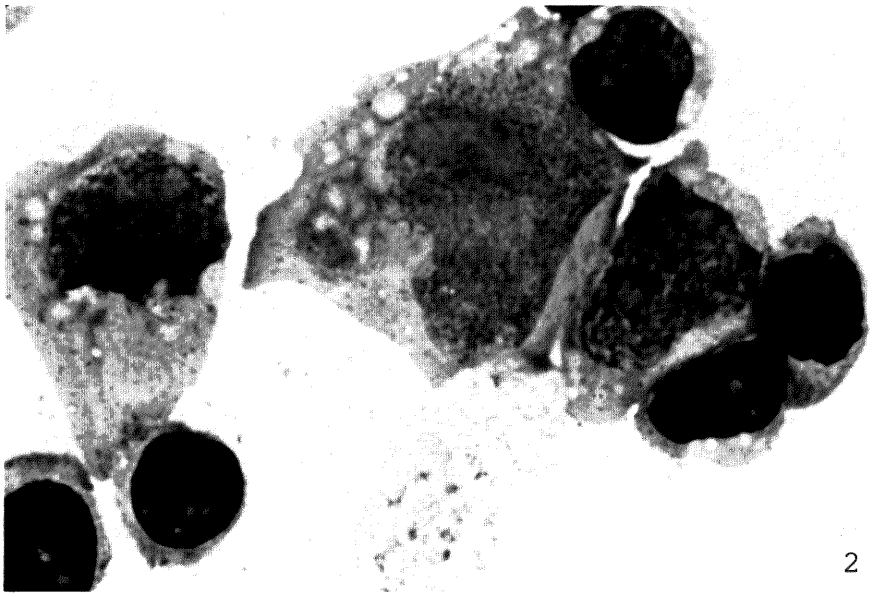

Fig. 2. Proliferated cells from pleural effusion revealing large, bizarre cells and small lymphoid cells. May-Giemsa stain, ×1,500.

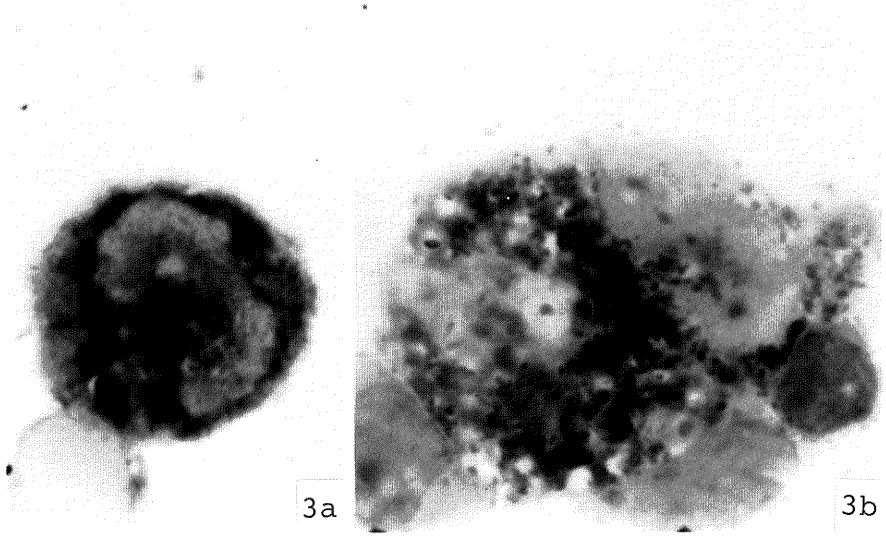

Fig. 3a. α naphthyl butyrate esterase stain on pleural effusion smear preparation, demonstrating heavy positivity in large, bizarre cell. ×1,500.

Fig. 3b. Smear preparation illustrating strong positivity acid phosphatase. ×1,500.

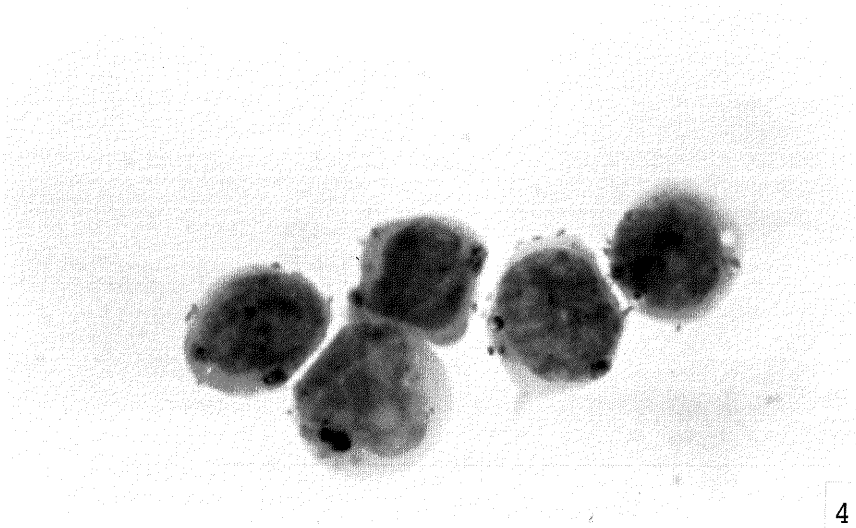

Fig. 4. Small lymphoid cells from pleural effusion aspirate, showing acid phosphatase reactive, dot-like localization. ×1,500.

Table 4. Immunological Analysis of Proliferated Cells in the Chest Cavity

	Small Cells	Large, Bizarre cells
Ia	−	+
J5	−	−
Leu 7	(+)	−
Leu 3a	++	−
Leu 2a	(+)	±
T11	++	− ~ ±
B1	−	− ~ ±
B4	−	−
Mo2	−	++++
My4	−	+
My7	−	−
My9	−	−

( ) a very small number

positive reactions for Ia-like antigen, Mo 2 and My 4. On the other hand, the lymphoid cells expressed a phenotype of T cells (T 11 and Leu 3a positive).

ULTRASTRUCTURE

The large, bizarre cells in the pleural cavity contained an irregular folding nucleus, a prominent nucleous, small mitochondria, irregular cytoplasmic projections, and some-

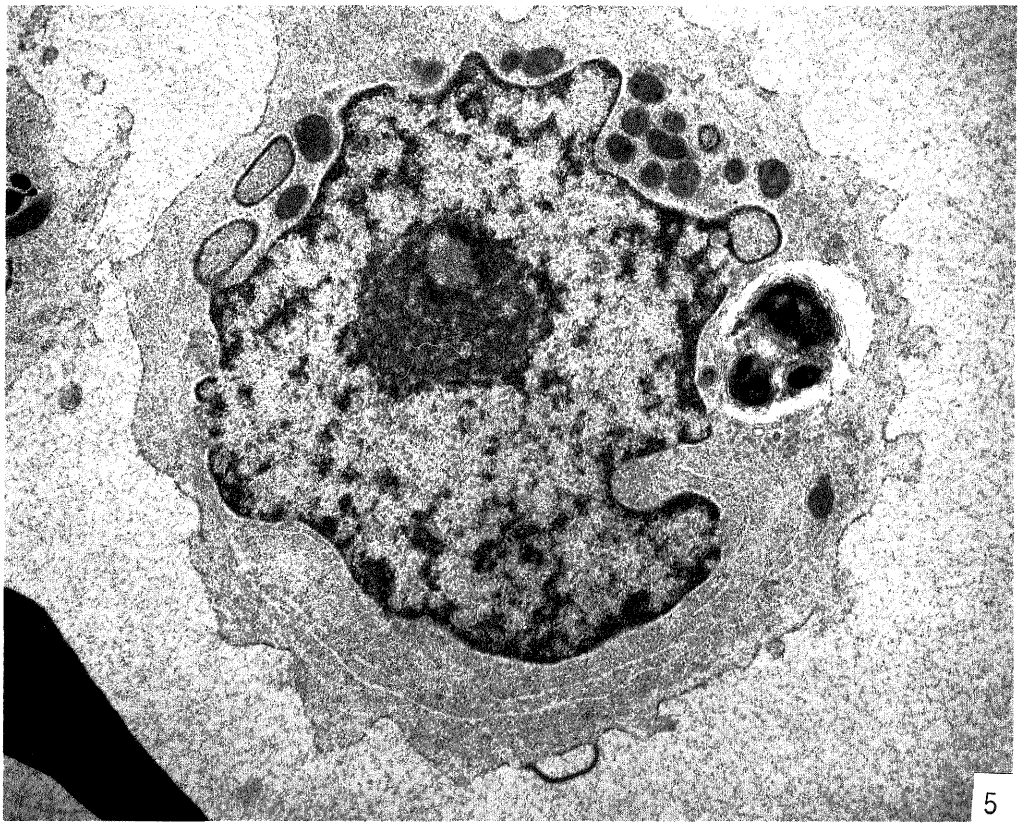

Fig. 5. Electron micrograph of large, bizarre cell from pleural effusion, demonstrating slight folded nucleus with nuclear pocket and a prominent nucleolus, small mitochondria, phagolysosomes, and long strands of rough endoplasmic reticula in the cytoplasm. ×10,000.

times phagolysosomes (Fig. 5). Nuclear pockets were often observed. In the lymphoid cells the nucleus was hyperchromatic and sometimes convoluted (Fig. 6). A small number of mitochondria and Gall bodies were also noted.

DISCUSSION

The present case is an unusual case of monocyte/macrophage proliferative disorder. The characteristic points of the case are as follows: 1) localized proliferation of neoplastic cells in the pleura and pleural cavity, 2) no leukemic manifestation, 3) no evidence of hepatosplenomegaly or lymphoadenopathy, 4) neoplastic cells were not only of the monocyte/macrophage series but also lymphocytes (T cells). Although most of the neoplastic cells in the chest cavity were suspected of being malignant lymphoma cells, cytochemical findings indicated the cells had a monocytic nature, i. e., positive reaction with α naphthyl butyrate esterase, acid phosphatase, and aminopeptidase.[7] Moreover, ultrastructurally, the cells had phagolysosomes in the cytoplasm, and after surface

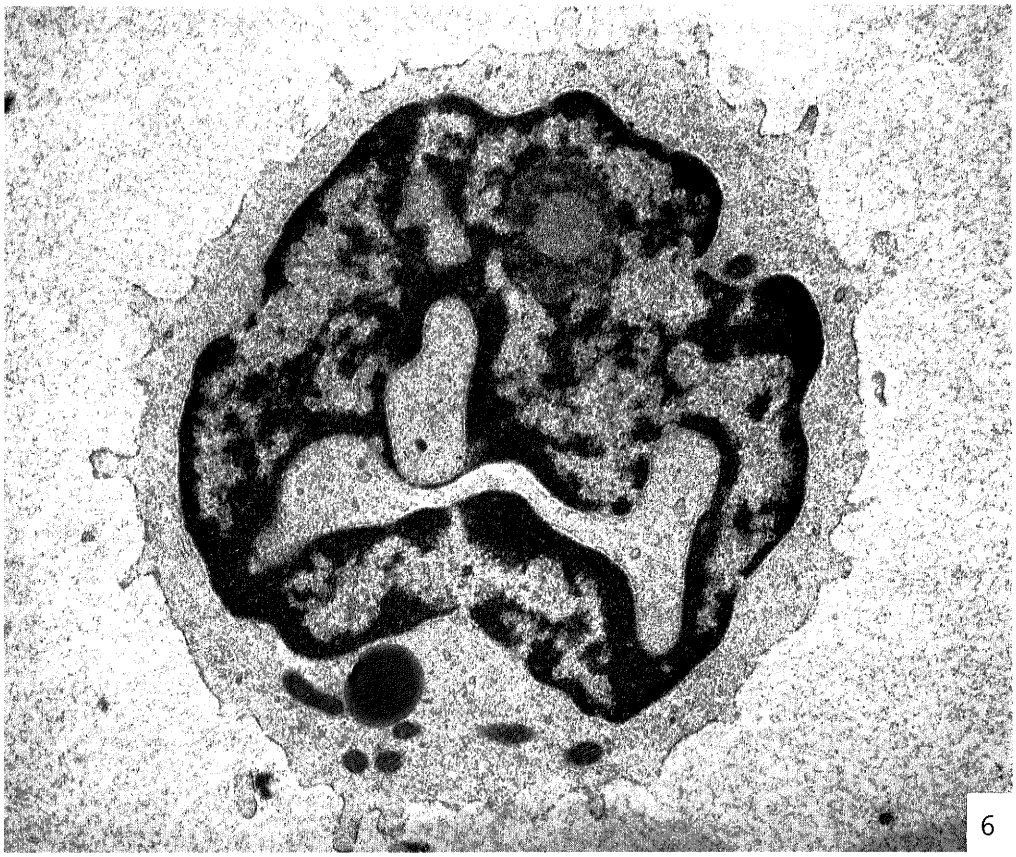

Fig. 6. Electron microscope of lymphoid cell from pleural effusion, showing convoluted nucleus with marked condensation of heterochromatin and very small amounts of cell organella. ×12,000.

phenotype, these showed a positive reaction for Ia-like antigen, Mo 2 and My 4.

Since the report of van Furth et al.[11], it has been generally accepted that tissue macrophage (histiocyte) is derived from the circulating monocytes.

Cline and Golde[1] documented a review and reevaluation of the histiocytic disorders. In their paper, the principal features of normal and malignant histiocyte differentiation are reviewed and correlated with clinical syndromes. According to their findings, the blood monocyte is an intermediate cell between the bone marrow precursor and the tissue macrophages, which are further subdivided into immature cells and mature ones. Moreover, they reported that monocytic leukemia was recognized morphologically by the presence of immature cells of the monocyte-macrophage cell line in the blood, bone marrow, and tissues.

Malignant histiocytosis (MH) is a malignant neoplastic process of the histiomonocytic series. Scott and Robb-Smith[10] first described the disease in 1939 under the name of histiocytic medullary reticulosis (HMR). The disease is characterized by

fever, weight loss, jaundice, lymphoadenopathy, hepatosplenomegaly, pancytopenia, and systemic proliferation of atypical histiocytes and their precursors. In 1966, Rappaport introduced the term "malignant histiocytosis."[9] Generally, HMR and MH are considered the same disorder. Cline and Golde[1] considered that the cells in the HMR resembled moderately, well-differentiated histiocytes with a high proliferative capacity and a well-developed phagocytic activity.

The present case differs from MH in several respects, for example, clinical features, morphology, and distribution of neoplastic cells.

On the other hand, chloroma and granulocytic sarcoma, which revealed an extramedullary solid tumor composed of non-lymphocytic hemopoietic cells, have been reported.[4,5,6,9] These tumors occur most frequency in the periostium and bone, soft tissue, lymph nodes, and skin.[6] By analyzing clinical data of 61 biopsy cases of granulocytic sarcoma, Neiman et al.[6] divided the cases into three clinical settings: 1) the tumor with no known hematologic disease, 2) known myeloproliferative disorders, and 3) acute myeloid leukemia. Moreover, they mentioned 13 of the 15 patients with no known disease having developed acute leukemia in from one to 49 months after the biopsy of their tumors (mean: 10 months). Concerning the frequency of tumor formation, Kojima et al.[4] demonstrated chloroleukemia had the highest rate, followed by monocytic leukemia, while myeloid leukemia showed a considerably lower rate. In contradistinction to granulocytic sarcoma, Deura et al.[2] reported a case of monocytic sarcoma forming tumor masses composed of a monocytic series in the peritoneum, omentum, mesenterium, and retroperitoneum. In their case also, there was no leukemic manifestation until 6 months from the time of initial diagnosis. The present case is very similar to that reported by Deura et al. Table 5 is a summary of the monocytic leukemia we have experienced. In our classification, the present case belongs to an unusual form (tumor-forming cases) without leukemic manifestation. If we could have followed the condition of the patient'

Table 5. Monocytic Leukemia

- Usual Form
  - Monocytic Leukemia
    - without Maturation
    - with Maturation
  - Myelomonocytic Leukemia
    - Acute
    - Chronic
- Unusual Form
  - Tumor-Forming Cases
    - without Leukemic Manifestation
    - ⋮
    - ↓
    - with Leukemic Manifestation

s disease for a longer period, a picture of monocytic leukemia might have been identifiable. We consider monocytic sarcoma is a peculiar type of monocytic leukemia in which the neoplastic cells have an affinity to tissues rather than bone marrow and peripheral blood.

Finally, the proliferated cells in the chest cavity were not only of the monocytic series but also lymphoid cells. The coexisting lymphoid cells were thought to be T cells as a result of cytochemical and immunological studies. Concerning lymphohistiocytosis, Jaffe et al.[3] have reported on 6 interesting patients with malignant lymphoma, in whom appeared a syndrome that mimicked an MH which developed as a terminal event. They postulated that the erythrophagocytic syndrome might be secondary to the production of macrophage-activating factors by the neoplastic T cells. The authors mentioned[8] a familial hemophagocytic reticulosis which was characterized by an extensive proliferation of histiocytes showing active phagocytosis of blood cells in various organs but was also a special type of lymphoproliferative disease probably involving T cells rather than a true histiocytic disease. In the present case, it cannot be denied that the lymphocytosis may play some role as a cause for monocytic proliferation.

ACKNOWLEDGMENT

The authors thank Mr. T. Hasegawa, Mr. K. Satoh, Mr. S. Momozaki, and Mrs. M. Tanabe for their excellent technical assistance.

REFERENCES

1) Cline, M. J. and Golde, D. W.: A review and reevaluation of the histiocytic disorders. *Amer. J. Med.* 55: 49-60, 1973.
2) Deura K., Ishii Z., Shimoyama M., Minato K., and Matsuda M.: A case of monocytic sarcoma of the peritoneal type with minimal involvement of the bone marrow, liver, spleen, and lymph node. *Jpn J. Clin. Hematol.* 19: 1372-1378, 1978 (in Japanese).
3) Jaffe, E. S., Costa, J., Fauci, A. S., Cossman, J. and Tsokos, M.: Malignant lymphoma and erythrophagocytosis simulating malignant histiocytosis. *Am. J. Med.* 75: 741-749, 1983.
4) Kojima M., Kikuta K., and Dazai A.: Tumor-forming leukemia. *Tohoku J. Exper. Med.* 81: 256-266, 1963.
5) Meis, J. M., Butler, J. J., Osborne, B. M., and Manning, J. T.: Granulocytic sarcoma in nonleukemic patients. *Cancer* 58: 2697-2709, 1986.
6) Neiman, R. S., Barcos, M., Berard, C., Bonner, H., Mann, R., Rydell, R. E., and Bennett, J. M.: Granulocytic sarcoma: A clinicopathologic study of 61 biopsied cases. *Cancer* 48: 1426-1437, 1981.
7) Nemoto K. and Ohnishi Y.: Studies on aminopeptidase activity in acute non-lymphocytic leukemia. The relation to peroxidase reaction. *Acta Pathol. Jpn.* 33: 495-499, 1983.
8) Nemoto K. and Ohnishi Y.: Familial hemophagocytic reticulosis: Clinicopathologic findings, and cytochemical, immunohistochemical and electron microscopic studies. *Acta Pathol. Jpn.* 37: 1811-1822, 1987.
9) Rappaport, H.: Tumors of the hematopoietic system. In Atlas of Tumor Pathology. Washington, D. C., Armed Forces Institute of Pathology, 1966.
10) Scott, R. B. and Robb-Smith, A, H. T.: Histiocytic medullary reticulosis. *Lancet* 2: 194-198, 1939.
11) van Furth, R., Cohn, Z. A., Hirsch, J. G., Spector, W. G., and Langevoort, H. L.: The mononuclear phagocyte system: A new classification of macrophages, monocytes, and their precursor cells. *Bull. Wld. Hlth. Org.* 46: 845-852, 1972.