An Autopsy Case of Leukemic Lymphosarcoma Arised at the Thymic Region

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Leukemia is merely the result of a release of tumor cells into the blood stream due to increased production and failure of maturation of white cells. A leukemic blood picture frequently occurs in malignant lymphomas with wide spread of tumor cells to the various organs. When tumor mass is formed prior to leukemic manifestation or leukemia coexsists with tumorous condition, the term "tumoriferous leukemia" is commonly applied.

The authors recently experienced an autopsy case in which large tumor mass was found in the thymic region with accompany of a leukemic blood picture. Histological examination followed the conclusion that the thymus was the possible origin of the primary neoplastic proliferation.

Report of a Case

Clinical History. — The patient was a 25-year-old male who had been well until nine days before admission, when he suddenly began to have disturbance in swallowing, general fatigue, nausea and vomitting. At that time he also complained of pain of the eye and disturbance in gait. Loss of appetite and general fatigue gradually increased in their severity, so the patient was admitted to Yamaguchi Prefectural Central Hospital on August 15, 1967. He had not been exposed to atomic bomb.

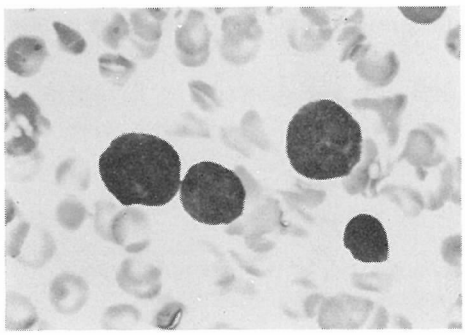


Fig. 1. Leukemic cells in the peripheral blood. They have soft chromatin texture and scanty cytoplasm.

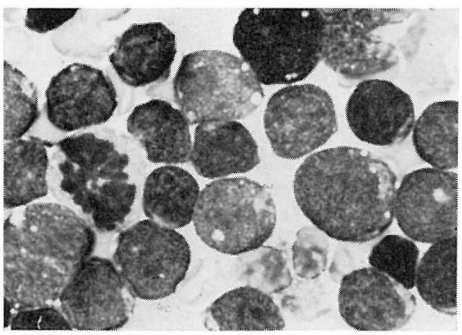


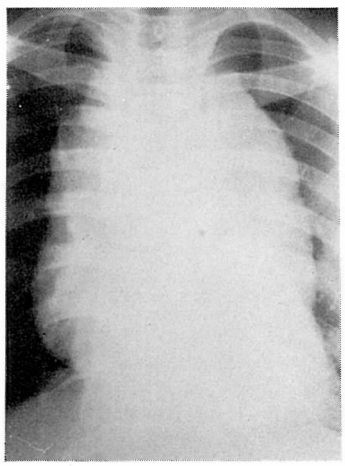
Fig. 2. The marrow smear reveals atypical cells which have large nucleus. Note numerous vacuoles in the cytoplasm.

On physical examination, he was well nourished, young man. Petechiae were scattered over the chest wall. Enlarged lymph nodes were palpable at the axillary and inguinal region on both sides. These lymph nodes, however, were smaller than the size of pea. The temperature was 37.0°C, the pulse was regular and 75 in frequency. The blood pressure was 150 systolic and 82 diastolic. The liver was smooth and palpable three finger-breadths below the right lower rib margin. Splenomegaly was also present and was palpated two finger-breadths. Facial palsy of the peripheral type was revealed on the left side.

Examination of the peripheral blood revealed 403×10^4 red blood cells and 53,200 white blood cells, with a differential count of 67 % atypical cells, 13 % neutrophils, 0.5 % eosinophils, 16.5 % lymphocytes and 1.5 % monocytes. The thrombocytes were extreamely reduced in number, being one per oil immersion field. The atypical cells were almost round in shape and had scanty basophilic cytoplasm with occasional small vacuoles (Fig. 1). The nucleus was almost round but occasionally indented with soft chromatin texture. One nucleolus was frequently found. Peroxidase stain for these atypical cells was negative. From these findings, acute lymphatic leukemia was suspected. Hemorrhagic study disclosed increased capillary fragility and poor clot retraction.

Examination of the sternal bone marrow disclosed the following: 89 % stem cells, 0.2 % nonsegmented neutrophils, 0.6 % segmented neutrophils, 9.4 % lymphocytes, 0.2 % rubricytes and 0.6% metarubricytes. WBC : nucleated RBC ratio was 124 : 1. The megakaryocytes were rarely found. The stem cells were a little larger than the atypical cells found in the peripheral blood, and had soft chromatin texture with one nucleolus and scanty basophilic cytoplasm (Fig. 2). Mitotic figures were frequently encountered.

Blood chemistry revealed slight depletion in nutritional condition, latent jaundice and azotemia (NPN. 59.0 mg/dl, urea N. 47.5 mg/dl.).



Examination of the urine revealed two plus albuminuria. The sediment contained a few white cells per high power field and numerous citrate crystals.

The electrocardiogram showed low Q waves in Leads I, aVL, V4 - V6. ST segments were also sagged in Leads I, aVL and V2 - V6.

Fig. 3. A chest film taken at the time of admission reveals a mediastinal tumor.

Rentogenographic examination of the upper gastro-intestinal tract was normal. A chest film disclosed large mediastinal tumor as shown in Figure 3.

On the 4th hospital day, the patient vomitted bloody fluid and suddenly became unconscious and expired.

Pathologic Findings

Gross Anatomical Findings. — An autopsy was performed three hours after the death. The body was that of a well nourished young man, measuring about 175 cm. in length. Petechial hemorrage was scattered on the chest wall and left axillary region. Superficial lymph nodes were not palpable.

The anterior mediastinum was filled with a large tumor mass measuring 20 × 17 × 10 cm. in size and 950 gms. in weight. The tumor mass was rather flat in shape and closely adherent to the anterior surface of the pericardial sac (Fig. 4,5). It was mostly encapsulated with thin fibroconnective tissue with scattered areas of petechial hemorrhage. Cut surface of the mass was grayish white and partially lobulated.

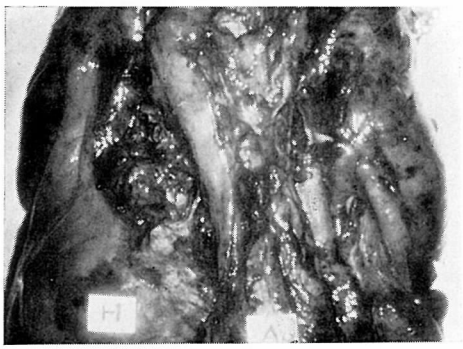


Fig. 4. A tumor mass in the anterior mediastinum is encapsulated with thin fibrous tissue and petechial hemorrhage is visible on the surface. H : heart, Ao : aorta.

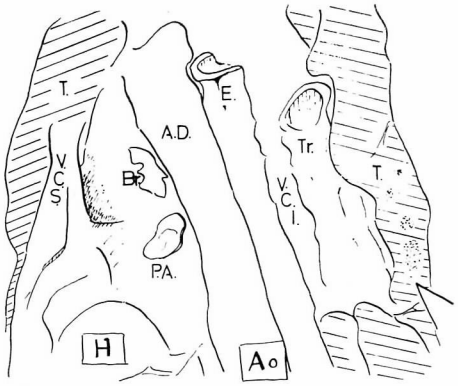


Fig. 5. Schematic figure of Fig. 4. T : Tumor, A.D. : Aorta descendens, V.C.S. : Vena cava superior, P.A. : Aorta pulmonalis, E. : Esophagus, Tr. : Trachea, V.CI. : Vena cava inferior, Br. : Bronchus.

Petechiae were scattered on the internal surface of the pericardial sac, which contained a little bloody fluid. The lymph nodes around the aortic arch were slightly enlarged and cut surface of them was grayish white with occasional hemorrhagic foci.

The heart was 425 gms. in weight and the epicardium showed numerous petechial hemorrhagic foci. On the posterior surface of the left ventricle hemorrhagic area measuring 3 × 10 mm. in size was observed and section of this area revealed grayish white lesion in the myocardium, which suggested metastatic focus of the tumor cells. The left ventricle was moderately dilated

and its wall was measured up to 2 cm. in thickness. All valves revealed no gross abnormalities.

The lungs were normal in shape and size but petechae were scattered over the pleural surface. Section through the lungs disclosed no abnormalities. The hilar lymph nodes were not enlarged.

In the abdominal cavity, neither fluid nor adhesion was noted. There were numerous spotted areas of hemorrhage on the serosal surface of the mesenterium and intestine. Lymphadenopathy was not found.

The spleen was markedly enlarged measuring $17 \times 11 \times 5$ cm. in size and 520 gms. in weight, and the consistency was slightly soft. On section, the parenchyma was brick red in color and the lymph follicles were hardly visible.

The liver was also enlarged and weighed 2500 gms. Section through the liver revealed normal architecture except for moderate congestion at the central area of the lobule.

Grossly, both kidneys looked approximately the same. They were remarkably enlarged weighing 412 gms. on the left and 406 gms. on the right. The capsule was striped with slight difficulty and the surface was slightly lobulated with scattered foci of petechial hemorrhage. The consistency was moderately soft. Section through the kidneys disclosed pale whitish gray parencyma, and the cortico-medullary junction could not be easily distinguished. On both kidney pelvis, spotted area of mucosal hemorrhage was observed.

Both adrenals were normal in size and no gross abnormalities were noted on section. The pancreas was normal in size and shape and lobular architecture was well preserved. The digestive tract revealed no gross abnormalities except for numerous petechiae over the gastric mucosa. The pelvic organs revealed no significant changes. The bone marrow of the ribs was markedly cellular. The hypophysis was slightly enlarged. The brain showed no gross abnormalities except for localized subarachnoid hemorrhage on the left temporal region. On section, no hemorrhagic lesions were found.

Microscopic Findings. — Histologically, mediastinal tumor showed monotonous appearance and was composed of cells with morphological characteristics similar to the lymphocyte series. Most tumor cells were round in shape and had scanty cytoplasm and hyperchromatic nuclei. The nucleolus was scarecely visible and karyorrhexis was remarkable (Fig. 6). The nuclei were almost round or oval but occasionally indented. Among these compactly arranged, neoplastic cells, large reticulum cells with abundant foamy cytoplasm were scatteringly observed. Such reticular cells revealed increased phagocytic activities and the cytoplasm contained nuclear fragments and hemosiderin-like particles (Fig. 7). The fibrous tissue was sparse and the reticulum fibers were poorly developed and showed no intimate relation with the tumor cells. Characteristic finding of this tumor was the presence of abortive Hassal's bodies, many of which appeared as hyalinized

or calcified foci (Fig. 6, 8). Though cellular elements were hardly visible, concentric lamellar arrangement of calcified and hyalinized materials strongly suggested that such foci were abortive or degenerated Hassal's bodies characteristic to the thymus.

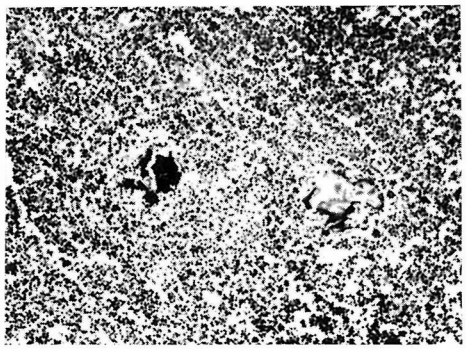


Fig. 6. Mediastinal tumor is consisted of lymphoid cells. Two calcified Hassal's bodies are visible. H.E. × 100

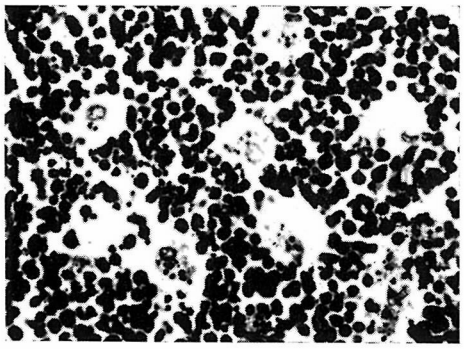


Fig. 7. High magnification of tumor cells with hyperchromatic nuclei. Reticulum cells contain nuclear fragments in the cytoplasm. H.E. ×400

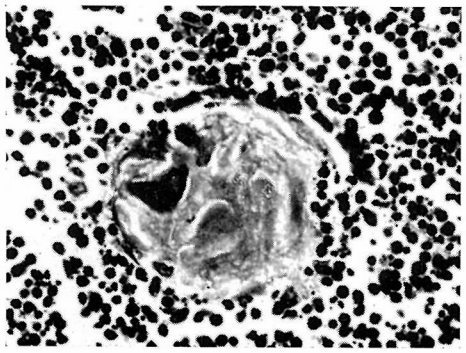


Fig. 8. Abortive Hassal's body in the mediastinal tumor. H.E. ×400

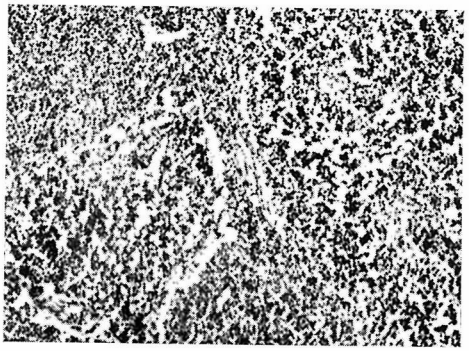


Fig. 9. The lymph node arround the aortic arch is diffusely infiltrated with leukemic cells. H.E. × 100

The lymph nodes were diffusely infiltrated by leukemic cells with loss of germinal center (Fig. 9). But distinction between the medullary cords and the sinus was discernible. The capsules were also infiltrated by the tumor cells with further invasion to the surrounding adipose tissue.

Grayish white lesion grossly observed in the left ventricular wall was markedly infiltrated with leukemic cells (Fig. 10). In the other area the myocardium and the epicardial fatty tissue were also infiltrated.

The spleen was moderately congestive, and both red and white pulps were severely infiltrated with the tumor cells. The lymphatic follicles were atrophic

and had indistinct outlines (Fig. 11). The macrophages were enlarged and showed increased phagocytic activity containing hemosiderin particles in the foamy cytoplasm.

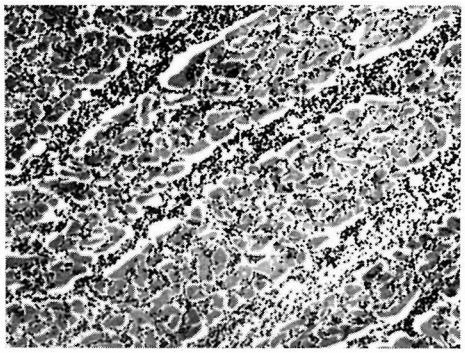


Fig. 10. Marked leukemic infiltration in the myocardium. H.E. × 100

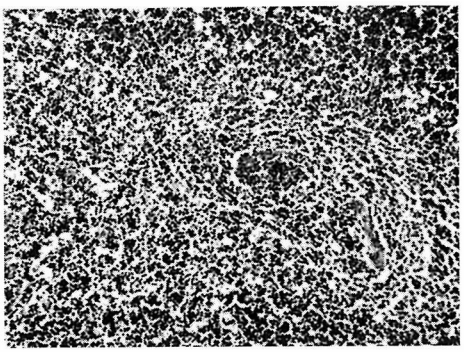


Fig. 11. The sinus of the spleen is filled with leukemic cells and lymph follicle is atrophic. H.E. × 100

In the liver, both the sinusoid and Glisson's capsule were moderately infiltrated with leukemic cells (Fig. 12, 13). Degenerative changes of the liver parenchyma was not prominent. Extramedullary hematopoiesis was not noted.

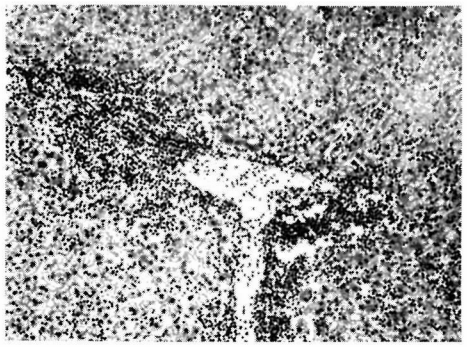


Fig. 12. Both the sinusoid and Glisson's capsule are markedly infiltrated. H.E. × 100

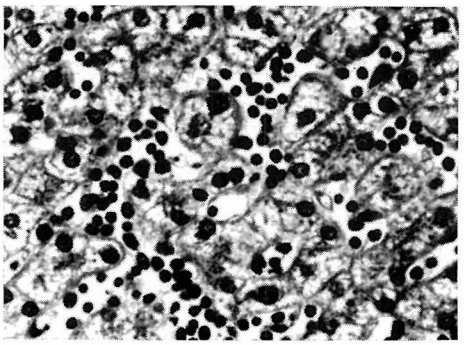


Fig. 13. High magnification of leukemic cells infiltrated in the sinusoid of the liver. H.E. × 400

The kidneys were also severely infiltrated with marked destruction of the parenchyma. Accumulation of leukemic cells was more prominent in the cortex than in the medulla (Fig. 14). Most glomeruli were intact except for slight thickening of the basement membrane of the glomerular tufts.

The bone marrow of the ribs was highly cellular and was markedly infiltrated by the immature-appearing cells of lyphocytes series. Megakaryocytes were hardly recognized (Fig. 15).

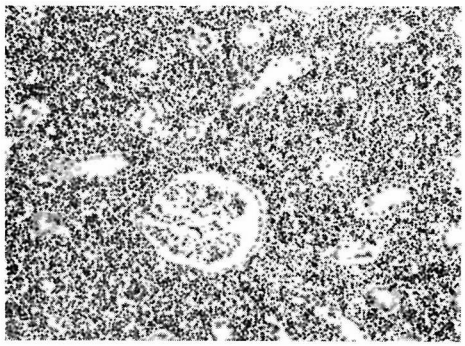


Fig. 14. Leukemic infiltration in the kidney with destruction of the parenchyma. H.E. × 100

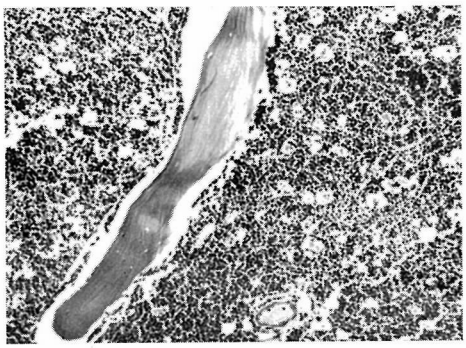


Fig. 15. Bone marrow of the rib is highly cellular and macrophages are scatteringly seen. H.E. × 100

The sinusoids of the hypophysis were obliterated with leukemic cells and the gland cells showed destructive changes.

In the central nervous system, the leptomeninges was slightly infiltrated and all the cranial nerves were markedly infiltrated with lymphoid cells (Fig. 16). Near the ventricular wall, infiltration of leukemic cells around the small blood vessels was prominent (Fig. 17).

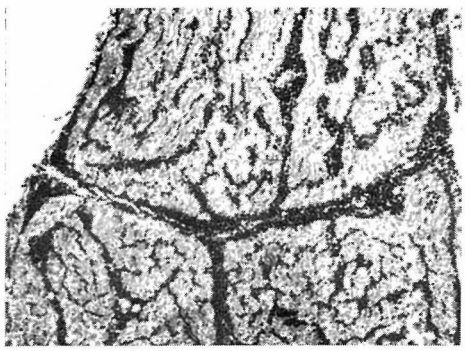


Fig. 16. The facial nerve on the left side is remarkably infiltrated by leukemic cells. H.E. × 100

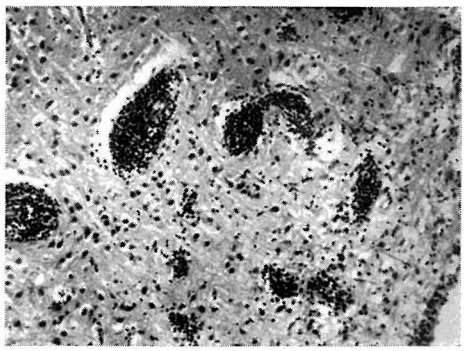


Fig. 17. Perivascular infiltration of the leukemic cells in the brain. × 100

Leukemic infiltration was also observed in the thyroid gland, gastro-intestinal wall, urinary bladder, testis, prostate and skin.

From above mentioned findings, leukemic lymphosarcoma with generalized infiltration to the various organs was made. The primary involvement of the neoplasm was presumed to be the thymus. The direct cause of the death was heart failure due to severe infiltration of leukemic cells in the myocardium.

COMMENT

The view that leukemia is devided into two main groups, myeloid leukemia and lymphatic one, has been widely accepted. This classification implicates not only the morphological characteristics of leukemic cells but also the primary site where the neoplastic cells proliferate. So, in case of myeloid leukemia the primary neoplastic proliferation do take place in the bone marrow and not in the other organs. In lymphatic leukemia,on the other hand, neoplastic cells are primarily produced not only in the lymph nodes or lymphoid tissues but also probably in the bone marrow. Since lymphatic neoplasm is generally considered to arise multicentrically, it is hardly possible to ascertain which group of nodes or lymphoid tissue are primarily affected.

Formation of tumor mass is occasionally encountered in both myeloid and lymphatic leukemias and such cases have been designated tumoriferous leukemia or leukemia with tumor formation. When leukemia is myeloid variant and tumor mass is entirely composed of myelogenous cells, it is clear that the tumor is formed by accumulation or colonization of leukemic cells, and in addition it is not the primary site of neoplastic proliferation. Though there may be some problems as to the relationship between lymphatic leukemia and lymphosarcoma, both two entities are only different manifestation of lymphoid tissue neoplasia as have been mentioned by Evans[1]. A leukemic blood picture frequently occurs in malignant lymphomas and the patterns of visceral involvement and infiltration are identical with those observed in leukemia. In this case, the neoplastic cells in the main tumor located in the mediastinum and those observed in the infiltrated organs or tissues were morphologically identical, and in addition tumor formation and leukemic blood picture coexisted at the time of admission. So it may be impossible to decide which feature was primary occurence. However, rapid clinical course, presence of large tumor mass in the anterior mediastinum and lack of lymphoadenopathy suggest that a leukemic blood picture is a late accompaniment of lymphosarcoma.

Infrequently lymphosarcoma arises in such extranodal sites as the pharynx, gastro-intestinal tract, lung, thymus, salivary glands and others[1]. The authors presume that a large tumor mass observed in this case primarily arised in the thymus. Presence of abortive Hassal's bodies scatteringly found in most preparations taken from the various portions of the mass and numerous foam cells which are morphologically identical with the epithelial reticular cell[2] would be histological evidences of our presumption.

Since Ceelen and Rabinowitsch[3] first applied the term "thymic lympatic leukemia" to such cases in which mediastinal tumor with accompany of lymphatic leukemia was disclosed both clinically and pathologically, similar cases have been

infrequently reported. In 1960, Suzuki[4] reported 11 cases of tumoriferous leukemia (10 cases of myelogenous type and one case of lymphatic type) in which the tumors were always found in the locality with the thymus as the center. Comparing 11 other cases of leukemia without macroscopic tumor formation at the thymic region, he concluded that the tumors at the thymic region were not the primary loci of occurence of leukemia but were formed by colonization of tumor cells primarily originated in the bone marrow or the lymphoid tissues. He also pointed out organ-specificity of the thymus to be easily affected by leukemic infiltration. Tsuboi[5], on the other hand, reported four cases of acute lymphatic leukemia with tumor formation at the thymic region and he affirmed lymphatic leukemia primarily arised in the thymus. Considering histogenesis of such neoplastic condition, he applied the term "thymoma with blastcytemia". Since the lymphocytes of the thymus are morphologically identical with those in the lymph nodes and other lymphoid tissues, it may be impossible to determine if the neoplastic lymphocytes have originated from the thymus or from the other lymphoid tissues. Exact nature and histogenesis of "thymic lymphatic leukemia" still remain to be determined.

SUMMARY

An autopsy case of leukemic lymphosarcoma with large tumor mass in the anterior mediastinum has been reported. Histological characteristics of the mediastinal tumor, and gross and microscopic findings of the lymph nodes, bone marrow and the other organs are highly suggestive of the view that the thymus is the primary locus of occurence of leukemia.

REFERENCES

1) R.W. Evans: *Histological Appearances of Tumours.* (2nd ed.) p. 242, 1966. (Livingstone LTD.)
2) W. Bloom and D.W. Faucett: *A Textbook of Histology.* (8th ed.) p. 318, 1962. (Saunders Co.)
3) W. Ceelen and L. Rabinowitsch: Über Lymphogranulomatose und ihre Beziehung zur Tuberkulose. *Z. Tbk.*, **27**: 175, 1917.
4) M. Suzuki: Tumoriferous Leukemia with Emphasis on the Histogenesis of Tumors at the Thymic Region. *Transactiones Societatis Pathologicae Japonicae*, **49**: 882, 1960. (Japanese with English abstract)
5) K. Tsuboi: Pathologisch-Histologische Untersuchung über die Leukaemie im Kindesalter. *Transcationes Societatis Pathologicae Japonicae*, **49**: 370, 1960. (Japanese with German abstract)