Pathological Studies on Lymphosarcoma in Swine

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Abstract. Pathological investigation was carried out on 10 cases of lymphosarcoma in swine. Cytologically, neoplastic cells in these cases presented essentially the same morphological characteristics as lymphocytes. Neoplastic lesions were recognizable predominantly in lymph nodes, liver, spleen, kidney and urinary bladder, and additionally in many other organs macroscopically or histologically. They were remarkable in tonsil, genital organs, bone marrow, nervous tissue, pancreas, adrenal, hypophysis, tongue, submaxillary gland and gallbladder. Their histogenesis was suggested to consist in the accumulation of neoplastic cells throughout perivascular areas, judging from the character of these cells.

Lymphosarcoma, synonymous to lymphocytoma or lymphoblastoma, in swine has been termed from the cytological characteristics of cells composing the respective neoplasm or from the anatomical situation of the respective neoplastic lesion [1, 2, 4, 5, 7–12, 15–19, 21–23]. The occurrence of the neoplasm was more frequent than any other neoplasm in swine leukemia originated from lymphatic and hematopoietic tissues [1, 2, 4–12, 15–19, 21–23]. Neoplastic lesions have frequently been recognized in liver, spleen and kidney in addition to lymph nodes [1, 2, 4, 5, 7, 9, 22]. On the other hand, the neoplasms of lymphoreticular tissues have been summarized under the general term, lymphosarcoma [3, 13, 14, 20] or malignant lymphoma [3], in several reports.

The present authors conducted cytological and histological investigations on 10 cases of lymphosarcoma to gain more detailed findings on the distribution of lesions and to discuss the histogenesis of the neoplasm.

Materials and Methods

The ten cases examined were obtained from the routine meat inspection in the Morioka municipal and Shiga and Kitakami country abattoirs over a period from July, 1965, to June, 1975. One (Case No. 3) of them had already been studied ultrastructurally in the previous paper [11]. Histological samples were collected from various parts of the whole body in each case after macroscopic observation, and fixed in 10% formalin solution. Paraffin sections were made from them and stained with hematoxylin and eosin and by Groenier's silver impregnation. For cytological examination, fresh tumor imprints were made from various lesions in each case. They were air-dried and stained with May-Giemsa solution.

Results

I. Macroscopic findings

Liver: Nodular lesions of various size were noted in the hepatic parenchyma. Some of them were projected from the parenchymal surface. The nodules were whitish and soft. They were spherical and well circumscribed with the parenchyma.
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Remarks:
- C: Castrated male, M: Splenomegaly.
- *: Positive for neoplastic lesion.

on the cut surface. Occasionally, the neoplastic tissues revealed the honeycomb-like appearance, together with the normal hepatic tissue.

Spleen: The splenic capsule was tight in the case of splenomegaly. The parenchyma was dark reddish in color and soft to the touch on the cut surface. Neither trabeculae nor follicles were obvious. On the other hand, neoplastic nodules of various size were distributed in the subcapsular region in some cases. Parenchymal atrophy was noted in the peripheral region on nodules in these cases.

Lung: The left apical lobe was replaced by whitish neoplastic tissue in one case. A neoplastic nodule of thumb-tip in size was present in the ventral margin of the apical lobe in another case revealing the infarct-like appearance. Two neoplastic nodules of pigeon-egg in size were also recognized in the subpleural tissue of the costal pleura of this case.

Heart: Cardiac muscle in the subendocardial area of the right ventricle and auricle was dispersedly whitish or faded to pale pink in color on the cut surface. The pericardium was thickened and displaced by neoplastic tissue.

Kidney: Neoplastic lesions were distributed on the parenchymal surface. On the cut surface, they were nodular in shape and soft in consistence.

Urinary bladder: The mucous mem-
brane was elevated to form foci, which were reddish or dark reddish in color and red bean to soybean in size. Beneath these foci whitish nodular neoplasms were noted. On the other hand, neoplastic nodules of soybean to pigeon-egg in size were dispersed in the subserous tissue of the organ.

Genital organs: In the one case the left ovary was swollen to baby's fist in size to contain soft and whitish sarcomatous tissue. In this case the uterus was also thickened and neoplastic in its submucosa. Neoplastic tissue was noted among Graafian follicles and corpora lutea on the cut surface in two cases. Neoplastic foci of poppy-seed size were distributed dispersedly on the tunica vaginale of the plexus pampiniformis.

Digestive canal: Thickened sarcomatous tissue was noted in the submucosa of the stomach, circumscribing the gastric mucosa. Neoplastic nodules from soybean to baby's head in size were distributed dispersedly in the subserous tissue of the small and large intestine. Some lesions were occasionally protruded into the intestinal lumen. The intestinal mucosa was ulcerous in these areas.

Lymph nodes: Most of the lymph nodes attached to organs affected with neoplastic lesions were swollen to various size. They were soft to the touch, whitish in color and structureless on the cut surface. Occasionally, petechiae were noted on the surface.

Other organs: The tonsil was thickened, from which follicles disappeared. The mesentery increased in thickness on the cut surface. Sarcomatous nodules were recognized dispersedly. Neoplastic nodules of pigeon-egg size were present in the subserosa of the diaphragm. Neoplastic growth was found in the bone marrow. Sarcomatous tissue was noted in the tentorium cerebelli and cavum epidurale spinalis of the sacral spine.

2. Cytological findings

In the imprints of sarcomatous lesions in eight cases, neoplastic cells were round in shape, ranging from 11 to 14 \( \mu \text{m} \) in diameter. The nucleus was round or occasionally horseshoe in shape, and 10 \( \mu \text{m} \) in diameter. It was rich in chromatin and contained 2 to 4 nucleoli. The narrow cytoplasm circumscribing the nucleus was generally pale basophilic and occasionally basophilic, containing vacuoles (Fig. 1). Neoplastic cells in one case were polymorphous shape. Of them the smaller ones were 8 to 10 \( \mu \text{m} \) in diameter, possessing dense chromatin and a nucleus 7 to 9 \( \mu \text{m} \) in diameter, containing 3 or 4 nucleoli. The larger ones were mingled with the smaller ones. They were basophilic and ranged from 14 to 17 \( \mu \text{m} \) in diameter. Their nucleus was 10 to 15 \( \mu \text{m} \) in diameter and contained a coarse chromatin net and 2 or 3 nucleoli.

In sections, neoplastic cells were homogeneous in shape, possessing dense chromatin and a round nucleus about 7 \( \mu \text{m} \) in diameter. On the other hand, cells in compact areas formed by a large amount of collagenous fibers contained a nucleus polymorphous in shape. Their cytoplasm had an obscure outline. Mitosis was noted occasionally. Plasma cells, eosinophils and fibroblasts were present together with neoplastic cells in some areas. In the neoplastic tissue stained by silver impregnation, coarse argyrophil fibers were distributed among neoplastic cells. They revealed, however, no close association with the cells (Fig. 2).

3. Histological findings

Liver: The interlobular tissue of the liver was enlarged with severe infiltration of neoplastic cells. Atrophy and destruction of hepatic lobules were also seen. Neoplastic cells were occasionally noted in
sinusoids in some cases (Fig. 3).

Spleen: Nodular accumulations of neoplastic cells were present between the serous membrane and splenic capsule in two cases. Atrophy of the parenchyma caused by an oppressive growth of the nodules was recognized in some areas. In some cases revealing splenomegaly, neoplastic cells were distributed in the splenic sinus. Megakaryocyte-like giant cells were also seen (Fig. 4). Accumulations of neoplastic cells were frequently present in the perivascular tissue of small arteries in the trabecula (Fig. 5).

Lung: Neoplastic cells accumulated in alveolar septa. Focal infiltration of neoplastic cells was noted in the peribronchiolar tissue. Destruction of the parenchymal structure was frequently seen (Fig. 6).

Heart: Accumulations of neoplastic cells were noted in the subendocardial tissue of the right ventricle and auricle. Atrophy and vacuolation of Purkinje nerve fibers were noted in these areas. Neoplastic cells invaded the intermuscular tissue, in which the fragmentation and partial disappearance of muscle fibers were frequently observed. Focal accumulations of neoplastic cells were also recognized in one case without macroscopic lesions.

Kidney: Neoplastic cells accumulated in perivascular tissue in the renal interstice. In this lesion, Bowman’s capsule and renal tubules degenerated (Fig. 7).

Urinary bladder: Focal accumulations of neoplastic cells were noted in the tunica propria of the organ. Nodular accumulations of the cells were also noted in the subserous tissue. The cells frequently invaded the muscular layer, in which fragmentation of muscle fibers were noted.

Genital organs: In the ovary, neoplastic cells were predominant in the stroma. They accumulated so severely that the proper structure of the ovary was destroyed in one case with a residual Graafian follicle. They accumulated also in the tunica propria of the uterus in this case. On the other hand, focal accumulations of neoplastic cells were attached dispersedly to the tunica vaginalis of the plexus pampiniformis.

Digestive canal: In a few cases with no macroscopic lesions, neoplastic cells were accumulated in the tunica propria and around glandular acini of the esophagus. They showed a massive infiltration in the submucosa of the stomach in one case. They invaded the muscular layer of the stomach in the case, causing fragmentation of muscle fibers. These changes were seen in two cases without macroscopic lesions. On the other hand, the tunica propria of the small and large intestine in two cases was thickened with massive accumulations of neoplastic cells. In this lesion, the intestinal mucosa was eroded away. The tunica muscularis mucosae was also destroyed. Neoplastic cells invaded the subserous tissue in the cases. They were also recognized in the tunica propria of the small intestine in 2 cases and in the mucosa of the large intestine in one case lacking macroscopic lesions.

Lymph node: Nodes invaded severely by neoplastic cells lost their proper structure (Fig. 8). In them, the central region degenerated and karyorrhexis and pyknosis were noted. Some nodes were residual in structure. Moreover, hypertrophic follicles and accumulations of neoplastic cells in both sinus and medullary cord were observed in numerous lymph nodes.

Other organs: Lymphatic tissue of the tonsil was thickened due to severe accumulations of neoplastic cells in the submucosa, in which atrophy and destruction of follicles and fossulae were found (Fig. 9). Nodular accumulations of neoplastic cells
were noted in the mesentery and the subperitoneal tissue of the diaphragm. Bone marrow was replaced with fat tissue. The interstice of fat cells was filled with accumulations of neoplastic cells and a few megakaryocytes (Fig. 10). Neoplastic cells did not invade the central nervous system, but accumulated in the tentorium cerebelli, cavum epidurale spinale, and endoneurium of the lumbar nerve (Fig. 11). Focal accumulations of neoplastic cells were also in the pancreatic interstice, perivascular tissues of the venous sinus of the adrenal medulla (Fig. 12), and the frontal lobe of the hypophysis. Moreover, these cells were distributed in intermuscular tissues of the tongue, interstice of the submaxillary gland, peripheral tissue of the aortic adventitia (Fig. 13), and submucosa of the gallbladder in several cases.

**Discussion**

The present cases were diagnosed as lymphosarcoma, which was composed of neoplastic cells similar to lymphocytes when examined cytologically and histologically in detail. It is well known from a macroscopical survey that neoplastic lesions are quite frequently noted in liver, spleen and kidney, in addition to lymph nodes [1, 2, 4, 5, 7, 9, 22]. Neoplastic lesions, however, were also recognized in the urinary bladder in most of the present cases. Moreover, it should be noted that macroscopical lesions occurred in tonsil, genital organs, bone marrow and nervous tissues, and histological changes in adrenal, hypophysis, tongue, submaxillary gland and gallbladder.

Histologically, the liver is one of the organs quite frequently affected with neoplastic cells [5]. These cells revealed a tendency to accumulate in interlobular tissues of the organ [5, 9, 10, 19]. Their accumulation also focused on the periportal area in the present cases. It has been accepted in the spleen that neoplastic cells accumulate to form nodules in subserous tissue [1, 23] or are present diffusely in the splenic sinus [5, 9, 21, 22]. Moreover, megakaryocyte-like giant cells similar to Langhans' or Sternberg's giant cells have been observed in the splenic sinus [5]. In the present cases, two types of neoplastic changes were noted. In one type, neoplastic nodules were formed in subserous tissue. In the other type, splenomegaly was shown and the splenic sinus contained a large number of neoplastic cells and megakaryocyte-like giant cells. It was impossible, however, to find any severe infectious lesion associated with the origin of such giant cells in the present cases. These cells have been presumed to have their origin in an extramedullary hematopoietic focus produced in infectious diseases [5].

As for the route of invasion of accumulating neoplastic cells, an investigator asserted that these cells might invade the periportal area in the liver [5]. In the present investigation, an accumulation of neoplastic cells was noted in the perivascular tissue of arteries in splenic trabeculae, in addition to the periportal area in the liver. It also showed a tendency to occur in perivascular areas, especially in the periadventitial areas of the aortae. Further, arteries were frequently found in the central area of a focus of accumulation of neoplastic cells. These findings suggested that neoplastic cells might tend to accumulate in perivascular areas. The lymphatic tissues, including lymph nodes and tonsils have such histological characteristics that it is reasonable to assume that they may be ready to be neoplastic. The remarkable accumulation of neoplastic cells in the subserous tissue of visceral organs must be closely as-
associated with the structure of the tissue rich in blood and lymph vessels.

Acknowledgments: The authors wish to express their gratitude to Professor Sadao Miura, of the Faculty of Agriculture, Iwate University, for valuable advice to their studies.

References

Explanation of Figures

Fig. 1. Fresh tumor imprints from neoplastic tissues. May-Giemsa staining, ×780.
Fig. 2. Argyrophil fibers in neoplastic tissue. Gomori’s silver impregnation, ×170.
Fig. 3. Infiltration of neoplastic cells in interlobular tissue of liver. Hematoxylin and eosin staining (HE), ×70.
Fig. 4. Megakaryocyte-like giant cells in splenic sinus. HE, ×170.
Fig. 5. Accumulation of neoplastic cells in perivascular area of artery in splenic trabecula. HE, ×170.
Fig. 6. Accumulations of neoplastic cells in alveolar septa in lung. HE, ×170.
Fig. 7. Infiltration of neoplastic cells in renal interstice. HE, ×170.
Fig. 8. Neoplastic cells in bronchial lymph node. HE, ×340.
Fig. 9. Neoplastic lesion in tonsil. HE, ×70.
Fig. 10. Neoplastic cells in bone marrow. HE, ×340.
Fig. 11. Accumulations of neoplastic cells in cavum epidurale spinale of lumbar spine. HE, ×70.
Fig. 12. Infiltration of neoplastic cells in adrenal. HE, ×170.
Fig. 13. Accumulation of neoplastic cells in aortic adventitia. HE, ×170.