MAST-CELL LEUKOSIS IN CATS—A REPORT OF TWO CASES

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Mast-cell leukemia is characterized by splenomegaly in which basophilic granular cells show a marked neoplastic increase in the spleen. Vomiting is known as a significant clinical symptom of the disease. The occurrences of the disease have been reported by several investigators, most of whom have dealt with the cases as those of "leukemia". It is obscure, however, whether the animals involved really possessed characteristics of blood neoplasms. On the other hand, those workers have dealt with the neoplastic cells as mast cells or basophil myelocytes indiscriminately. In the present situation, such confusion seems not so unreasonable, in view of the obscurity regarding the histogenesis of these cells.

According to HOLZWORTH, the report made by ANTONIE in 1907 on a feline case with an enlarged spleen showing histologically great masses of mast cells, seems to be the first of its kind. Since then publications on the disease have been made by LILLIE, MONLUX, STÜNZI, MEIER and GOURLEY, HEAD, LABIE and FONTAINE, SEAWRIGHT and GRONO, and LUCKE. Recently, the authors also encountered two cases of the disease and had a chance to conduct pathological studies on them.

CASE REPORT

Case 1

E786, a sixteen-year-old female cat, kept in Morioka City. The patient was examined by a veterinarian on September 13, 1961. About a week prior to the examination, the distended and fluctuated abdomen, as well as inappetence, was recognized by the owner. On the day of examination, an abdominal paracentesis yielded about 140cc of turbid, greyish-yellow fluid in the morning and the patient died in the afternoon.

Autopsy findings

The palpebral conjunctivae were pale. The abdomen was distended. The subcutaneous tissue was edematous and predominantly dirty yellowish-brown in color. The abdominal cavity was filled with cloudy yellowish fluid. The peritoneum, omentum, and mesenterium were congested and dirty brown in color. The left kidney was capsulated with a thick fibrous membrane, to the inner surface of which adhered a fibrinous substance. It contained yellowish fluid turbid with pus.

The liver was enlarged, weighing 210g and measuring 13 by 13 by 3cm. A dark-red nodule of sparrow-egg size was present on the ventral surface of the center portion of the caudal lobe. No significant changes were noted on any cut surface of the organ, which presented an indistinct lobular structure.

The spleen was enormously enlarged, weighing 45g and measuring 21.5 by 4.5 by 2.0cm. It was soft in consistency, with rounded borders. The cut surface was swollen. The parenchyma was pale brick-red and scraped off easily. The trabecules and follicles were indistinct.

In the brain, a soybean-sized tumor was recognized in the third cerebral ventricle,

attached to the meninges in the longitudinal fissure.

Histological findings

Liver: The sinusoid was markedly dilated and contained numerous cells which had a round nucleus and reddish broad protoplasm. The protoplasm had not always a distinct demarcation. It contained large or small vacuoles in many cells. Pictures of nuclear division were occasionally seen (Fig. 1). The protoplasm was filled with numerous fine granules stained bluish-violet by Giemsa stain (Fig. 3). These granules were stained reddish-violet with cresyl violet, showing metachromasia. One-third of these cells had oxidase-positive granules in the protoplasm. No proliferative picture of argyrophil fibers was recognized. On the other hand, transformation of the endothelial portions into collagenous fibers was distinct (Fig. 2). Dissociation was evident in the hepatic cell cords, the cell of which had become atrophic. Fibrosis and accumulation of numerous tumor cells were shown in the periportal areas. In the dark-reddish nodule of the caudal lobe, the sinusoid was markedly dilated and congested. The tumor cells were collected in and around the lymphatic space.

Spleen: The tumor cells increased diffusely and filled up the pulp. Especially they tended to accumulate densely in the marginal portions located in the vicinity of the capsule (Fig. 8). Cell infiltration was occasionally observed also in the trabeculae. The follicles were rather small and recognized as small foci consisting of small round cells. No increase was noted in argyrophil fibers, which were rather torn in pieces by the increased tumor cells (Fig. 7).

Mesenteric lymph nodes. Numerous mast cells were accumulated in the medullary sinuses (Fig. 11).

Serous membrane of the intestine: Accumulations of tumor cells were recognized in some portions of the serous membrane, which was thickened to some extent (Fig. 10).

Other organs: Nephrotic changes were noted in the right kidney and suppurative interstitial nephritis was in the left kidney. There was also fibrinous suppurative peritonitis. Carnification was recognized in some portions of the lungs. Neoplastic mast cells showed no increase in the other tissues of the whole body. A tumor in the third cerebral ventricle was diagnosed histologically as endotheliomatous meningioma (Fig. 12).

Case 2

Pr. 438, a twelve-year-old female cat, kept in Morioka City. She seemed to have some ill feeling for ten days. On September 2, 1963, she was examined by a veterinarian. Her body temperature was 37.5°C and pulse rate 175. Remarkable anemia, difficulty in walking, and splenomegaly were recognized. She received heart drugs, but died the next morning.

Autopsy findings

Anemia was recognized on the visible mucous membranes. Subcutaneous fatty tissue was retrogressive. Capillaries in subcutaneous tissues were anemic. Abdominal fluid was yellowish but clear and increased in quantity.

The liver was enlarged, weighing 170g and measuring 15 by 12 by 2cm. It was icteric in appearance. On its section, slight granular swelling in accordance with the acinal figure was seen.

The spleen was markedly enlarged, weighing 175g and measuring 22 by 6 by 2cm (Fig. 5). Its posterior end reached the abdominal median line, covering the surface of the gut. It was elastic and hard in consistency. Its border was rounded. On its section, its parenchyma was swollen and pale brick-red in color and could be scraped easily. The trabeculae and follicles were barely seen.

Atelectatic lesions were found in the lungs. No obvious changes were recognized macroscopically in the other organs and tissues.

Histological findings

Liver: The sinusoid was dilated. Central disorder was distinct in the lobules. In these portions, numerous cells were noted to have the same characteristics as observed in Case 1. There was a tendency that the tumor cells showed more marked vacuolization and karyopyknosis and more irregular protoplasmic borders than those in Case 1 (Fig. 4). Oxidase-reaction-positive cells were less in this case than in Case 1. Argyrophil fibers appeared as in Case 1, but collagenous fibers increased in the central portions of the lobules. Hemosiderin granules were scattered diffusely.

Spleen: The tumor cells increased diffusely in the pulp. On the other hand, they gathered here and there, forming dense cell foci. Degenerative changes of the cells were noted in some of these foci and other portions. The cells showed karyopyknosis or contained scattering protoplasmic granules. There was hemosiderosis. The follicles were rather atrophic (Figs. 6 and 7).

Lungs: There was edema. The alveolar wall was thickened as a result of the increase of tumor cells which formed no cell foci (Fig. 9). There was epithelization in some parts of the alveolar walls. Infarct picture was also seen.

Other organs: The kidneys and the heart were edematous. Senile atrophy was noted in nerve cells of the end-brain. The other organs and tissues of the whole body showed no obvious changes.

DISCUSSION

Prior to general discussion, the authors wish to explain the title of this report. The disease in question has been treated as "leukemia" by most of the previous workers. It is considered, however, that the disease might not be regarded as leukemia in a strict sense of the word, all cases of such disease have not manifested the characteristics of blood neoplasm.

It is a well-known fact that mast-cell tumor originated from the skin of dogs is very common^{2,10}. WEISS regarded his canine case as one of "leukosis", in which mast cells proliferated in the skin and the lymph nodes. Recently, a canine case of mast-cytoma was reported in Japan¹⁴, in which tumors were in the udders, bone marrow, liver, spleen, and lymph nodes. It is considered that this case might naturally be included in the concept of "leukosis". In the two present cases, though no bone marrow nor peripheral blood was examined, the increase in mast cells was considered to be due to proliferation, except that in the alveolar walls. Accordingly, the present authors intended to treat their cases as "leukosis".

HEAD reported 9 feline cases of the disease in his investigation on "Cutaneous mast-cell tumours in the dog, cat and ox". He also made an attempt to classify the disease on the basis of lesions produced, and divided the tumors into two groups, one involving the skin and subcutis and the other involving only internal organs. The latter included internal mast-cytoma and internal mast-cell sarcoma. Furthermore, he stated that whether internal mast-cell sarcoma and basophil-cell leukemia were one and the same disease or not was bound up with the question of the relationship between the blood basophil cell and the tissue mast cell. He also mentioned that he could not decide whether the basophil-cell leukemia might be classified as a distinct group or not. The neoplastic proliferation of the skin shown in his cases is very interesting, since the skin mast-cell tumor appears in cats, as well as in dogs.

On the other hand, NIELSEN and COLE investigated one hundred canine cases of mast-cytoma and assumed that the disease might be different from basophil-cell leukemia. They cited ROMANELLI's canine case of basophil-cell leukemia in which no skin lesions

had been detected.

In any case, many problems still remain to be solved until it is determined whether the neoplastic diseases produced by basophilic granular cells should be treated with the concept of one and the same disease. One of the keys to solve the entity of the diseases is to clarify the histogenesis of the mast cell and basophil myelocyte. No definite conclusions, however, might be drawn on the basis of knowledge obtained so far. Furthermore, it is impossible to determine the origin of the tumor cells from the morphological characteristics of the cells increased in neoplastic proliferation. Accordingly, it is considered that there would be no means to know the true nature of this disease other than a presumption based on a histo-morphological point of view. The true nature of the disease will gradually be disclosed in future in accordance with the advance of cytology.

Only two cases were reported here. It is suggested, however, that the occurrence of the disease might not be infrequent in cats, since the two cases were detected from among only eight feline cases autopsied at the authors' laboratory during a considerably short period. It may be the reason why case reports on this feline disease have been comparatively small in number that the investigation of the feline disease has not presumably fully been conducted.

The present cases may be the first ones that have been reported in Japan. Hereafter, further detailed observation of this disease will contribute to the expansion of cytological knowledge of the basophilic granular cell involving a mast cell and a basophil myelocyte.

In regard to such endotheliomatous meningioma as detected in the third cerebral ventricle of Case 1, LUGINBUHL mentioned from his investigation that meningioma was not so seldom in cats. In this case, meningesoma as well as nephritis and peritonitis, may have no direct relations with the mast-cell neoplasm.

SUMMARY

A pathological study was conducted on two feline cases of mast-cell leukemia. Both cases were concerned with old female cats. The spleen and liver were markedly enlarged, since mast cells proliferated and infiltrated in both organs. The proliferation and infiltration were recognized also in the medullary sinuses of the mesenteric lymph nodes, alveolar walls of the lungs, and serous membrane of the intestine. On the basis of the findings obtained, the authors made some discussion about nosological opinions.

In one of the cases, endotheliomatous meningioma was noted as a type of multiple neoplasm.

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猫における肥満細胞白血症 2 例について

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猫の肥満細胞白血症に関しては、すでに 1907 年以来、十数例の報告をみるが、その多くは、単に白血病として取り扱っている。しかし、白血病とは血液腫瘍であるという概念からみれば、既報の症例をすべて白血病と呼ぶことが妥当であるとは考えられない。まして、この腫瘍構成細胞が、組織肥満細胞であるか、または骨髓好塩基球であるかは、今日の細胞学的知見では容易に断定し得ない。したがって本症の命名については、なお多くの論議があるように見受けられる。

著者らは、教室剖検例の中 2 例に本症を経験した。いずれも老令の雌猫で、著明な脾腫と肝腫を主徴としたものである。組織学的には、脾髄は腫瘍細胞によってみたされ、肝では、静脈洞および門脈周囲の結合組織における腫瘍細胞の増生がみられた。このほか、腸間膜リンパ節髄洞、腸漿膜、肺胞壁などに腫瘍細胞の集簇をみとめ、肺胞壁における以外のものは、明らかに増殖性浸潤性の性格をそなえていた。

これらの腫瘍細胞は、円形核を有しヘマトキシリン・エオジン染色で、原形質は赤味を帯びて染まり大小の空胞を有するものが多く、原形質縁は必ずしも明瞭でない。原形質内には、Giemsa 染色で青紫色、cresyl violet で赤紫色にメタクロマシアを呈する微細顆粒がみたまわっている。また酸化酵素反応陽性顆粒を有するものが、およそ 1/3 に認められている。細胞増殖巣における嗜銀線維の発達はみられず肝では膠原化、脾髄では断裂を示すものが多い。

このうち 1 例に endotheliomatous meningioma を認めた。これについては、いうまでもなく本症と直接の関連がみられなかったが、重複腫瘍として興味あるものであった。

これらの 2 例を得た同期間中の教室における猫剖検例は、わずかに 8 例であることから、本症の存在は決してまれでないことがうかがわれた。今後における本症の追究は、肥満細胞および骨髓好塩基球を含む、塩基性顆粒細胞の細胞学の進展に寄与するものと考えられる。

EXPLANATION OF PLATES

PLATE I

- Fig. 1. Liver of Case 1. Increased tumor cells in the sinusoids. Hematoxylin and eosin (H-E) stain, $\times 400$.
Fig. 2. Liver of Case 1. Distinct collagenous-fiber formation in the endothelium. Argyrophil-fiber stain, $\times 400$.
Fig. 3. Liver of Case 1. Basophilic granules in the cytoplasm of tumor cells. Giemsa stain, $\times 400$.
Fig. 4. Liver of Case 2. Vacuolated and binucleated tumor cells. H-E stain, $\times 400$.
Fig. 5. Spleen of Case 2. Transverse section.
Fig. 6. Spleen of Case 2. Increased tumor cells in the pulp. H-E stain, $\times 400$.

PLATE II

- Fig. 7. Spleen of Case 2. Torn argyrophil fibers in the pulp. Argyrophil-fiber stain, $\times 400$.
Fig. 8. Spleen of Case 1. Basophilic granules in the cytoplasm of the tumor cells. Giemsa stain, $\times 400$.
Fig. 9. Lung of Case 2. Mast cells (dark spots in the figure) in the alveolar wall. Giemsa stain, $\times 400$.
Fig. 10. Intestinal serosa of Case 1. Accumulation of mast cells. Giemsa stain, $\times 400$.
Fig. 11. Mesenteric lymph node of Case 1. Accumulation of mast cells (dark spots in the figure) in medullary sinuses. Giemsa stain, $\times 100$.
Fig. 12. Endotheliomatous meningioma of Case 1. H-E stain, $\times 100$.