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NEW TYPE OF TUMOR IN COW, "*LYMPHOGONIOMA*"

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PREFACE

As to the tumors which grow in the lymph nodes of the domestic animals, not many detailed pathological studies have been published although the existence of such growths has long been known. The description of the tumors in text books is also poor; NIEBERLE in his text book has given a brief explanation of lymphadenosis, lymphosarcoma and lymphosarcomatosis. However, the differentiation of these lesions is not clearly stated in that text book. It may be mentioned that DOBBERSTEIN and PAARMANN (1934) and LÜBKE (1938/39) have made a pathohistological survey concerning the lymphadenosis in cattle which shows a swelling mainly on the lymph node and sometimes of the spleen, liver etc. On the other hand, in human medicine, the lymph node tumors have been studied in great detail patho-, histo- and cytologically together with hematological studies, because such growths play an important role in the malignant tumors. Especially in our country, many excellent researchers have been prosecuting outstanding investigations and it is not too much to say that studies in the lymph node tumor have made much progress in Japan.

The author has recently had a chance to obtain a lymph node tumor from the abdominal cavity in a cow at the Sapporo slaughter house, and having conducted a detailed pathological study, the author would like to make comments on the results as follows as well as on the Japanese and foreign literature.

MATERIAL AND METHODS

A cross-bred Holstein cow. Age and habitat unknown. Material number T. 544. Was slaughtered on December 15, 1953 at the Sapporo slaughter house. A meat inspector of the slaughter house detected a lymph node hanging down from the abdominal cavity of the slaughtered animal, and brought it to the writer's laboratory for pathological examination. Seeing its hanging position, the author suspects it may be an iliac lymph node.

The material was fixed with formalin and CARNOY's solution, several tissue blocks were made vertically to the hilum of the lymph node. Paraffin sections were made adopting hematoxyline-eosin (H.-E.), HEIDENHAIN's Azan, UNNA-PAPPENHEIM's pyronin-methylgreen, GIEMSA, thionin and SCHIFF's periodic acid staining as well as BIELSCHOWSKY-MARESCH's silver-impregnation method for detailed histological examination.

RESULT

1. Macroscopical Findings

The lymph node is $13 \times 9.5 \times 2$ cm in size, and 150 g in weight. Fatty tissue covers the lymph node tightly; it is difficult to strip the fatty tissue from the capsule. Several millet-sized haemolymphonodi are detected in the fatty tissue. The lymph node is about palm size and shows surface as uneven as hills. The portion of the hilum is extended, and is measured 6.5×3.5 cm in size; the thickness of the concave hilum paretchyma is reduced to 1 cm. Neither dilatation of the lymph vessels nor development of the blood vessels is especially remarkable. The consistency of the lymph node is elastic and hard. Cut surface is light greyish yellow in color, hydrous and slightly swollen. The follicles are almost unrecognizable, the trabeculae are rather rough and their tracks appear as irregular grooves on the cut surface.

2. Histological Findings

One of the most noticeable changes is the increase of closely packed tumor cells in the medullary cord. These cells take large and round or oval shape. The protoplasm is basophilic. The nucleus is situated nearly at the center of the cells, is poor in chromatin and has two or several basophilic nucleoli. Some nuclei show pyknosis; amitosis and mitosis are rarely seen. The argyrophil fiber is highly developed as is also the great quantity of tumor cells. By pyronin-methylgreen staining, the protoplasm and nucleoli of the tumor cell are shown to be pyroninophilic; the protoplasm can be stained by thionin and shows negative result to the periodic acid SCHIFF's reaction. In the Azan-staining of these cells, they are observed to be free from the reticular fiber nets but in a few of them the surface of cell is closely connected with the fibers stained by anilin-blue. Among the tumor cells, the reticular cells are found sporadically which have slightly stained protoplasm containing several granules which respond to the periodic acid SCHIFF's reaction.

As a result of the increase of the tumor cells, the other tissue structure of the lymph node is oppressed; the follicles are atrophic and are barely recognized as foci made up of small scattering lymphocytes. Some of the lymph follicles show lymph stasis in the center and the formation of the argyrophil fiber is very poor. As the sinus endothelium is almost destroyed and many tumor cells infiltrate and increase in the lymph sinus, the figure of the lymph sinus is indistinct but some of the sinuses distinctly show lymph stasis. The lymph node capsule is thickened, the trabeculae are fairly developed, and a slight sporadic infiltration by the tumor cells is observed in the trabeculae. On the lymph and blood vessels of the hilum region, embolism or other changes are not observed.

The author, therefore, histologically diagnosed the present case as "*Lymphogonioma*" based on the above findings.

DISCUSSION

A tumor in the abdominal cavity of a cow was histologically examined and was diagnosed as "*Lymphogonioma*". At the beginning of the examination, the author felt that it would be a lymphadenoma (lymphoma) macroscopically from

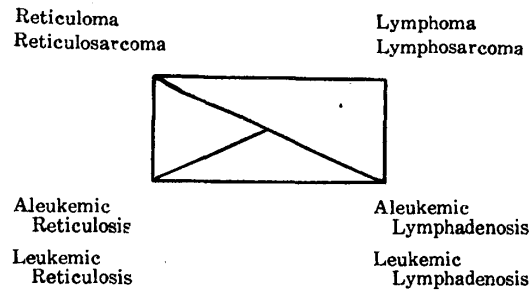
the fact that the tumor shows simple hyperplasia of the lymph node and is not a systematic disease of the whole lymph nodes. Of course the diagnosis was given only macroscopically to the material sent to the laboratory and neither hematological nor patho-anatomical examination had been conducted. However, histological examination revealed that the tumor cells were increased diffusely in the medullary cord accompanied by the intense increase of argyrophil fibers. Atrophy of the follicles and the disappearance of the originally existing lymphocytes were noticed, consequently the author found that the tumor should be taken out of the category of lymphadenoma. On the silvering preparation as well as on H.-E. staining, there was observed neither the development of blood vessels nor the new formation of follicular structures which are the characteristic changes for lymphosarcoma²⁰. With regard to the histological findings, this tumor should be considered as a lymphatic reticulosarcoma.

As to the original lymph node tumors as well as to the reticulosarcoma, many studies have been made in human cases. The author would like to add his comment on the literature concerning the original lymph node tumors as follows.

1. Reports on Human Cases

As to the studies on reticulosarcomas in our country, reports have been made by OGATA, AMANO^{4,5)} and AKAZAKI. AMANO and his coworkers⁶⁾ classified the original reticulosarcoma into immature and mature types and asserted that the mature type of lymph node tumor can be separated into two types of fibro-cellular-differentiated form and polymorpho-cellular form. AKAZAKI classified the reticulosarcoma as undifferentiated, differentiated and transitional types, and the differentiated type was further divided to reticular, histiocytic and polymorpho-cellular types. In addition to this, OLIVEIRA (1936/37), ROULET (1930) and others abroad have made detailed studies of these tumors, and they also attempted to classify them. Further investigations are still considered to be required in order to make the present case fit into the above-mentioned classifications. However, the author's case is forcibly categorized into the classifications of AMANO and OLIVEIRA's fibro-cellular-differentiated form and AKAZAKI's differentiated reticular type. Recently, there have been many reports made on reticulosarcoma^{9,12,15,24,30,31,37,39)} and the majority of them recognize it as reticulosarcomatosis systematically affects the whole lymph nodes.

There are reticulosis, reticulosarcoma (-sarcomatosis), lymphosarcoma (-sarcomatosis), lymphadenosis and lymphatic leukemia etc. included under the term "lymph node tumor"; many workers state that the differential diagnosis is difficult to conduct for these tumors and that transitional types of lesions are frequently recognized. More specifically, since FRAENKEL had noticed the transition between lymphosarcomatosis and leukemia back in 1914, NORDMANN (1932) pointed out the coexistence and transition of lymphatic and myeloid leukemia, ROULET (1932) that of reticulosis, reticulosarcoma and lymphatic leukemia, and APITZ (1937) that of lymphadenosis, lymphosarcomatosis and lymphosarcoma respectively. In Japan also, MIYAGAWA and SAITO (1941) consider the relation among the above as follows;



Furthermore, many other investigators indicated the relations of coexistence and transition among them as follows: reticulosarcoma and lymphosarcoma by AMANO and NAGATA (1941); leukemic reticuloendotheliosis and reticulosarcoma with monocytic leukemia by AMANO (1943); lymphadenosis and lymphosarcomatosis by MIYAKE (1951); lymphosarcoma, lymphatic leukosarcoma and lymphatic leukemia by MATSUI (1952); reticulosarcoma and lymphosarcoma, lymphatic leukemia, reticulosis or lymphoblastoma by AKAZAKI (1952/53/54); reticulosarcomatosis and reticulosarcoma by HARAGUCHI and MORI (1954); and reticulosarcoma and monocytoma by MARUYAMA and ÔTANI (1954). Quoting the report made by MATSUI, HANSWIRTH et al. (1948) and KATO and BRUNSCHWIG (1933) also consider the existence of the transition between lymphosarcoma and lymphatic leukosarcomatosis. At present, the predominant opinion, in academic circles, is that it can not be denied that the lymphosarcoma and reticulosarcoma are to be included in the category of leukemia. Since the histological diagnosis of these tumors has some questions as stressed by many workers, a diagnosis should be decided depending on the cytological examinations. ÔSAKI (1953) carried out cytological examinations about the reticulosarcoma and determined the characters of the tumor cells.

2. Similar Tumors in Domestic Animals

On the other hand, regarding the lymph node tumor in domestic animals, not many reports have been made as far as the author knows. In our country, leukemia cases were reported only at the Veterinary Medical Society by OHBAYASHI et al. (1951) on horses and MISHIMA et al. (1952) on a calf. JENNINGS (1953), in 8 cases of canine lymphadenosis, attached importance to the lymphoblast which shows large and round shape and is stained by neutral red. As to the so-called bovine leukosis which has recently been attracting attention as a mineral deficiency disease^{17,30}, LÛBKE (1938/39) has reported an interesting finding to the effect that the lesions in the lymph nodes in bovine leukosis are much like to the lesions in human retiothelsarcoma (reticulosarcoma). About the bovine leukosis, ARONSOHN (1917) and KNUTH and DU TOIT (1917) in Germany, JONES (1928) in England and, according to DOBBERSTEIN's report, FELDMANN (1928) in America reported the existence of the disease, but it is regretful that none of them has presented the detailed histological information. In 1934, DOBBERSTEIN and PAARMANN investigated lymphadenosis in cattle centering around the slaughtered cases, from the view points of hematology and pathology. Then the workers named the disease as "bovine leukosis" which had previously been called by various names, and classified it into 4 types—lymphoid form, myeloic form,

lymphatic form and sarcomatous form. According to the description of the report, enlargement of one or more lymph nodes was macroscopically detected and some of them were more than 600 g in weight. As to the cells in these lesions, the nucleus is large and poor in chromatin with two or three nucleoli, the protoplasm is stained basophilic and some of them have some vacuoles. Some of the cells having a polygonal-shaped protoplasm are connected with the reticular tissue. Sometimes mitotic nuclei are also seen. Histological findings prove distinct or almost broken original structure of the lymph nodes. On the pathogenesis of the disease, they considered that the lymphoid-cytomatosis will change into lymphadenosis, myelosis or lymphosarcomatosis.

With regard to the great problems concerning the leukemia in domestic animals, it is considered that many unknown factors about it still exist. Speaking of the leukemia in domestic animals, a discussion on the avian leukemia should not be neglected because many excellent studies of it have been recently reported also in Japan. The author, however, intentionally, has not incorporated any discussion thereof at this time it is different from the category of lymph node tumor.

3. Author's Opinion in This Case

The foregoing is the author's comment pertaining to many investigator's reports. Reviewing the present case, the author cannot state with assurance whether or not the case is a leukemic type for the clinico-hematological observations have not yet been concluded. As the lesion is obviously found on a lymph node and is made up of mononuclear round and large tumor cells, it is considered that the tumor has to be histologically diagnosed as lymphosarcoma, reticulosarcoma or reticuloendothelioma (AKAZAKI doubts the existence of this tumor on lymph node). As previously stated, this case can be proved not to be a lymphosarcoma in respect to its histological figure, and the factors of lack of intensive phagocytosis and of the development of the tumor cells in the lymph sinus, argue against its being reticuloendothelioma. Consequently, it seems to be capable of diagnosis as a reticulosarcoma. As noted in the foregoing description, this case might histologically belong to the differentiated reticular type (AKAZAKI) and to the fibro-cellular-differentiated form (AMANO).

However, the characters of the tumor cell are strikingly noteworthy; it is identical to the "L-cell" according to the results of the examination conducted by the author. The "L-cell" was pointed out by YAMAGIWA and OHSHIMA in the medullary cord of the lymph node in equine infectious anemia. The present author reported his cytological studies about the "L-cell" as a part of the studies on equine infectious anemia. The "L-cell" is characterized by its comparatively large size, basophilic and syrupy protoplasm, two to several nucleoli, slight staining reaction to neutral red and non-phagocytosis to carbon particles by supravital staining, etc; it is identified as the lymphogonia reported by AMANO et al., in 1951. In author's present case, the tumor cell was identified as the "L-cell",

lymphogonia, and the tumor developed in a lymph node as a benign one which was temporarily named as "Lymphogonioma". As most cases of reticulosarcoma are recognized as reticulosarcomatosis according to recent publications, the author considers that the newly proposed name is much more suitable for this case because the whole lymph nodes have not yet been examined.

From the fact that the lesions of bovine leukosis resemble reticulosarcoma according both to LÜBKE and to the cytological and histological observations by DOBBERSTEIN and PAARMANN, it can be said that this case may be so-called bovine leukosis. The author, being not content with the vague name of the disease group, wishes to clarify the nature of so-called leukemia as well as the similar diseases in domestic animals by conducting a systematic research by means of patho-histological and cytological examinations.

SUMMARY AND CONCLUSION

Patho-histological study was conducted on the lymph node tumor found in the abdominal cavity of a cow killed at the Sapporo slaughter house.

The tumor cell has basophilic protoplasm and large nucleus which is poor in chromatin; it is identified as the author's "L-cell". The lesion, however, was not observed systematically and for the time being it is proposed to name it "Lymphogonioma (OHSHIMA)"

Histologically, the tumor is similar to the human reticulosarcoma and it might belong to AKAZAKI's differentiated reticular type and AMANO and OLIVEIRA's fibro-cellular-differentiated form.

From the observations reported in this paper it should not be denied that the case may be so-called bovine leukosis.

The author, taking this case a basis for furthering his study, wishes to clarify the nature of so-called leukemia as well as the similar diseases in domestic animals.

To this end, the author desires to extend his gratitude to Prof. YAMAGIWA for reviewing and to the staff of the Sapporo slaughter house for their cooperation in supplying the material.

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EXPLANATION OF PLATE

- Fig. 1. Intensely developed argyrophil fiber and F-atrophic lymph follicle. × 100.
- Fig. 2. Magnification of a portion of fig. 1. × 400.
- Fig. 3. Tumor cell increased in the medullary cord. H.-E. staining. × 400.
- Fig. 4. Destroyed sinus endothelia and S—the lymph sinus. H.-E. staining. × 400.
- Fig. 5. Strongly magnified tumor cells and nucleoli showing distinct appearance, and M—a mitotic tumor cell. H.-E. staining. × 1100.
- Fig. 6. Relation between the tumor cell and the reticular net. Azans-staining. × 1100.

