Tumors of the Thymus in Cattle, Sheep, and Pigs

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SUMMARY

A histologic survey has been made of all neoplasms found in slaughtered cattle, sheep, and pigs during one year in 100 abattoirs throughout Great Britain. A total of 302 tumors from cattle, 107 from sheep, and 139 from pigs was collected. The specimens included 16 thymomas (15 from cattle and one from sheep) and 80 thymic lymphosarcomas (40 from cattle, 5 from sheep, and 35 from pigs). Thymomas were found only in adults, whereas thymic lymphosarcoma had a high incidence in immature animals. Of the 16 thymomas, 13 were predominantly epithelial tumors and 3 were predominantly lymphocytic. The findings are considered in relation to the characteristics of thymic neoplasms in man.

INTRODUCTION

Intensive investigations have been in progress for some years to elucidate the function of the thymus, the histogenesis of its component cells, and the role of neoplasia of the thymus in the etiology of associated disorders in man. Recently it has been shown that the rodent Mastomys natalensis tends to develop spontaneous thymomas, often with an associated polymyositis and dacryoadenitis (13), but there are few records in veterinary literature, and the incidence of such tumors in the domestic species is unknown. In Britain, the common neoplasm of the thymus in domestic animals is lymphosarcoma, which may affect the thymus apparently exdusively or in association with lesser involvement of other organs. There are no recent reports of animal thymomas in this country.

A pathologic survey of all neoplasms found in slaughtered cattle, sheep, and pigs in 100 abattoirs throughout Great Britain during one year has been carried out in collaboration with the Ministry of Agriculture, Fisheries and Food. During the survey, we have examined 16 thymomas and 80 thymic lymphosarcomas. In this paper, the incidence of these two conditions and the histologic features of the thymomas are described.

MATERIALS AND METHODS

Meat inspectors in 100 abattoirs throughout Great Britain agreed to participate in a survey of tumors found in slaughtered animals in one year. During the period October 1965 to September 1966 they submitted tissue for histologic diagnosis to the University of Glasgow Veterinary Hospital from all suspected neoplasms encountered in cattle, sheep, and pigs. The specimens were fixed in 10% formol-saline in the abattoir and sent to the laboratory in polythene-lined bags, with prepaid labels provided for this purpose. An accompanying form was also sent, giving the owner's name and address, the abattoir address, and details of the species, breed, age, and sex of the animal, and the organs seen to be affected. In the laboratory, the specimens were trimmed and further fixed for 24 hours in formol-saline, then processed for paraffin section in the usual way.

Sections from all blocks were stained with hematoxylin and eosin. Special stains used on selected sections included picro-Mallory, the reticulin stain of Slidders, Fraser, and Lendrum, van Gieson's method, periodic acid-Schiff (PAS), and Southgate's mucicarmine.

RESULTS

Incidence of Thymic Neoplasms

The survey included approximately one-third of all animals slaughtered throughout Great Britain during the year. A total of 713 specimens were received for histologic examination, and 548 of these were diagnosed as true neoplasms. The incidence of thymoma and thymic lymphosarcoma in the 3 species is shown in Table 1.

The thymomas occurred almost exdusively in adult animals. In cattle, the youngest with thymoma was a 2-year-old bullock; all other thymomas were from adults of 6 years or more. The single example from a sheep was found in an adult ewe of uncertain age. Two bovine thymomas were from male animals and the remaining 13 from females. The affected animals were from several common British breeds. The tumors occurred in the thoracic thymus in 11 cattle and in the cervical portion in 4; in the sheep, the precise location was not stated. None had metastasized. Adhesion to visceral pleura was noted in 3 cases.

From these observations, it appears that thymoma is essentially a neoplasm of adult animals. The low incidence in sheep and the absence of any cases in pigs may be due to the fact that the majority of sheep and pigs are slaughtered before reaching maturity, whereas the cattle population included a high proportion of adults. Of the 1,300,000 cattle surveyed in the present study, 890,000 were over 2 years of age. The sex incidence is modified since most adult cattle are females:

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hence, our result does not indicate any sex predisposition. The thymomas found in cattle comprise 5% of all bovine neoplasms in our series and therefore, are not uncommon in this species.

Thymic lymphosarcoma in animals is a form of lymphosarcoma which appears to start or grow most rapidly in the thymus. The thymus may be the only site apparently affected, or there may be lesser involvement of lymph nodes and other organs. The proportion of all lymphosarcomas which were of the thymic type and the age incidence in the three species are shown in Table 2. In 8 of the 40 cases from cattle, one of the 5 from sheep, and 6 of the 35 from pigs in this series, the lesion was observed only in the thymus. When the condition was disseminated, the organs most commonly involved were lymph nodes, liver, spleen, kidney, and lung. Lymphosarcoma is the outstanding malignancy of domestic animals, and this is reflected in the larger number of thymic lymphosarcomas than thymomas. Most of the nonthymic lymphosarcomas were multicentric in distribution; lymphosarcoma, as found in this survey, has been fully described elsewhere (1).

Thymic lymphosarcoma differed considerably in age incidence from thymoma, having a high incidence in immature cattle and pigs. However, in cattle more than 4 years of age, thymoma and thymic lymphosarcoma occurred with equal frequency. Thymic lymphosarcoma was found only in adult sheep, possibly due to the economics of sheep farming, where by clinically affected young lambs would not be marketed. There was no significant sex or breed incidence in any species.

**Histologic Appearances**

The thymomas were subdivided into predominantly epithelial and predominantly lymphocytic tumors. There was a lymphangiomatous component in 6 cases, forming cystic spaces of varying size — sometimes visible macroscopically — lined by a single layer of flattened cells filled with faintly eosinophilic amorphous material, in which a few tumor cells were suspended (Figs. 2, 3). In one tumor in which the lymphangiomatous spaces were prominent, pseudorosette formation around blood vessels was also evident. Formation of numerous rudimentary Hassall's corpuscles had occurred in one tumor (Fig. 4), but this differentiation was not found in any others. Four of the thymomas contained calcispherites scattered in groups among the epithelial cells; usually they lay in spaces bounded by flattened cells.

The tumor cells were usually plump with abundant cytoplasm but tended to become spindle shaped in places. In one, the spindle shape predominated, and the cells tended to form whorls. Mitotic activity was usually minimal, but in two, mitotic figures were moderately frequent. Nonneoplastic thymic tissue was included in three of the specimens received, and this was normal except for compression on the border adjacent to the tumor.

The predominantly lymphocytic thymomas were composed of sheets of uniform, tiny, round lymphoid cells with small, dense nuclei. An irregular lobulated structure was formed by subdividing fibrous bands (Fig. 5). In the ovine case, a reticular framework was appreciable in places where small groups or cords of epithelial cells lay among the lymphoid cells. Again, occasional eosinophils were present in each. There were no lymphangiomatous spaces or calcispherites. In the two predominantly lymphocytic thymomas from cattle, an abundant hyalinised stroma was distributed focally throughout the tumor (Fig. 6). The lymphocytes were scattered singly and in small groups through an amorphous eosinophilic matrix, which showed the staining affinities of collagen; these cases were referred to Professor A. C. Lendrum, University of Dundee, who considered that the matrix contained aging fibrin but that the origin of the material was not evident. Both tumors also contained small groups of plasma cells. Mitotic figures were not found in any of the lymphocytic thymomas.

The histologic appearances of thymic lymphosarcoma are well known and will be summarized here for comparison with the lymphocytic thymomas. In thymic lymphosarcoma, the thymus became totally replaced by sheets of cells of the

### Table 1

<table>
<thead>
<tr>
<th>Animal</th>
<th>Total No. of Tumors Examined</th>
<th>No. of Thymomas</th>
<th>No. of Thymic Lymphosarcomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td>1.3</td>
<td>302</td>
<td>15</td>
</tr>
<tr>
<td>Sheep</td>
<td>4.3</td>
<td>107</td>
<td>1</td>
</tr>
<tr>
<td>Pigs</td>
<td>3.7</td>
<td>139</td>
<td>0</td>
</tr>
</tbody>
</table>

Incidence of thymoma and thymic lymphosarcoma in slaughtered cattle, sheep, and pigs.

### Table 2

<table>
<thead>
<tr>
<th>Animal</th>
<th>Total No. of Lymphomas</th>
<th>No. of Thymic Lymphomas</th>
<th>Age Incidence of Thymic Lymphomas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle</td>
<td>75</td>
<td>40</td>
<td>Under 1 yr., 6 cases</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1–2 yr., 7 cases</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2–3 yr., 10 cases</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3–4 yr., 2 cases</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Over 4 yr., 15 cases</td>
</tr>
<tr>
<td>Sheep</td>
<td>44</td>
<td>5</td>
<td>All adult</td>
</tr>
<tr>
<td>Pigs</td>
<td>92</td>
<td>35</td>
<td>3–6 months, 25 cases</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Over 6 months, 10 cases</td>
</tr>
</tbody>
</table>

Thymic lymphosarcoma: proportion of all lymphomas and age incidence.
lymphoid series, which were usually large lymphocytes or lymphoblasts, with large nuclei, obvious cytoplasm and a high mitotic rate. Direct invasion of adjacent structures was a common finding. The cytologic features of malignancy were invariably present, in contrast to the uniform masses of tiny, dense, round cells without mitotic figures, found in lymphocytic thymomas. The lobular pattern and fibrous stroma of the thymomas were further differentiating features.

**DISCUSSION**

The results of our survey indicate that thymoma is a more common neoplasm of cattle than the scarcity of reports in veterinary literature would suggest. The tumor may have escaped more general recognition because of lack of associated clinical signs or failure to relate any presenting signs to an underlying thymic lesion.

In a few collections of animal tumors from several parts of the world, a low incidence of thymoma in cattle has been reported, but more often, such surveys have included no thymomas. Trotter (16) examined 300 bovine tumors at the Glasgow abattoir and found 16 (5.3%) tumors of the thymus, which he separated into 11 round cell sarcomas and 5 mixed cell sarcomas: in 4, lymph nodes were also involved, and it is almost certain that some of these tumors were thymic lymphosarcomas. In South Africa, Jackson (8) described 4 thymomas in 108 (4%) neoplasms from cattle, a result approximating our own, and 2 in 39 (5%) from sheep. However, a frequency of less than 1% of tumors in cattle was found in two large series: in Canada, Plummer (12) reported 4 thymomas in 447 bovine neoplasms, and in the United States, Brandly and Migaki (4) noted 5 thymomas in 737 neoplasms from cattle, 2 in 34 from sheep and 1 in 187 from pigs. One thymoma was found in a series of 40 tumors from slaughtered sheep (7).

There have been a small number of specific reports of thymomas in domestic animals in addition to those encountered during surveys. Blanchard et al. (3) reviewed the veterinary literature and described in detail thymomas from 4 horses, one piglet, one sheep, one calf, one dog, and two rabbits. A single case of thymoma in a heifer has been noted (2). Five thymomas from slaughtered cattle were reported by Pellegrini and Pierrotti (11), who considered the tumor to be relatively common in cattle. Two infiltrative lymphocytic neoplasms of the thymus found in young cattle by Vismara (17) were probably thymic lymphosarcomas. Further investigations may lead to a wider recognition of thymomas in animals.

Classification of human thymic tumors remains unsatisfactory, but it is generally accepted that the majority of human thymic tumors are thymomas in which reticular epithelial cells are always present although sometimes migrant lymphocytes obscure a scanty epithelial content. Thymomas may, therefore, be predominantly epithelial or predominantly lymphocytic in appearance. The mixed types are sometimes termed lymphoepitheliomas. The epithelial cells may be ovoid, spindle, squamoid, organoid, or undifferentiated and may be arranged in trabecular, retiform, whorled, or rosetted fashions. Castleman (5), a leading authority, makes no attempt to name formally variant forms of thymoma and Evans (6) points out that several architectural patterns may occur in the same neoplasm and that the ratio of epithelial cells to lymphocytes may also vary in different parts of the same tumor. Lattes (9), who studied 107 cases from the United States, does not believe that clinical outcome can be predicted on the basis of histologic appearance; his series included 42 predominantly lymphoid, 26 predominantly spindle cell, 20 predominantly epithelial, 4 predominantly rosette forming, 3 atypical epithelial with granulomatous foci, 7 granulomatous, and 4 clinically benign seminoma-like tumors. Thomson and Thackray (15) collected 67 thymic tumors in the United Kingdom and reported these as 10 lymphoid, 7 differentiated, 7 oval or spindle cell, 5 lymphoepitheliomatous, 15 granulomatous, and 20 frequently metastasizing undifferentiated epithelial tumors and three malignant teratomas; however, Evans (6) believes lymphoepithelioma to be the most common form of human thymoma.

Castleman (5) described thymoma epithelial cells as being three to ten times larger than the associated lymphocytes: in a given tumor, however, the cells tend to be uniform in size and are usually oval, often with an indistinct outline and unidentifiable cell membrane. The cytoplasm appears clear, but cases associated with myasthenia gravis may contain PAS-positive granules. The nucleus is large, pale, vesicular, and well-demarcated with one or two nucleoli and may be ovoid, elongated, or indented. Mitoses are usually rare. Occasionally the epithelial cells are thin and spindle shaped and may simulate a connective tissue stroma; when whorled there may be a resemblance to Hassall's corpuscles which are, however, rare in thymoma. Occasionally a lymphangiectatic or lymphangiomatous appearance is evident (18). Fibrous trabeculae may be prominent and extensive and may sequesterate areas of tumor (6). It is probable that large plaques of calcification indicate a tumor of long duration (5). Most thymomas are benign and well circumscribed; adjacent structures including pleura may be invaded, but metastasis is rare. The animal thymomas in the present series were benign, with extension to pleura in a few instances.

There have been few published descriptions of the histologic appearances of animal thymomas. Jackson's examples (8) were reported in detail and had many features in common with the predominantly epithelial tumors in our own series. Plummer's cases (12) were classified as 2 lymphoid and 2 epithelial forms and those of Pellegrini and Pierrotti (13) were composed of mixed epithelial and lymphoid elements. Of the thymomas reported by Blanchard et al. (3), 4 were predominantly lymphocytic, 4 were predominantly epithelial, and in 2 the elements were mixed. Feldman's thymoma (7) from a sheep, not described in detail, showed sheets of epithelial cells.

The differential diagnosis of thymoma raises separate problems in animals and man. In animals, the tumor must be distinguished from the more common thymic lymphosarcoma: in our series, differentiating features included the age incidence and likelihood of lymph node involvement in thymic lymphosarcoma as well as the histologic characteristics described. In man, intrinsic thymomas and secondary bronchial cancers have in the past been confused, and the true incidence of the thymic tumor has only recently become apparent. True malignant lymphomas, which are rare in man, must be differentiated from the predominantly lymphocytic thymomas; teratomas and metastatic carcinoma may be mistaken for
lymphoid and 8 of the predominantly epithelial cases had myasthenia gravis (6). In Lattes’ series, 20 of the predominantly lymphoid and 8 of the predominantly epithelial cases had myasthenia gravis while in Thomsson and Thackray’s series, 7 of the epithelial cases were similarly affected. Spindle cell tumors may be associated with refractory anemia (9). The rodent mastomys has been shown to develop spontaneous thymomas (13); in a colony of 113 mastomys, 27 developed thymomas and 7 of these had an associated polymyositis. In one such animal, a high-titer serum immunoglobulin to the I-band of striated muscle was demonstrated (14). This syndrome in mastomys thus resembles thymoma with myasthenia gravis in man. No such relationship has yet been shown in the domestic species, possibly due to failure of recognition both of the tumor and of the nature of any associated disease. Recently at the University of Glasgow Veterinary Hospital, a thymoma was found at autopsy in a cat which had shown muscle weakness in life. Clearly there is a need for detailed and comprehensive investigations in future cases of this type.

Thymic lymphosarcoma has a higher incidence in British cattle than in Scandinavia, Germany, and the United States, where the majority of lymphosarcomas are of the multicentric form. One of the primary aims of the present tumor survey was to determine whether the “enzootic” form of bovine lymphosarcoma found in those areas is present in Britain. The results revealed no evidence of the enzootic condition, and lymphosarcoma occurred entirely sporadically in the cattle surveyed (1). Among several features that were found to differ in sporadic and enzootic lymphosarcoma was the frequency of the thymic form among sporadic cases. Our survey has also shown that thymic lymphosarcoma is relatively common in pigs while in sheep it is infrequent.

ACKNOWLEDGMENTS

The authors thank the Ministry of Agriculture, Fisheries and Food for their cooperation in organizing the survey and providing data concerning numbers of animals slaughtered in the participating abattoirs; the meat inspectors who submitted the specimens for histopathological examination; and Professor W. F. H. Jarrett, Department of Medicine Veterinary Pathology, University of Glasgow, for planning the survey and providing laboratory facilities. Mr. N. L. Russell carried out the technical work, and Mr. A. Finney took the photographs.

REFERENCES


Fig. 1. Predominantly epithelial bovine thymoma, showing a diffuse sheet of epithelial cells which have indistinct cell membranes and large nuclei with small nucleoli. Small lymphocytes are scattered singly among the epithelial cells. H and E, × 500.
Fig. 2. Predominantly epithelial bovine thymoma, showing lymphangial spaces containing amorphous eosinophilic fluid. H and E, × 300.
Fig. 3. Predominantly epithelial bovine thymoma, showing the edge of a large cyst lined by flattened cells, with tumor cells suspended in the faintly eosinophilic fluid. H and E, × 500.
Fig. 4. Predominantly epithelial bovine thymoma, showing rudimentary Hassall's corpuscles. H and E, × 300.
Fig. 5. Predominantly lymphocytic thymoma from a sheep showing sequestration of groups of tumor cells by prominent bands of fibrous tissue. H and E, × 130.
Fig. 6. Predominantly lymphocytic bovine thymoma showing an area with intercellular matrix which stains as collagen. H and E, × 300.
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