

# A TUMOUR (HÆMORRHAGIC ADENO-CHONDRO-SARCOMA) OF THE ANTERIOR MEDIASTINUM ARISING FROM THE THYMUS GLAND.

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(PLATE XX.)

## INTRODUCTORY REMARKS.

MEDIASTINAL tumours may be divided into two main groups—(1) those of the anterior mediastinum, and (2) those starting in the bronchial lymphatic glands in the posterior mediastinum, which largely produce symptoms by narrowing and compressing the bronchi, while tumours in the anterior mediastinum are especially liable to lead to obstruction of the superior vena cava and symptoms of venous engorgement.

Wilson Fox <sup>(1)</sup> says that of these two situations tumours commence nearly twice as frequently in the anterior mediastinum.

In his collection of 520 cases of mediastinal disease, H. A. Hare <sup>(2)</sup> tabulates 134 as carcinoma, of which 48 occurred in the anterior mediastinum alone; 98 as sarcoma, of which 33 were limited to the anterior mediastinum, and 21 cases as lymphoma and lymphadenoma, of which 11 occurred in the anterior mediastinum. In addition, many cases were described as being in the anterior, and also in the middle or in the posterior mediastina. In Dr. Hare's cases it does not appear that primary growths are only recorded, some being secondary, and, as J. L. Steven <sup>(3)</sup> has pointed out, the terms carcinoma, sarcoma, and lymphadenoma must not be taken as strictly correct, inasmuch as many of the records quoted are antecedent to modern histology. Many of the cases called carcinoma would probably now be called sarcoma.

Nevertheless, these tables indicate the comparative frequency of tumour in the anterior mediastinum. Pepper and Stengel <sup>(4)</sup> speak of mediastinal tumours as being three or four times more frequent in the anterior than in the posterior mediastinum. In 9 cases of primary malignant disease in the mediastinum, recorded by V.

D. Harris (<sup>4</sup>), 8 were in the anterior mediastinum, and 1 in the posterior. In 9 cases which I have personally examined there were six primary tumours in the anterior mediastinum, and three in the posterior.

#### POSSIBLE SOURCES OF ORIGIN OF TUMOURS IN THE ANTERIOR MEDIASTINUM.

With regard to the origin of tumours in the anterior mediastinum, the following situations have been thought, in different cases, to be the starting-points:—

*Thymus gland.*—Astley Cooper (<sup>5</sup>) described the thymus gland as the starting-point of a medullary sarcoma in a girl aged 19, and since then the same view has often been taken. Virchow (<sup>6</sup>) pointed out that tumours arising there were softer than those starting in the bronchial glands, and have a regular outline and a smooth unlobulated surface. Jacobi (<sup>7</sup>), in a critical paper on the anatomy and pathology of the thymus, quotes 7 cases in which the thymus was thought to be the site of mediastinal growth. Letulle (<sup>8</sup>) records 8 cases of tumour which he regards as being of this nature, and after discussing the subject sums up in favour of this origin for carcinomatous tumours in the anterior mediastinum. Other cases have been recorded by Cayley (<sup>9</sup>), Church (<sup>10</sup>), R. Douglas Powell (<sup>11</sup>), Dansac (<sup>12</sup>), and Denmanké (<sup>13</sup>), in which a similar opinion is expressed. J. L. Steven, in his recent monograph, mentions the possible origin of tumours in connection with the thymus, but dismisses it somewhat briefly as one of which he had no personal experience. According to Pepper and Stengel (<sup>14</sup>), the form and outline of the tumour may at once recall those of the thymus gland.

*Sternum.*—From the periosteum on its inner surface a sarcoma may arise (Kaulich quoted by Wilson Fox). The occurrence of syphilitic nodes on the posterior surface of the bone has been described by Symes Thompson (<sup>15</sup>) and Burney Yeo (<sup>16</sup>). Tumours also may possibly arise from the costal cartilages of the ribs, and project into the anterior mediastinum.

*Lymphatic glands in the anterior mediastinum.*—It is important to find some criterion which will distinguish growths starting in the anterior mediastinal glands from those arising in the thymus gland or its remains. Letulle has insisted on the presence of epithelial cells in growths arising from the thymus gland or its remains, and has drawn attention to the polymorphic character of these cells.

It is natural to regard the presence or absence of the concentric corpuscles of Hassall as of diagnostic importance in considering the origin of a tumour in the anterior mediastinum. This point will be referred to later, but at present it may be conceded that a connective tissue growth showing neither epithelial elements nor concentric

corpuscles may quite conceivably arise in these lymphatic glands, and that in this way lymphadenoma, etc., can be explained most satisfactorily.

*Connective tissues of the mediastinum.*—Tumours may arise—

(a) From subpleural connective tissue. Several examples are given by J. L. Steven.<sup>1</sup>

(b) From the adventitia of the large vessels, Pastau (<sup>17</sup>).

(c) From the pericardium, Kaulich (quoted by Wilson Fox) and Broadbent (<sup>18</sup>) describe examples of sarcoma of the pericardium.

*Thyroid gland.*—Osler (<sup>19</sup>) gives 2 cases of his own, both in women, and refers to two others—the case of a woman recorded by Dettrich, and another, in which the sex was not mentioned, by Kretschy. B. Pitts (<sup>20</sup>) records a substernal goitre developed in an accessory thyroid, but it did not simulate a mediastinal tumour.

In addition, reference may be made to

*Dermoid cysts.*—Dr. H. A. Hare has collected 11 dermoid cysts in the thorax, of which seven were situated on the anterior mediastinum.

The following case, which was under my care in St. George's Hospital, is of interest, as bearing on the origin of mediastinal tumours from the thymus gland:—

#### CLINICAL ABSTRACT.

Male, æt. 20, was admitted with swelling of face, neck, and left arm, dulness behind the sternum and in the left infraclavicular fossa, near the sternum, as far down as the third costal cartilage. There was bronchial breathing near the root of the left lung, and enlarged veins over the front of the sternum—signs pointing to a growth in the superior mediastinum.

The heart's apex beat, which was felt on admission, ceased to be palpable after a time, and the heart sounds became extremely distant. Dulness and loss of breath sounds over the left lung developed, and were thought to be the signs of effusion due to pressure. Accordingly paracentesis was performed in the left mid-axillary line, and 40 oz. of blood-stained fluid were withdrawn, to the great relief of the patient's dyspnœa and distress. This fluid was shown post-mortem to have been withdrawn, not from the pleura, but from the greatly displaced pericardium.

The patient, though better for a while, became more dyspnœic and delirious, and eventually died 2 months after admission; some weeks before death the swelling of the left arm went down, and the dilated veins disappeared, due in all probability to development of collateral circulation.

#### MORBID APPEARANCES.

*The post-mortem examination* was performed by Dr. Cyril Ogle. Both pleuræ contained clear serum. Occupying the superior and anterior mediastina, and covering over the upper half of the pericardium, with which it was firmly blended, was a mass of growth, 18 in. in circumference, and measuring 7 × 6 in. It was on the median line, and extended laterally so as to touch the roots of both lungs. It was fairly smooth and encapsuled on its anterior surface, except at one point towards the right border, where a mass of red growth

<sup>1</sup> "Mediastinal Tumours," p. 31.

projected from it. In consistency it was soft, and gave a feeling of semi-fluctuation.

On section the tumour was composed of two parts—(a) a more superficial anterior stratum, about a quarter of an inch thick, white in colour, and excavated into a number of small cysts. A colourless syrupy fluid containing cholesterol crystals was found in these cavities; (b) the remainder and greater part of the tumour was composed of hæmorrhagic new growth, soft and almost diffuent. The glands at the bifurcation of the trachea were not enlarged, and except for a few nodules in the lungs there were no secondary growths. The trachea was flattened antero-posteriorly, but was not invaded by the growth, and was easily dissected from it. The thyroid gland was quite free from invasion by the tumour. The œsophagus was compressed for a short distance, and its mucosa in this situation thickened (chronic œsophagitis), but it was not infiltrated by the growth.

On opening the pericardial sac it was seen that the growth had eaten its way through the upper part of the pericardium, and that it projected in front of the intra-pericardial portions of the aorta and pulmonary artery, thus hiding them from view. Both these vessels were much constricted, but were not invaded by the growth. The superior vena cava, however, was completely obstructed and lost in the substance of the tumour. The lower part of the vein could be traced; it contained soft growth, but above the entrance of the azygos vein its walls appeared to have been completely destroyed. The left innominate and jugular veins contained blood clot. The azygos vein was dilated, and at its junction with the superior vena cava it was obstructed. The pulmonary veins were somewhat compressed, but did not contain any growth or clot. The growth did not spread down in front of the lower part of the pericardium, near the diaphragm, and, as stated above, it was chiefly confined to the region of the base of the heart and great vessels; anatomically it was, therefore, in the position of the remains of the thymus gland.

The cavity of the pericardium was distended with 12 oz. of blood-stained fluid, and both serous surfaces were coated with shaggy lymph, firmly adherent, and evidently of some standing.

*Lungs* somewhat collapsed, containing a few nodules of hæmorrhagic growth.

*Liver*, 3½ lbs., fatty, but otherwise healthy.

*Spleen*, 6 oz., healthy.

*Suprarenals* and *pancreas* normal.

*Intestines* natural.

*Kidneys* showed the effects of chronic venous congestion.

Microscopically no spermatozoa were found in the contents of the vesiculæ seminales.

*Testes* small; microscopically interstitial increase and thickening of the basement membrane of the seminiferous tubules.

#### MICROSCOPICAL EXAMINATION.

The more superficial white part containing the small cysts was composed of cavities lined by simple mucous glands (Plate XX. Figs. 1, 2) of the same type as Lieberkühn's crypts, and containing numerous goblet cells. Lying around the base of these glands there were in places collections of small round cells like those normally found in a young thymus (Plate XX. Fig. 2a). More externally there were strands of fibrous tissue and smooth muscle fibres (Plate XX. Fig. 2b), and occasionally groups of fat cells (Plate XX. Fig. 1a). The combination of these various tissue elements produced a distorted image or caricature of a structure of a bronchus. But from the preponder-

ance of the glandular tissue it may be described as an adenoma. The more extensive and hæmorrhagic part of the tumour was composed of a basis of cells and of large irregular spaces filled with both fresh and coagulated blood; there were in addition small blood channels running between groups of spindle cells. The cells were of varying size and form (Plate XX. Fig. 3), mostly oval or spindle shaped, but some resembled the small round cells seen normally in a young thymus. Some of the cells were oblong, others had a superficial resemblance to ganglion cells. The latter cells are evidently the same as the "polymorphic" cells described by Letulle, and the "voluminous cells" mentioned by Dansac. The last named author suggests that these cells are modifications of the epithelial cells temporarily present in the foetus, which may be permanent in pathological conditions. The spindle and oval cells being of a connective tissue type, this part of the tumour is sarcomatous, but in addition it contains peculiar cells, possibly of epithelial (hypoblastic) origin. Scattered at intervals in this sarcomatous tissue were islands of well-formed hyaline cartilage (Plate XX. Fig. 1a).

The two parts of the tumour ran into each other and gradually blended; in the area of transition gland tubes may be seen to be surrounded by hæmorrhagic sarcomatous tissue. In no part were any concentric corpuscles of Hassall seen.

The tumour then is partly a cystic adenoma and partly a hæmorrhagic chondro-sarcoma. Although these portions are to some extent distinct it may be described as a whole by calling it a hæmorrhagic adeno-chondro-sarcoma.

On comparing these appearances with those described as occurring in tumours in the anterior mediastinum, it is seen—

1. That this tumour is remarkable in containing well-formed glands. In Letulle's article<sup>(8)</sup> special attention is drawn to the presence of epithelial cells in tumours arising in the position of the thymus, and in the first of his 8 cases a description is given of large polymorphic cells forming columns, which he compares to those seen in an adenoma of the suprarenal or of the liver. Cells of this character were abundant in the hæmorrhagic part of the tumour in this case. Two others (Nos. 6, 7) of his cases are described as carcinomata, and another as a "tubular pavement epithelioma." In Case No. 7 the polymorphic cells are said to be undergoing mucoid change. The comparative structural regularity of the glands in this case contrasts with the generally atypical arrangement in Letulle's cases, and on the whole justifies the term adenoma rather than carcinoma.

2. That it contains large polymorphic cells like those described by Letulle and Dansac.

3. That it contains cartilage. This may in rare instances be present in tumours derived from the bronchus or root of the lung, or from the costal cartilages, but seems to be unique in tumours presumably derived from the thymus.

4. That it agrees with most or at least with a large number of these tumours, namely, those arising in the thymus, in containing hæmorrhagic sarcomatous tissue.

#### ORIGIN OF THE TUMOUR.

Some of the sources for growths in the anterior mediastinum mentioned above can be readily dismissed. The tumour was not connected with the sternum, and so could not be regarded as a periosteal sarcoma, and its glandular contents again would have rendered this view impossible. The latter fact puts out of court its having arisen in the lymphatic glands of the anterior mediastinum, or from the connective tissue in that situation, or from the pericardium with which it was so closely related.

Two possibilities suggest themselves—

1. That it is derived by a rapid and uncontrollable proliferation taking place in a rudimentary bronchus. The presence of smooth muscle, fibrous tissue, and mucous glands together suggested this tempting speculation. I have on one occasion seen a cul-de-sac in connection with the superior surface of a main bronchus, which might be called a rudimentary bronchus.

The "accessory" bronchi are the most likely to vary, they are found chiefly in the lower lobe, and the most important—the azygos bronchus—is on the posterior aspect of the right lung.

The median position of the tumour in the superior mediastinum is against the view that it is derived from the bronchial tubes, inasmuch as carcinoma<sup>(21)</sup> and enchondroma<sup>(22)</sup> when originating in the bronchi give rise to tumours in the lung rather than in the mediastinum. In addition, the connection between this growth and the bronchi was but slight, dissection easily separating adhesions and not revealing any absolute continuity between them. These anatomical considerations render it improbable that the growth was bronchial in origin.

2. The resemblance of the tumour to the structure of the bronchial wall suggests at all events that they have a like origin. Although it is improbable that the growth has sprung from the bronchial tubes, it is quite possible that embryologically they are both derived from the hypoblast of the fore-gut. Since the tumour was anatomically in the situation of the remains of the thymus gland, it may be well to refer briefly to the developmental history of that organ. It is developed from the hypoblast of the third, and according to de Meuron, from the fourth visceral cleft<sup>(23)</sup>. The epithelial tube thus formed has a narrow lumen and is surrounded by vascular connective tissue. An ingrowth of lymphoid cells takes place into the epithelial tube, the constituents of which early degenerate and eventually are represented only by the concentric corpuscles of Hassall. If from

any cause this process of involution of the primitive epithelium does not occur, there will be an absence of Hassall's corpuscles. Hence, the fact, that there are none of these bodies, which characterise a normal thymus, in this tumour, is not opposed to the suggestion that the growth is thymic in origin. On the contrary, if along with such a glandular growth concentric corpuscles had been found, it would be more, rather than less, difficult to assign the thymus as the starting-point. For regarding the concentric bodies as epithelial débris, and not as vascular occlusions, it would be necessary to assume either (1) that different portions of the primitive epithelium had undergone the two opposite processes of involution and evolution much at the same time, namely, in early foetal life; or (2) that the thymus had been invaded by a glandular growth derived from some external source, thus giving up the idea that the tumour started in the thymus gland proper.

If this growth be derived from the thymus, the development of that gland must have been radically affected, and that early in foetal life. The process of involution of the primitive epithelium must have never taken place; and for years the hypoblastic tube must have remained much in its original condition. Then rapid proliferation, set up by some unknown stimulus, gave rise in it to an adenomatous overgrowth, and, as the result of similar activity in the surrounding vascular connective tissue, hæmorrhagic sarcomatous growth was produced. This association of cartilage, glands, and embryonic connective tissue forcibly recalls the structure of some parotid tumours, and renders a common origin for both not improbable. So that from the resemblance of this growth to mixed parotid tumours derived from embryonic remains of visceral arches, a somewhat similar origin for this tumour—namely, from the thymus diverticulum—gains some support.

The cartilage in this tumour might conceivably be derived either from the remains of a branchial arch, as in the case of parotid tumours, or from a chondrification taking place in the sarcomatous part of the growth. But the well-formed character of the islands of cartilage, and the absence of any signs of the development of cartilage, show that the cartilage is of old standing and slow growth, and favour the view that it is a development of tissue belonging to an embryonic branchial arch and not of the more recent sarcomatous growth.

To sum up—

1. The tumour arising in the position of the thymus gland is complex, and is partly a cystic adenoma of mucous glands, and partly a hæmorrhagic chondro-sarcoma.

2. The appearances present considerable resemblance to those seen in some parotid tumours.

3. It is reasonable to believe that this tumour arose from the thymus gland.

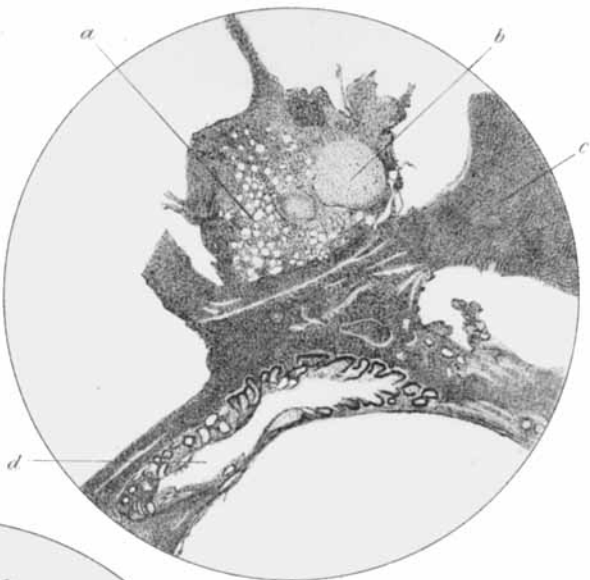


Fig 1.

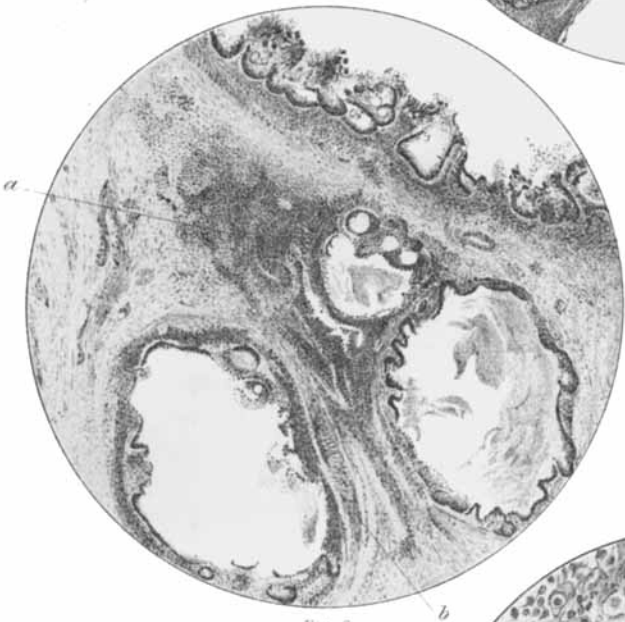


Fig 2.

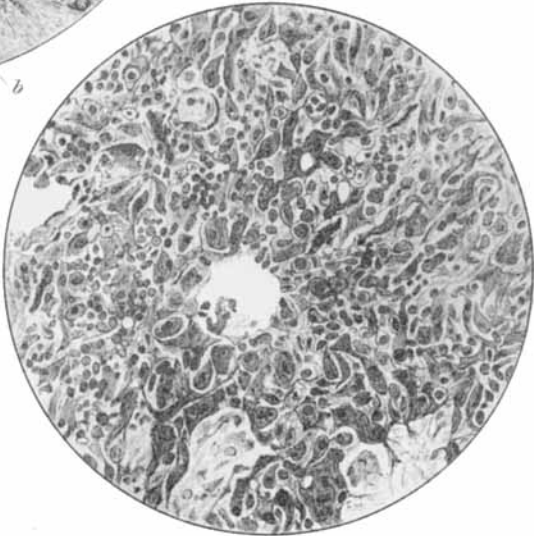


Fig 3



4. Consideration of this specimen shows that it is by no means necessary to find Hassall's concentric bodies in a tumour derived from the thymus gland.

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#### DESCRIPTION OF PLATE XX.

- FIG. 1.—Shows fat (*a*), hyaline cartilage (*b*), sarcomatous tissue (*c*), and spaces lined by gland tubes (*d*). It also shows the junction of the two parts of the tumour. ( $\times 25$ .)
- FIG. 2.—This section from the more superficial part of the tumour shows, under a somewhat higher magnification, spaces lined by gland tubes and containing the coagulated products of their epithelial activity. Around the bases of the gland tubes there are, in parts, collections of small round cells (*a*) like those of thymus gland. In other parts bundles of smooth muscular fibres (*b*) are visible. ( $\times 50$ .)
- FIG. 3.—Shows the polymorphic character of the cells in some parts of the deeper sarcomatous portion of the tumour. They are round, spindle-shaped, and some resemble ganglion cells. In the centre of the field there is a blood space. ( $\times 120$ .)