LYMPHO-EPITHELIOMA OF THE THYMUS
NERVOUS AND OTHER CLINICAL SYMPTOMS IN THE ADULT

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In this paper we are concerned, not with the simple
tumours—fibroma, lipoma, lymphangioma, lympho-
sarcoma, round-cell sarcoma—which occasionally
(though rarely) arise in the thymus, as in other parts
of the body, but with those which arise from the
essential epithelioid cells of the thymic medulla
associated in greater or lesser proportion with
lymphocyte-like cells (probably really lymphocytes),
such as constitute the normal thymic cortex. These
primary thymic tumours—true " thymomata "—
may be termed " lympho-epitheliomata " (Grand-
homme, 1900; Schmincke, 1921; Regaud, 1921),
and are much less often malignant than are the
primary lympho-epitheliomata of the tonsils,
pharynx, and naso-pharynx (Cappell, 1934; Harvey,
Dawson and Innes, 1937). For recent histological
accounts of thymic lympho-epitheliomata, see Wu
(1935) and Obiditsch (1937).

The thymic lympho-epitheliomata seem in some
cases to exert an endocrine effect, and are specially
related to myasthenia gravis. Most important and
interesting was the original observation by Weigert
(1901) of a thymus tumour in a case of myasthenia
gravis in which he wrongly interpreted the
" lymphorrhages " in the muscles as tumour-
metastases. To these questions we will return in
the discussion further on, but for a summary of the
literature of the subject we must refer to the recent
papers by Gold (1935), Meister (1936), Norris
(1936), Miller (1940), Blalock et al. (1941), and Poer
(1942).

Case Record

The patient, Mrs. F. F., aged 58 years, was admitted
on 5th November, 1941, with irregular pyrexia of un-
certain origin. The history was that after a sore throat
6 weeks ago she had been suffering from pains in various
parts. Blood-count: Hæmoglobin, 60 per cent.; ery-
throcytes, 3,610,000; colour-index, 0·8; leucocytes,
9,000 (polymorphs, 53 per cent.; lymphocytes, 40 per
cent.; monocytes, 7 per cent.). Blood-sedimentation:
first hour, 70; two hours, 120. Blood-culture: negative.
Urine: nothing abnormal. By auscultation a blowing
systolic murmur could be heard in the left intercostal
space close to the sternal margin. X-ray examination
of the heart (Dr. F. G. Wood) showed a rounded mass
projecting to the left of, and apparently continuous with,
the heart shadow and moving with it; right and left
oblique views were thought to point to this projection
being an enlargement of the pulmonary artery and
conus (Fig. 1). Brachial blood-pressure: 135/80 mm. Hg.
Blood-Wassermann reaction: negative. Ophthalm-
oscopic examinations (Dr. C. Markus) showed hyperaemia,
especially left eye, apparently connected with hyper-
metropia. The patient at various times complained of
a severe kind of acroparasthesia and of numbness (no
real anaesthesia) of the right lower limb and afterwards
of the right upper limb and both lower limbs. Severe
cramps were sometimes complained of. The knee-jerks,
which were equal and normal on admission, were
unequal at the end of November, the left one being
greatly exaggerated. In March 1942 the patellar and
Achilles reflexes were absent on both sides; the triceps
reflex was absent on the right side, present on the left
side; the plantar reflex was of the normal flexor type
on both sides; no superficial abdominal reflexes were
obtained. Both pupils reacted normally. The speech
was rather sluggish. Very little tactile responses in
either lower limb; some hypersensitiveness to pressure
over the sciatic nerve, both sides. The patient tended
to keep her knee-joints flexed. Although general
asthenia was very marked, no definite characteristic
features of myasthenia gravis were noted.

Focal infection was thought of, but no focus could be
discovered. There was moderate fever from admission
to 25th November—then a little at the commencement
of December and from 10th December to the com-
 mencement of January 1942. About 5th February
there was again fever, and then from 22nd February to
the patient's death on 17th March, 1942, which was due
to a final broncho-pneumonia with some decubitus.
Frequent profuse night sweats constituted also a
clinical feature. The last blood-culture yielded a growth
of staphylococcus albus. Amongst the drugs tried
sulphapyridine on one or two occasions seemed to exert
temporary beneficial effect.

Necropsy

Over the front upper part of the heart and slightly
to the left, firmly connected with the fibrous layers
of the parietal pericardium, was a bun-shaped mass,
about the size of half a large orange, 14 x 8 cm.
in measurement (weight after preparation as a
museum specimen: 112 gm.). The multilocular
cystic central portion of the mass had a honeycomb
appearance on section; most of the cysts freely
communicated with each other and were filled with
a slimy, translucent mucoid fluid; their walls had
a smooth inner surface. In the upper portion of the
" tumour " was a slightly larger cavity, which
was filled with what macroscopically appeared
to be pus, but no microbes could be detected in a film
stained with methylene blue, or by Gram's method.

Thymus gland: slightly enlarged, showing nodular
adenomatous condition, one of the nodules in the
left lobe having a calcified capsule. Broncho-
pneumonia of the lower lobe of the right lung; puru-
 lent bronchitis. Nothing specially noteworthy in
the other organs: brain, heart, liver, spleen,
pancreas, adrenals, kidneys, uterus, ovaries, gastro-
intestinal tract, larynx.
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**Microscopical Examination**

The solid part of the mass consisted of a dense collagenous fibrous framework, in which were embedded cellular islands consisting of delicate spindle and epithelioid cells with vesicular nuclei, associated with lymphocyte-like cells as in so-called thymic lympho-epitheliomata (Fig. 2). No Hassal's corpuscles were seen, but at one spot several elongated, slightly curved ("banana-shaped") vesicular nuclei were noted, grouped together, so as to suggest a differentiated in sections stained in other ways. The honeycomb cystic portion of the tumour represented apparently a further stage of aseptic necrotic involution of the lympho-epitheliomatous tissue. The process was probably analogous to the occasional changes in the thymus gland of children leading to the formation of Dubois's "abscesses" or pseudo-abscesses formerly supposed to be necessarily connected with congenital syphilis.

Is the mass to be regarded as a real lympho-

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**Fig. 1.—Radiogram of the thorax taken on 20th November, 1941.**

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of cells is not sufficiently clearly marked out into cortex and medulla to permit the mass to be regarded as the result of mere thymic hypertrophy; nor does the complete absence of Hassal's corpuscles favour the view of mere hypertrophy. The mass must therefore, we think, be regarded as a true primary thymic lympho-epitheliomatous tumour ("thymoma"). Whether the tumour is a primary one of an ectopic thymus or of a thymic "rest" makes no difference from the pathological point of view; we did not specially search for any thymic remnant in the normal position. By our term "ectopic" we do not imply that the position of the tumour, in front of the pericardium, is abnormal for thymic tissue in early childhood. In the present case there were no cells functionally still resemble the cells of simple hyperplasia.

In something like 55 per cent. of cases of myasthenia gravis hypertrophy or primary tumour (lympho-epithelioma) of the thymus has been present, but in reality the percentage is probably considerably higher, for in many cases thymus or thymic tumour has not been sufficiently looked for. On the other hand, myasthenic symptoms may have been overlooked in some cases of thymic tumour in surgical wards (Mann, 1934). Although in our present case characteristic symptoms of myasthenia gravis were absent, it is highly probable that the great general asthenia, the extreme acroparaesthesia, numbness and other nervous symptoms were in some way con-

metastases and nothing in the microscopical examination pointed to malignancy.

Discussion

Clinical symptoms from thymic hypertrophy or tumour may of course be mechanical, from local pressure, and in the present case the systolic murmur heard to the left of the sternum was probably due to tumour pressure. If the thymus is an endocrine organ one would expect that constitutional endocrine symptoms would often result—as they often do in primary tumours of other endocrine organs—from a primary neoplasia arising from the essential (endocrine) cells, that is to say, so long as the neoplastic cells still retain something of the original functional (endocrine) activity, in fact, so long as the neoplastic cells functionally still resemble the cells of simple hyperplasia. The recurrent sweating and pyrexial periods may possibly, by analogy with what happens in some cases of lymphgranulatosis maligna, be attributed to the necrotic softening and formation of "pseudo-pus" in the lympho-epithelioma, with resulting toxic absorption. Patients with thymic lympho-epithelioma, according to the literature (Matras and Priesel, 1928; Zajewloschin, 1929 and 1933; Nemenow, 1932; Ercklentz, 1936), have died of pleuritis, empyema, pneumonia, furunculosis, and decubitus. The loss of resistance to toxic-infectious agents culminated in our case with the decubitus and broncho-pneumonia, the latter first manifest 4 days before the patient's death, the former a week earlier. It is possible that the absence of definite symptoms of myasthenia gravis might be due to the diminution of the (pre-

Fig. 2.—Photomicrograph of part of the tumour, showing the characteristic epithelioid and lymphocyte-like cells (×400).
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SUMMARY

The tumour is well circumscribed and usually contains a combination of lymphoid, epithelioid, and phlegetitic cells. In some cases, the epithelioid cells may be predominant, and in others, the lymphoid cells. The tumour is usually located in the anterior mediastinum, overlapping the parietal pericardium on the left. In the differential diagnosis, it may be confused with thymic tumours, mediastinal lymphogranuloma, mediastinal tumour, and mediastinal gumma. The examination of the tumour is of great importance. It may be completely lost in the treatment. The possible part played by the thymus gland in some cases of Graves’s Disease is suggested by the occasional occurrence of myasthenic symptoms in the latter disease and even by satisfactory results of thymectomy (Schumacher and Roth, 1913; Russell Brain, 1938; Adler, 1939). Fraser (1937) recorded the case of a woman suffering from myasthenia gravis and Graves’s Disease, who temporarily completely lost her myasthenic opthalmoplegic symptoms under the influence of prostatim. Dudgeon and Urquhart (1926) in nine cases of Graves’s Disease found muscle “lymphorrhages” similar to those of myasthenia gravis.

It seems that in very rare cases malignant thymoma or primary carcinoma of the thymus may be by some unknown process disturb the endocrine balance in such a way as to give rise to symptoms somewhat resembling Cushing’s syndrome (Leyton, Turnbull and Bratton, 1931), but into this question of the “Leyton-Turnbull-Bratton syndrome” we cannot enter here.

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REFERENCES
