THE DIAGNOSIS OF RETICULOSARCOMA OF THE THYROID GLAND

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The difficulty of making a histological distinction between reticulosarcomata and certain anaplastic carcinomata is well known and this applies particularly to the thyroid gland. From a study of the literature it is not easy to obtain an accurate idea of the frequency of reticulosarcomata of the thyroid, using the term reticulosarcoma to include lymphoblastic and lymphocytic (lymphosarcoma) tumours as well as the reticulum cell and other varieties (Robb-Smith, 1938).

Rice (1932) described four cases of lymphoblastic reticulosarcoma of the thyroid and one of a more primitive type, possibly a reticulum cell tumour, these cases occurring between the years 1922 and 1929. Vaux (1937) described a case of dictyocytic reticulosarcoma of the thyroid occurring amongst 25 malignant thyroid tumours. Portmann (1940), in a review of 184 malignant thyroid tumours, recorded the presence of 11 cases of lymphosarcoma, but did not subdivide them into their predominant cell types. He also recorded 14 cases as "unclassifiable," but did not state why this was so or give any description of these tumours. Joll (1941) reviewed 127 malignant thyroid tumours and recorded seven cases of sarcoma. He stated that the reticulum cell variety was the commonest, but gave no figures. The Massachusetts General Hospital recorded, with necropsy findings, four examples of reticulosarcoma of the kidneys (1939, 1941, 1948), one of which (Case No. 34032, 1948) showed coexistent reticulosarcoma of the thyroid. Kellett and Sutherland (1949) recorded five cases of thyroid reticulosarcoma. From the description given of them, one appeared to be of polymorphic type, two reticulum cell, and two lymphoblastic. However, they did not state over what period of time these tumours occurred nor what percentage they formed of the total malignant thyroid tumours encountered in that period. Of the 43 primary malignant thyroid tumours examined histologically in this department between January 1, 1938, and January 1, 1951, 13 were predominantly anaplastic but with small foci of obvious carcinoma, while nine were completely anaplastic, and, of these, only one (Case 3 below) was proved by subsequent events to be a lymphoblastic reticulosarcoma.

There can be no doubt that the frequency with which a diagnosis of reticulosarcoma of the thyroid is made varies greatly according to the criteria acceptable to different observers, and it is with the intention of evaluating these diagnostic criteria that the following case of anaplastic carcinoma and two cases of authenticated reticulosarcoma of the thyroid gland are presented.

FIG. 1.—Anaplastic thyroid tumour in Case 1. Haematoxylin and eosin. $\times 700$.

FIG. 2.—Anaplastic thyroid tumour in Case 1, showing reticulin network. Silver impregnation. $\times 700$.

FIG. 3.—Area of papillary carcinoma in Case 1. Haematoxylin and eosin. $\times 180$.

Case Histories

Case 1.—J. K., a man aged 49, was admitted to Woodend Hospital, Aberdeen, on June 2, 1950, complaining of pain in the left side of the face and neck and of dysphagia of four months' duration. On June 7 he was operated upon for the removal of a retrosternal mass, which proved to be a malignant tumour, partially necrotic, arising from the left lobe of the thyroid gland and adherent to the great vessels, trachea, and oesophagus. Only part of the mass could be removed and x-ray therapy was begun. He subsequently developed radiological evidence of metastases in both lungs, pelvis, and right femur. He died on November 11, 1950. No necropsy was performed.

Histology.—In general, the tumour was anaplastic and highly cellular with some pleomorphism (Fig. 1). The predominant cell possessed a large oval nucleus with a prominent nucleolus, not unlike a reticulum cell. Also, silver impregnation revealed a fine supporting reticulin network (Fig. 2) in intimate relationship to the anaplastic cells, although numerous fragmented strands of pre-existing reticulin could be identified. Other small areas, however, presented the unmistakable features of a carcinoma, evidenced by cuboidal cells and a papillary structure (Fig. 3).

The conjunction of neoplastic cells resembling reticulum cells and a fine intercellular reticulin network might well have led to an erroneous diagnosis of reticulosarcoma, had not the presence of a relatively inconspicuous carcinomatous foci indicated beyond all doubt the true nature of the thyroid tumour.

Case 2.—E. A., a married woman aged 63, was admitted to the Broadstone Jubilee Hospital, Port Glasgow, on January 1, 1949, complaining of a swelling of the thyroid gland which had been present for three months without producing any respiratory distress. Examination revealed that, although the

whole thyroid gland was affected, the enlargement was most marked in the right lobe, which was hard and fixed to the deep tissues. A clinical diagnosis of a malignant thyroid tumour was made and partial removal of the right lobe was carried out, no enlarged lymph nodes being encountered. The post-operative course was uneventful and x-ray therapy was subsequently given.

She was admitted to the Aberdeen Royal Infirmary on July 8, 1949, having suffered from intermittent haematuria for approximately four and a half months, associated with a dull ache in the lumbar region and clot colic. Investigation indicated the presence of a renal tumour on the right side. An enlarged and hard right kidney was removed. X-ray examination failed to reveal any signs of tumour deposits in the lungs, humeri, femora, or vertebrae.

She was readmitted to the Broadstone Jubilee Hospital on September 23, because of persistent vomiting of four weeks' duration. A barium meal showed the presence of a duodenal ulcer, but there was no clinical evidence of either a local recurrence of the thyroid tumour or of metastases. She died on October 17, 1949, no necropsy being performed.

Thyroid.—The specimen from the thyroid consisted of 42 g. of firm pale tissue.

The lesion was a highly cellular and anaplastic tumour showing considerable variation in cell size and nuclear density (Figs. 4 and 5). Numerous cells of reticulum cell type were seen, some binucleate, and mitoses were plentiful. Although considerable coarse, preformed reticulin was present, there was also much that was apparently of recent origin and in close apposition to single cells or small groups of cells (Fig. 6). In addition, the tumour was intersected by ill-defined strands of fibrous tissue.

Right Kidney.—The organ, which was uniformly enlarged and measured 14 cm. from pole to pole, was bisected vertically from the convex border to the

FIG. 4.—Anaplastic thyroid tumour in Case 2. Haematoxylin and eosin. $\times 240$.

FIG. 5.—Anaplastic thyroid tumour in Case 2. Haematoxylin and eosin. $\times 700$.

FIG. 6.—Anaplastic thyroid tumour in Case 2, showing reticulin network. Silver impregnation. $\times 700$.

FIG. 7.—Renal tumour in Case 2, showing infiltration of tumour tissue with surviving islets of renal medulla. Measurements in centimetres (15 × 9 cm.)

hilum. Apart from small scattered areas of surviving renal medulla, the entire renal parenchyma had been replaced by a pale homogeneous tissue. There was no obvious penetration of the renal capsule and the calyces were flattened (Fig. 7).

The appearances were essentially the same as those of the thyroid tumour, as regards both the cellular elements and the reticulin network (Figs. 8, 9, and 10), and numbers of surviving glomeruli, some of them sclerosed, as well as renal tubules were present within the tumour tissue (Fig. 11).

The peculiar diffuse character of the renal tumour is similar to the renal lesions described in Case No. 34032, recorded by the Massachusetts General Hospital. It is quite unlike the usual circumscribed form of either a primary or metastatic growth and resembles the type of lesion seen in some cases of leukaemia. This, together with its histological appearance, indicates that it is a reticulosarcoma, while the histological similarity between it and the thyroid tumour shows that the latter is also a reticulosarcoma. It is impossible, however, to determine which, if either, is the primary focus, or whether the lesion is of multifocal origin.

Case 3.—M. C., a married woman aged 61, was admitted to Stracathro Hospital, Brechin, on July 21, 1947. About four weeks previously she had noticed a swelling in the region of the thyroid gland and at the same time her voice had become husky. An acute attack of dyspnoea occurred on the evening before her admission to hospital.

On examination, she was seen to be dyspnoeic and there was a slight tremor of the outstretched fingers but no exophthalmos; her pulse rate was 96 per minute. There was a diffuse enlargement of the thyroid gland, affecting the right lobe more than the left.

FIG. 8

FIG. 9

FIG. 10

FIG. 11

FIGS. 8, 9, 10, and 11.—Renal tumours in Case 2: (8) Showing anaplastic appearance. Haematoxylin and eosin. × 240. (9) Haematoxylin and eosin. × 700. (10) Showing reticulin network, silver impregnation. × 700. (11) Showing surviving renal tubules. Haematoxylin and eosin. × 240.

FIG. 12.—Ulcer of stomach in Case 3. Haematoxylin and eosin. $\times 2$.

FIG. 13.—Anaplastic thyroid tumour in Case 3. Haematoxylin and eosin. $\times 240$.

FIG. 14.—Anaplastic thyroid tumour in Case 3. Haematoxylin and eosin. $\times 700$.

FIG. 12

FIG. 13

FIG. 14

The gland extended downwards behind the suprasternal notch and the trachea was displaced to the left. There was no enlargement of the regional lymph nodes. She was transferred to the Aberdeen Royal Infirmary, where, on July 26, a partial thyroidectomy was performed, when it was found that the enlarged right lobe extended behind the trachea and oesophagus, being adherent to the latter. The thyroid tissue was pale and friable and appeared to invade the surrounding muscles. The immediate post-operative course was uneventful and x-ray therapy to the region of the thyroid was begun. She was readmitted to Stracathro Hospital on September 24 because of an erythematous rash on her face. At this time the total white blood cell count was 7,000 per c.mm. and the differential count normal. She was readmitted again to Stracathro Hospital on November 18 and January 11, 1948, because of recurrent attacks of increasingly severe dyspnoea with cyanosis and stridor, and she died on January 14, 1948.

Summary of Relevant Macroscopic Findings.—There was no emaciation, jaundice, or enlargement of the superficial lymph nodes. In the neck a small mass of apparently normal thyroid tissue, approximately 2 cm. in diameter, was found on the left side of the trachea and oesophagus. There was no evidence on the right side of any thyroid tissue or recurrence of the tumour and the neighbouring lymph nodes appeared normal. The tracheal bifurcation and main bronchi were enveloped in a mass of tumour tissue which

did not appear to be of bronchial origin. The tumour mass, which was white and homogeneous at its periphery, showed central necrosis and haemorrhage and, in general, had the appearance of a mass of confluent lymph nodes. No primary bronchial tumour could be demonstrated in either lung. The stomach contained two hard, discrete neoplastic ulcers with rolled edges and excavated centres. One, measuring 3 cm. in diameter, was situated on the anterior wall of the stomach, towards the cardia, while the other, measuring 5 cm. in diameter (Fig. 12), was situated on the greater curvature, midway between the cardia and the pylorus. The intervening gastric mucosa was normal, as was the rest of the stomach. The remainder of the alimentary tract was normal and there was no enlargement of the regional lymph nodes. No metastases were visible in the liver or in any of the other abdominal organs. Permission to examine the brain was withheld.

Histology.—The thyroid tumour was highly cellular and anaplastic, consisting predominantly of round cells, which possessed scanty cytoplasm and rather pale staining nuclei. Scanty cells of reticulum cell type were present, as well as lymphocytes and moderate numbers of mitoses (Figs. 13 and 14). Examination of the ulcers in the stomach showed that they also were composed of anaplastic tumour tissue, consisting predominantly of round cells similar to those seen in the thyroid tumour. Here again lymphocytes, cells of reticulum cell type, and mitoses were present in small numbers. The tumour in both cases was situated in the submucosa and was infiltrating the deeper layers of the mucosa as well as the muscularis. The appearances of the mass at the tracheal bifurcation were essentially the same as those of the gastric and thyroid tumours, and there was no evidence of reticulin formation in any of the tumours.

The cytological appearances of the gastric tumours indicate that they are of the lymphoblastic variety of reticulosarcoma. The histological similarity between them, the mediastinal mass and the thyroid tumour, shows that the latter two are also foci of lymphoblastic reticulosarcoma. It is impossible to decide which of the four foci is the primary tumour or whether the disease is of multifocal origin, but the absence of involvement of the regional lymph nodes in the neck suggests that the thyroid tumour may not be the primary focus.

Discussion

In the past, great reliance seems to have been placed on the presence of a fine reticulin network, lying in close apposition to the tumour cells, as well as on the cytological appearances of the latter, as diagnostic criteria of reticulosarcoma of the thyroid. However, Robb-Smith (1938) demonstrated that by no means all reticulosarcomata produce reticulin, and that, whereas it is abundant in the polymorphic and dictyocytic varieties, it is virtually non-existent in the syncytial and lymphoblastic tumours.

It has been demonstrated in Case 1 that the presence of a reticulin network in an anaplastic thyroid tumour by no means excludes the possibility of that tumour being a carcinoma. Also, it is well known that the degree of anaplasia and pleomorphism shown by some malignant tumours makes it impossible to decide, from the cytological appearances alone, whether these tumours are of epithelial or mesenchymal origin.

Thus the conclusion is reached that the cytological appearances of an anaplastic thyroid tumour and the presence or absence of reticulin production in that tumour are unreliable as diagnostic criteria of reticulosarcoma of the thyroid. Although these features in a thyroid tumour may raise the possibility of its being a reticulosarcoma, it is believed that the final diagnosis should not be made on examination of the thyroid tumour alone and that recourse should be had to collateral evidence

where possible. The absence of this collateral evidence has possibly led, in part at least, to the considerable variation in the incidence of these tumours between different observers. With the exception of Case 34032 of the Massachusetts General Hospital and Case 3 above, both of which came to necropsy, all the cases cited in the introduction to this paper were apparently diagnosed on histological examination of the thyroid tumour alone. Two of the cases presented by Rice (1932) and four of those presented by Kellett and Sutherland (1949) were dead at the time of these authors' reports, but no necropsies were performed.

It is only by the demonstration of other foci of tumour, which by their situation and macroscopical and microscopical appearances leave little doubt that they are foci of reticulosarcoma, that the final diagnosis can be made with any degree of certainty. This is well demonstrated in Cases 2 and 3, in which the diagnosis of reticulosarcoma, considered as a possibility at the time of the examination of the thyroid tumours, was confirmed only by the subsequent finding of collateral evidence of the type mentioned above.

Summary

Attention is drawn to the difficulty of making a histological distinction between reticulosarcomata and certain anaplastic carcinomata of the thyroid. The relevant literature is reviewed and the opinion expressed that the frequency with which a diagnosis of reticulosarcoma of the thyroid is made varies greatly between observers according to the diagnostic criteria employed. One case of anaplastic carcinoma and two cases of authenticated reticulosarcoma of the thyroid are presented. From a study of these cases, the conclusion is reached that the cytological appearances, as well as the presence or absence of reticulin, are unreliable diagnostic criteria and should not be used as a means of making the final diagnosis, the latter being withheld in the absence of collateral evidence, the nature of which is described.

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