Morphogenesis of testicular tumours

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SYNOPSIS A case is described in which death resulted from multiple trophoblastic teratomatous metastases arising, apparently, from a seminoma of the left testis. This occurrence is discussed and related to similar cases recorded in the literature. It is concluded that these cases continue to provide some evidence for the seminomatous origin of teratomas.

The occurrence of non-seminomatous metastases with primary seminoma of the testis was reported by Friedman (1951) who concluded from this and other evidence that seminomas were precursors of teratomas of the testis. This conclusion has been challenged by Azzopardi and Hoffbrand (1965) who, while studying retrogression of both seminomas and teratomas of the testis, claimed that the histology of the cases described by Friedman showed both seminoma and retrogression of a teratoma and that the retrogressed teratoma must have been the origin of the metastases.

The case described here is one in which the patient died from widespread trophoblastic teratomatous metastases associated with a seminoma of the left testis in which, despite the most careful histological examination, no trace of retrogressed teratoma could be found.

CASE HISTORY

J.C., a 25-year-old soldier, presented on 2 October 1965 complaining of abdominal pain and vomiting of a few weeks' duration. A chest radiograph taken on admission showed multiple bilateral pulmonary metastases. A careful search for a primary was made and a small nodule was felt on the anterior surface of the left testis and moderate bilateral gynaecomastia was noted. Hormone tests were carried out: Gravindex\(^{1}\) gave a positive result; Pregnosticon\(^{2}\) positive; Prepurerin\(^{3}\) positive 1:16,000; and the Hogben test was positive 1:100.

17-Ketosteroids showed an excretion of 7.8 mg./24 hr. (normal 10-20 mg./24 hr.) and pituitary gonadotrophins showed an excretion of 38 h.m.g. units/24 hr. (within normal limits). In view of the positive hormone tests, bilateral gynaecomastia, and multiple metastases, a diagnosis of trophoblastic teratoma was made and a left orchidectomy was performed. After orchidectomy the patient's condition continued to deteriorate and he died four days later, only three weeks after his first admission to hospital.

PATHOLOGY

ORCHIDECTOMY SPECIMEN The left testis was small and measured 4 × 3 × 2 cm. The cut surface showed a small homogeneous greyish tumour of about 2 × 1 cm. diameter with an irregular margin merging gradually with the testicular parenchyma (Fig. 1). Both the epididymis and vas deferens appeared normal. Histological examination showed that the tumour consisted of large, round, clear cells resembling seminoma cells with a stromal reaction and lymphocytic infiltration (Fig. 2). The seminoma cells were both intratubular and interstitial in position and they occurred in several foci in the testis surrounded by dense fibrosis associated with obliteration of the seminiferous tubules (Fig. 3). No haematoxylin-staining deposit was seen. The areas remaining of the testis which were unaffected by either tumour or dense fibrosis showed tubular atrophy with loss of spermatogenesis, thickening of the basement membrane and marked interstitial cell hyperplasia. Seminoma cells were found in the rete testis, the lower end of the cord, and the lymphatics.

The complete specimen was blocked and the material forwarded to the Testicular Tumour Panel and Registry where all the blocks were sectioned serially and the sections examined at 50-60 μ intervals throughout each block. This failed to reveal any tumour other than seminoma of the testis.

POST-MORTEM EXAMINATION The body was that of a well developed, somewhat emaciated young man with slight enlargement of both breasts and evidence of recent left orchidectomy. The right testis was present and felt normal.

Central nervous system The brain showed several haemorrhagic tumours both small and large (approx. 2.5 cm. diameter). There were three in the right frontal lobe, one in the left parietal lobe, one in the right cerebellar hemisphere, and one on the surface of the left parietal lobe.
FIG. 1. Cut surface of left testis showing small irregular greyish tumour (×2).

FIG. 2. Left testis. Seminoma showing stroma infiltrated with lymphocytes (haematoxylin and eosin ×50).

FIG. 3. Left testis. Zone of fibrosis around seminoma (haematoxylin and eosin ×6).
Morphogenesis of testicular tumours

all similar and typical of trophoblastic teratoma (Fig. 4). The tumour cells in general were limited to a narrow zone at the circumference of the blood clot and this feature was specially marked in the brain metastases. Apart from the gross metastases found on post-mortem examination, microscopic foci were also found on sectioning both kidneys and both adrenals.

The right testis showed normal seminiferous tubules with active spermatogenesis and a diffuse interstitial cell hyperplasia was present. The specimen was blocked completely and serial sections failed to reveal any tumour.

DISCUSSION

This case demonstrated the presence of widespread trophoblastic teratomatous metastases apparently arising from a primary seminoma of the left testis. Widespread metastases of trophoblastic teratoma associated with a fibrotic lesion of the testis was first reported by Prym (1927) and he interpreted the testicular lesion as being indicative of complete regression and fibrous replacement of a primary malignant testicular tumour which at some time had given rise to the trophoblastic metastases. Further similar cases have been reported in the literature, and Rather, Gardiner, and Frerichs (1954) reviewed 18 of these and described six new cases of their own. In seven of these 24 cases only scar tissue was found in the testis, in nine there were foci of seminomatous tissue in addition to fibrosis, and in the remaining eight there were cysts and tubular structures lying in zones of fibrosis containing foci of calcification and haemosiderin deposition. The first of the six new cases described in their paper has many features similar to those described in the case reported here.

Azzopardi, Mostofi, and Theiss (1961) made a detailed study of the testicular lesions in 17 cases from the files of the Testicular Tumour Registry of the American Armed Forces Institute of Pathology who had died with widespread trophoblastic and teratomatous neoplasms frequently associated with gynaecomastia. In all these cases a distinct and well defined fibrous scar was found in the testis. In addition, in 13 of the cases peculiar amorphous haematoxylin-staining deposits were observed in dilated seminiferous tubules which probably represented burnt-out primary testicular tumour. In eight of the cases there were remnants of differentiated teratoma and in four cases there were microscopic foci of seminoma in relation to the scars. In the unscarred zones of the testis atrophy and hyalinization of the seminiferous tubules were noted with hyperplasia of the interstitial cells.

The testicular histology of the case reported here differs from any of the cases reported by Azzopardi et al. (1961) in that the seminoma of the testis was

Thorax There was a haemorrhagic tumour of the right parietal pleura and the hilar lymph nodes were enlarged and haemorrhagic on both sides. Both lungs contained about 15 round haemorrhagic tumour masses, varying in size from 1 to 4 cm., with congestion and oedema of the intervening lung tissue. The pericardium, heart, and great vessels showed no abnormality.

Abdomen A 200 ml. blood clot was found on the right lateral surface of the liver and the liver itself contained about 10 round tumour masses varying in size from 1 to 4 cm. All were markedly haemorrhagic on cross section and most were in the right lobe, some just under the surface.

The left retroperitoneal lymph nodes were greatly enlarged and displaced the left kidney upwards and laterally. They consisted of a haemorrhagic mass measuring $10 \times 6 \times 7.5$ cm. which surrounded the left ureter and was adjacent to the aorta, left adrenal, and the duodenum. The spleen, pancreas, and the gastrointestinal tract were normal and no gross abnormality was noted in the genito-urinary tract or in the endocrine glands. The right testis showed a normal cut surface.

HISTOLOGY Sections of the tumour masses in the brain lungs, liver, and left retroperitoneal lymph nodes were

FIG. 4. Liver. Trophoblastic teratoma with clearly defined syncytial and cytrophoblastic elements (haematoxylin and eosin ×50).
much larger and, although it was associated with fibrosis and diffuse atrophy and scarring of the testis, there were no haematoxylin-staining deposits present nor was there any evidence of differentiated teratomatous structures. In this case the histological appearances more closely resemble those described by Dixon and Moore (1952) as indicative of a fibrous stromal response to seminoma together with the tubular atrophy and interstitial cell hyperplasia which are described as frequent concomitants of malignant testicular tumours by Field (1963).

In a further report Azzopardi and Hoffbrand (1965) described a case of retrogression of a testicular seminoma associated with seminomatous metastases and they made a clear histological differentiation between retrogressed seminoma and retrogressed teratoma of the testis. They felt that this distinction was extremely important as it helped to disprove Friedman's (1951) conclusion that seminoma is the precursor of malignant teratoma. Friedman had described four cases of seminoma with non-seminomatous metastases in which the testis was studied by the multiple block method and found to be pure seminoma. Azzopardi and Hoffbrand (1965) have suggested that in these cases retrogressed teratoma may have been present as well as seminoma and that this retrogressed teratoma was responsible for the non-seminomatous metastases — not the seminoma.

However, in at least one of the cases described by Rather et al. (1954), in which a primary seminoma was associated with trophoblastic metastases, no evidence for a retrogressed teratoma was given and in the case described in this paper there was no evidence either so it would seem that the occurrence of cases such as described here will continue to raise questions about the morphogenesis of testicular tumours.

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