

CHORIOCARCINOMA ARISING IN THE MALE MEDIASTINUM

BY

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(RECEIVED FOR PUBLICATION AUGUST 14, 1952)

Choriocarcinoma of extragenital origin is a rare condition. Bonn and Evans (1942) could find only 30 reports in the literature, and rarer still are tumours of this nature which grow from the mediastinum. The following case, therefore, appears to merit reporting.

CASE REPORT

A 26-year-old man, the father of two children, was admitted on May 2, 1949, complaining of pain in the chest, coughing up blood, feverishness, and shortness of breath. His illness began four weeks before this date with a pleuritic pain in the left upper chest. Three days after first experiencing this pain he coughed up the first of daily half-cupfuls of blood-stained sputum. Intermittent fever had set in some three weeks before admission. Till then, but for these symptoms and signs, the patient had felt in fair general condition, and

had not lost weight. During the week preceding admission he had noticed enlargement of the left breast which, like its fellow, had previously been normal.

Clinical examination revealed a young man, not obviously seriously ill. There was no dyspnoea or cyanosis at rest. A large area of stony dullness was outlined from the hilum to the anterior axillary line on the left side. There was bilateral gynaecomastia amounting to a protrusion of 1 inch. Radiographs of the chest showed a large, dense opacity (Fig. 1) occupying most of the lower two-thirds of the left chest, with many round opacities in the opposite lung field.

The patient's condition deteriorated rapidly. Small haemoptyses occurred daily, and dyspnoea and cyanosis increased. Radiographs of the skeleton revealed no bony metastases. He died two weeks after admission, the total duration of the illness having been six weeks.

NECROPSY.—Both breasts showed diffuse symmetrical enlargement, forming smooth discs 4 in. in diameter and $1\frac{1}{2}$ to 2 in. high. No secretion could be expressed. Cutting into them on the pectoral aspect, the appearance resembled the immature female breast—only firmer and less fatty. The left pleural cavity was filled with clotted blood. There was a large, dark red, roughly lobulated tumour extending from the mid-sternum to the left chest wall and from the third costal cartilage to three-quarters of the way down on the anterior pericardial aspect (Fig. 2). It was growing into the hilum of the left lung, had penetrated the pericardium, and had begun to invade the left auricle and anterior left chest wall. Both lungs contained numerous spherical deposits up to 2 in. in diameter. The main tumour and the satellites were partly necrotic, grossly haemorrhagic, and presented a friable, brownish-red to murky grey cut surface, which showed a honeycombing in parts.

A search of the bronchi failed to reveal a primary tumour. The liver and kidneys showed smaller but similar deposits of tumour. All organs, including the cranial contents, were examined for a possible primary tumour, and, in view of the gynaecomastia, both testes were cut into thin slices in the fresh state and re-sliced at 2 to 3 mm. intervals after fixation; but no possible primary, other than the tumour in the anterior mediastinum, was found.

Histopathology.—Thirty-five blocks were taken from different sites of the mediastinal tumour, and 23 from

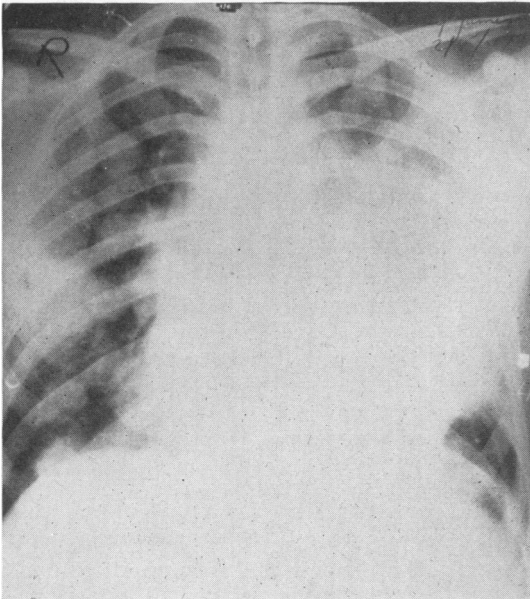


FIG. 1.—Radiograph on the day of admission. Mediastinal tumour extending to left: secondaries right lung and left apex.

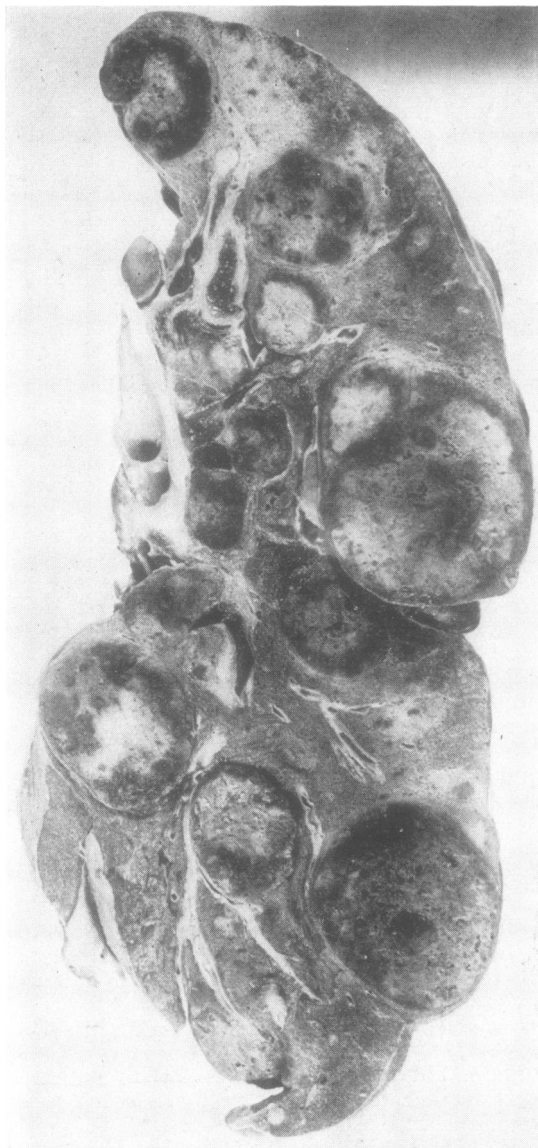


FIG. 2.—Sagittal section of the right lung showing haemorrhagic spherical deposits of choriocarcinoma.

the nodules in the lungs, liver, and kidneys. All these showed a uniform appearance, and varied only in the extent of necrosis and haemorrhage. Figs. 3 and 4 show the details of the histology. There was invasion of veins by tumour cells at the periphery of the various deposits, but within the tumour itself blood vessels were not found, but pools of blood bathed the broad syncytial-covered columns and sheets of cells. No teratomatous structure was seen in any of the sections. Slides of numerous blocks from each testis showed only complete depression of spermatogenesis, slight atrophy of tubules, and relative prominence of Leydig cells.

DISCUSSION

The history of the establishment of choriocarcinoma as a specific neoplasm is stormy. Teacher (1903) gives Sanger the credit for recognizing it in 1889 as a specific disease of pregnancy. Later, Marchand (1895a and b) identified the site of origin as the chorionic epithelium.

Before Marchand peculiar tumours of the testes had been recognized and described under a variety of names, e.g., "myxoma intravasculare" of Waldeyer (quoted by Bonney, 1907), "sarcoma angioplastique" of Malassez and Monod (1878), "perithelial sarcoma" or "haemangioendothelioma" of Sternberg (quoted by Hornicke, 1923). In 1902 Wlassow (quoted by Frank, 1932) saw in these tumours a resemblance to chorionic elements. In the same year Schlagenhauser (1902) recognized choriocarcinomata arising in teratomata, though Teacher (1903) states that Kanthack, Pigg, and Eden were the first (1897–8) to notice chorion-epithelioma occurring unrelated to pregnancy. Soon the discovery of similar growths in virgins and in the male testes caused the British Chorion-epithelioma Commission to revert to the name "decidual sarcoma."

Extragenital choriocarcinoma is now well established, though some authorities (Willis, 1948) remain sceptical. Bostroem's (1902) case was probably an example of retroperitoneal origin. Askanazy (1906) recorded a tumour arising in the pineal gland of a youth of 19 years, while Bonney (1907) described a primary site in the omentum. Ritchie (1903) was apparently the first to describe choriocarcinoma arising in a mediastinal teratoma.

Prym's case (1927) led to scepticism in the interpretation of extragenital chorionepitheliomata. He noted a vascularized scar in the right testis of the patient, and this, associated with a distribution of metastases in keeping with a testicular origin, led him to postulate spontaneous healing of a primary testicular growth. Following this observation, the criteria of acceptance of primary extragenital cases have become more strict. Hirsch, Robbins, and Houghton (1946) stress the necessity for taking multiple sections from the testes, and on this basis they admit 14 cases to the literature. Others (Bonn and Evans, 1942; Erdmann, Brown, and Shaw, 1941; Laipply and Shipley, 1945) demand serial block sections of the testes together with hormonal studies of the urine and of the tumour, and they accept only five to eight cases as authentic.

Many tumours resembling Prym's case have been recorded (Bonn and Evans, 1942; Heaney, 1933;

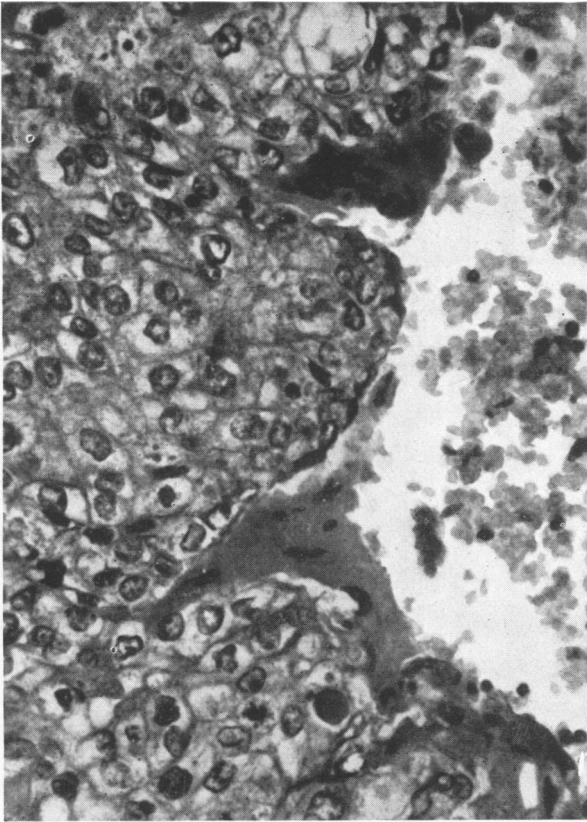
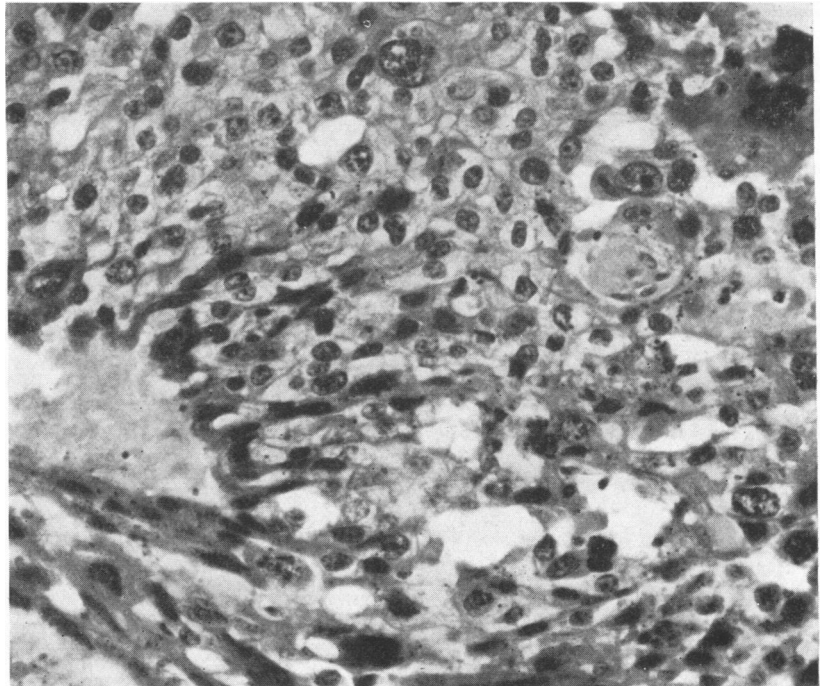


FIG. 3.—Deposit in liver, showing a sheet of vacuolated cells clothed on the free surface by syncytium bordering a blood lake. Haematoxylin and eosin, $\times 375$.

FIG. 4.—Primary (mediastinal) tumour showing characteristic cell types and arrangement. Haematoxylin and eosin, $\times 240$.



Craver and Stewart, 1936 ; Rottino and DeBellis, 1944). Bonn and Evans (1942) attributed the soft testicular scar with small round-cell infiltration to trauma suffered five years previously. Two small nodules in the left testis of Craver and Stewart's (1936) case showed squamous epithelial and mucous gland structures.

While the tendency has been to interpret these testicular scars, teratomata, and areas of haemorrhage in the testicles as the origin of choriocarcinomata, no one has considered that the scars might themselves be the results of extragenital growths. Moreover, a traumatic origin for such scars cannot be overlooked. Further, it is possible that the intense hormonal stimulation may cause totipotent gonadal cells to develop into small teratomata such as Craver and Stewart and Rottino and DeBellis found, while deposits on the tunica vaginalis of the latter show how secondary spread to the testis may occur by way of the left testicular vein. That there are a number of recorded examples (Park and Lees, 1950) of spontaneous regression of primary choriocarcinoma does not mean that this may be invoked to explain testicular scarring or haemorrhage found in association with an otherwise apparently primary extragenital choriocarcinoma.

Klemperer (1932) reminds us that teratomata may metastasize with all their structures (Virchow, 1871). Frank (1906) was of the opinion that such

composite metastases derived from the entry into the circulation of totipotent blastomere-like cells. Choriocarcinoma may arise in the secondary deposits, while the primary teratoma retains its characteristics.

The strictness of criteria of interpretation arising out of Prym's observations has been criticized by many. Houghton (1936) points out that in Greiling's study of 220 cases of metastasizing testicular tumours there was not a single case which showed secondary deposits in the anterior mediastinum. Some (Stowell, Sachs, and Russell, 1945) go so far as to question the spontaneous healing of primary chorionepithelioma.

The origin of extragenital choriocarcinoma is bound up with the origin of dermoids and teratomata. The most acceptable theory of origin of these growths is that they develop from multipotent or totipotent cells split off at the morula or blastula stages, or from the totipotent cells of the gonads. Staemmler (1934) was able to find testicular rests in the retroperitoneal tissues at the roots of the mesenteric vessels. This is not surprising in view of the fact that the urogenital ridge in the 8 mm. embryo extends a distance of 15 somites, viz., from the definitive sixth cervical to the third lumbar segment (Arey, 1940). The origins of retroperitoneal (Erdmann *et al.*, 1941; Fenster, 1934; Gerber, 1935) and mediastinal (Bonn and Evans, 1942; Arendt, 1931; Houghton, 1936; Laipply and Shipley, 1945; Hirsch *et al.*, 1946) choriocarcinomata have been attributed to elements of this structure. Ewing (1940) believed that complex teratomata grew from aberrant sex cells.

The origin of mediastinal dermoids and teratomata has been attributed by many to a branchiogenic source (Christian, 1902; Hedblom, 1933); such inclusions have been noted to have connexions with the thymus (Ekehorn, 1898). Hence, a derivation has been postulated from the third branchial pouch and cervical sinus. However, the majority of mediastinal dermoids are cystic structures, in which if choriocarcinoma were to develop, one would expect to find remnants of hairs and bone. In fact, records of such tissues being found in mediastinal chorionepitheliomata are few, for example, in the cases of Ritchie (1903) and Laipply and Shipley (1945). The possibility of a small teratoma being overgrown by choriocarcinoma developing in it, and of its dying and being obliterated by haemorrhagic ischaemic necrosis, has been emphasized by Hörnicke. It seems to us, however, that the majority of choriocarcinomata developing in teratomata do so at an early stage in the life of the latter, possibly from the very start

of unusual proliferation of the totipotent cell, though exceptions are on record.

Of 185 cases of intrathoracic dermoids reviewed, and six personal cases added, Hedblom (1933) found 17 (8.9%) to have been malignant. Up to the time of Houghton's (1936) writing 25 more cases of intrathoracic dermoids had been recorded, i.e., a total of 216 cases, of which 25 in all were malignant. Of these Houghton listed five as being choriocarcinoma. In Hedblom's series, where the sex was given, 79 were men and 92 were women, yet none of the latter developed choriocarcinoma. Stowell *et al.* (1945) found in the literature 16 reports of extragenital choriocarcinoma in the female, and in most of these an association with pregnancy could not be excluded. This has been the experience of one of the authors in an ovarian chorionepithelioma, and we are not aware of any case in the literature of primary choriocarcinoma in the female mediastinum. If we are to assume that extragenital and, in particular, mediastinal choriocarcinoma in the male derives from the same type of totipotent cell, which in the female develops to a dermoid or teratoma, we must come to the conclusion that a difference of environment accounts for this unequal fate of a similar cell type. From the reviews of Ekehorn (1898) and Hedblom (1933) it is apparent that the majority of dermoids and teratomata come to light shortly after puberty. In 15 recorded cases of extragenital choriocarcinoma—12 of which occurred in the mediastinum—the average age was 26.1 years. Thus, the onset of both types of tumour follows the attainment of sexual maturity, and the action of androgenic hormones appears to predispose to the development of choriocarcinoma from a misplaced totipotent cell.

SUMMARY

A case of choriocarcinoma arising in the mediastinum of a young man is described. The literature is reviewed, and the sex difference in incidence stressed. Possible aetiological implications of the latter are discussed.

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