CHORIONEPITHELIOMA IN THE MALE

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Chorionepithelioma in the male is of rare occurrence, although many cases in the female have been reported. In 120 cases of teratoma testis Ferguson found none of chorionepithelioma. Our own tumor records, containing over 100 reports of teratoma testis, include three cases of chorionepithelioma, of which two are reported here. Quantitative biological assays of the urine for prolan were made in both cases. Search of the literature reveals not over 12 cases of chorionepithelioma testis in which biologic hormonal assays were conducted, the case of Heidrich, Fels and Mathias being the first reported.

ETIOLOGY

Since Marchand in 1895 first used the term chorionepithelioma to describe these tumors in the female, a variety of theories have been advanced as to the probable origin or cause of these growths. While no positive statement can be made at present concerning the origin, there are many interesting facts worthy of consideration. Valuable information has been obtained from a study of these tumors in the female. The trophoblast is known to be normally an invasive type of tissue and chorionic cells are reputed to possess the property of digesting the maternal tissues. The embedding of the ovum is thought to be accomplished by the aid of this characteristic. The cells of the trophoblast are naturally endowed with great capacity for growth. Schmorl has reported trophoblastic emboli in 80 per cent of women during normal pregnancies. This parasitic tissue then is able physiologically to invade and wander. Blair Bell offers the opinion that chorionic epithelium, more particularly the syncytium, is originally of a malignant nature, although after a few weeks it comes naturally under the influence of the developing fetus and its growth is arrested at a stage where it becomes subservient to the dependent embryo. Support for this theory exists in the work of Fraenkel, who demonstrated that the serum of normal pregnant women is lytic to chorionic epithelium while the serum of women with chorionepithelioma lacks this property.

In explaining chorionepithelioma in the female it is assumed that the growth arises from a previous hydatid mole or from a placental

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FIG. 1. CASE I: PRIMARY CHORIONEPITHELIOMA OF THE RIGHT TESTIS SHOWING A RESEMBLANCE TO CHORIONEPITHELIOMA IN THE FEMALE

FIG. 2. CASE I: MICRO-SECTION OF MALE BREAST (GYNECOMASTIA) SHOWING ACTIVITY OF COMPONENT PARTS IN CASE OF CHORIONEPITHELIOMA TESTIS

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remnant. Usually in these cases a history of pregnancy may be obtained. In the male, where tissues associated with pregnancy do not exist, other explanations must be sought. It is difficult to believe that males may have a structure with the morphologic value of an included ovum, which in turn may possess trophoblastic tissue, as has been suggested by Schlagenaufener, who first recognized that certain tumors of the testicle were histologically similar to the chorionepitheliomas of the uterus. Bostroem believed that these tumors in the male might arise from undifferentiated germ cells (serotinal wandering cells), which, being affected by humoral influences, proliferate to form primary tumor cells. It is possible that some humoral agent may be concerned

in the etiology, since in the male an excessive amount of the anterior pituitary-like sex hormone is associated with these growths. Frank has regarded the formation of chorionepitheliomatous tissue in the male merely as evidence of a metaplastic change in an embryonal ectodermic structure which, under certain unrecognized conditions, is capable of producing this variety of tumor tissue, just as in response to other stimuli these tissues may undergo carcinomatous changes. Ross, in commenting on a case with pulmonary metastasis, states that it is unnecessary to presuppose even the presence of fetal ectoderm. She considers the tumor to be the expression of a process of specific partial differentiation of pluripotential cells in the testis. The pluripotential tendency in her case was not apparent from a study of the primary growth, which might be regarded as carcinoma. Local differentiation
may take place, as has been suggested by Ahlstrom. This would explain cases of carcinoma with chorionepithelioma in the absence of a teratoma.

Embryologically primary chorionepithelioma above the diaphragm would be difficult to explain since the diaphragm is said to arise from the fifth cervical segment, while the urogenital ridge is believed to arise from the sixth cervical segment.

Diagnosis

Tissues from orchidectomies are of value for diagnosis, but classification may be difficult because of necrosis and the fact, accepted by several workers, that the original growth may be exceedingly small and obscure. Prym reports a case where the primary tumor had undergone spontaneous regression.

The biological assay of the urine for prolan offers great hope for timely diagnosis, although such tests are usually not obtained early, due to the painless character of the growth. Chorionepithelioma testis is associated with a urinary output of prolan varying from 10,000 to 150,000 mouse units per liter. The teratomas are likewise associated with excessive amounts of prolan in the urine, but here the quantities range from 50 to 10,000 mouse units per liter depending upon the type of tumor. Since normal male urine contains less than 50 mouse units of prolan per liter, it is apparent that the increased amount of the hormone offers an index of diagnostic value in these cases. We have found quantitative biological assay for prolan especially useful in teratoma testis.

Treatment

Since these tumors consist of anaplastic and undifferentiated tissue, they may be expected to be highly radiosensitive. Once a diagnosis has been made, preoperative irradiation may be followed by radical surgical removal of the primary growth, with subsequent postoperative irradiation to the primary site. For metastatic areas, irradiation is at present the method of choice.

There is a possibility that treatment of these tumors may eventually be non-surgical, consisting in serum injections or endocrine therapy. In view of the observations made by Fraenkel it would seem that serum from pregnant animals holds promise of being beneficial. Such sera are now being utilized but it is too early to expect accurate findings. The very infrequency of chorionepithelioma testis will delay for some time an adequate report on this method of therapy, although results in chorionepithelioma in the female should be reported at an early date. Due to the close association of teratoma testis with chorionepithelioma, as evidenced by their endocrine relationship, it might be expected that the lytic agents occurring in pregnancy sera would also affect the teratomas. This is a problem worthy of investigation.
CASE REPORTS

Case I: A white male, aged about thirty-eight years, entered the hospital in March 1934, complaining of pain and aching in the right serotum, extending upward into the lower abdomen. Two years previously he had noticed beginning enlargement in the serotum. For several weeks before admission he had been unable to work. Examination revealed a tense enlargement of the serotum with a hydrocele on the right. Large tortuous veins were present, some the size of an ordinary lead pencil. The left testicle was palpable, but no structures were outlined on the right until about 350 c.c. of amber-colored fluid were removed, when all the structures were found to be involved in a hard nodular mass of tumor tissue. A diagnosis of teratoma of the right testis was made. The patient was transferred to another Veterans' Facility, where confirmation of the diagnosis was made and it was found that metastases were present in the lungs and in the inguinal and axillary lymph nodes. Prolan tests in March and in May of this same year yielded 10,000 and 16,000 mouse units of the hormone per liter of urine respectively. Death occurred in May, two months after the first hospitalization.

Post-mortem Findings: Palpable lymph nodes were present in the right axillary and in both inguinal regions. Both nipple regions were prominent, firm, and disc-shaped, measuring about 5 cm. in diameter. The bony structure of the hands appeared to be slightly enlarged. Along the mesenteric attachment, small yellowish and moderately firm masses were seen and felt. Similar but conglomerate masses were present over the ascending colon from the ileocecal junction to the hepatic flexure of the colon. A large conglomerate mass was present between the pancreas and the left kidney. On the superior surface of the liver was a mottled grayish and reddish tinged irregular area measuring 6 cm. in diameter. The heart presented no gross pathology.

In the lungs were numerous discrete nodules, some gray but most of them mottled red and gray. On section the nodules showed a spongy appearance, the gray tissue being quite friable. The right lung contained a few more than the left.

The spleen presented one grayish-red nodule which on section showed yellowish friable tissue interspersed with small hemorrhagic areas displaying a suggestion of encapsulation.

The gastro-intestinal tract disclosed no invasion of the mucosa, but slight pressure induced by the mass in the region of the cecum was observed. The liver contained sev-
eral smaller hemorrhagic and yellowish nodules in addition to a large area. The pancreas and suprarenal glands presented no gross pathology.

The kidneys displayed moderate dilatation of the calyces and the left contained two nodules of tumor tissue. Both ureters were dilated to about twice the normal diameter. A tumor mass definitely obstructed the right ureter near the urinary bladder and partially obstructed the left ureter. The urinary bladder was normal. The prostate contained a small abscess in the left lobe. The left testis was normal in size, shape, and appearance on section. The right testis was greatly enlarged, measuring 10 by 8.5 cm. in its two diameters. On section it appeared to be encapsulated and composed of yellowish friable tissue interspersed with small hemorrhagic areas.

The vascular system presented no marked changes. The lymphatic system showed marked involvement of the nodes adjacent to the esophagus, aorta and left kidney, and of the retroperitoneal node group.

The neck organs and skeletal system contained no tumor tissue. There were some areas of exostosis in the spine. The bone marrow and brain were not studied.

Case II: A white male of forty years entered the hospital in December 1934, complaining of severe headaches, difficulty in speech, and haziness, following a fall about one week earlier. He had observed a gradual enlargement of the left testicle since August 1934. Examination revealed some mental confusion, with spasticity of the left extremities. Voluntary movements of these showed marked awkwardness. There was some discoloration of the skin over the left ankle. Deep reflexes were exaggerated and there was an inconstant ankle clonus. The Babinski reflex was indefinite. The left scrotal sac contained a tumor mass about 10 by 8 by 6 cm. The right testis was of normal size and consistency. No lymphadenopathy was discovered. X-rays of the chest showed spherical masses, probably metastatic, in both lungs. The skull plates were negative. A diagnosis of teratoma of the left testis with metastases to the lungs and brain was made. Assay of the urine on Dec. 18, 1934, revealed 125,000 mouse units of prolan per liter.
FIG. 6. CASE II: METASTATIC, HEMORRHAGIC NODULES IN RIGHT PARIEtal LOBE OF THE CEREBRUM

FIG. 7. CASE II: INFRA-RED PHOTOGRAPH OF LUNG SHOWING METASTATIC CHORIONEPITHELIOMATOUS AREAS WITH HEMORRHAGIC FEATURES
Post-mortem Findings: Externally slight enlargement of the breasts was observed. Bloody fluid was present in both pleural cavities, about 400 c.c. in the left and about 300 c.c. in the right. One nodule of tumor tissue was found beneath the parietal pleura on the left, near the vertebral column. Section showed it to consist of grayish friable tissue with hemorrhagic areas.

The lungs presented many small and large nodules of tumor tissue, most of which were located in or near the pleural surfaces. Most of these nodules when sectioned showed hemorrhagic areas located chiefly along their peripheries. Lung tissue between the nodules was rather wet and boggy.

The spleen was somewhat soft and mushy. The jejunum contained several nodules of tumor tissue. These were located intramurally but one had penetrated the mucosa and presented a small ulcerated spot. The liver displayed three nodules in the posterior region of the right lobe. These on section did not disclose such large hemorrhagic areas as the pulmonary nodules and the necrosis was not so pronounced. The gallbladder, pancreas, suprarenal glands, and kidneys presented no gross changes. A tumor mass was found back of the peritoneum in the inguinal ring.

The urinary bladder, prostate and right testis were grossly negative. The left testis was greatly enlarged and measured 9 by 7 by 5 cm. It was moderately firm in consistency. On cut section it presented numerous bloody cystic areas with islands and strands of pinkish gray friable tissue. This tissue was streaked with a fine reddish network.

The vascular system and neck organs presented no marked abnormal changes. The only lymph nodes containing tumor tissue were those of the retroperitoneal region. The brain showed four reddish hemorrhagic nodules in the parietal region of the right cerebral hemisphere.

Sections from the primary tumors and metastatic nodules in both these cases disclosed typical characteristics of chorionepithelioma. In addition to the syncytial masses dipping into large areas filled with red blood cells, some strands appeared to have central connective-tissue cores with capillaries, thus resembling chorionic villi. Sections through the mammary glands presented an increase in number of acini, with an increased amount of fibrous tissue between them. The acini were moderately dilated and displayed evidence of activity.

Summary

1. Two cases of chorionepithelioma testis are presented, with gross and microscopic illustrations.
2. Prolan tests in each case offered confirmation of the diagnoses.
3. The urinary prolain output in chorionepithelioma testis exceeds that associated with pregnancy and testicular tumors of the teratoma type.
4. Evidence is cited which indicates that future treatment of these tumors may be serological in nature.
5. A study of the literature as to etiology is given, with comments and additions from the authors’ observations.

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REFERENCES


