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Sclerosing stromal tumor of the ovary

A hormonal, histochemical and ultrastructural study

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Summary. Three new cases of sclerosing stromal tumor of the ovary have been studied by hormonal, immunohistochemical and electron microscopic analysis. The results confirm that this tumor may have hormonal activity. Ultrastructural study shows findings different from those previously reported. The authors propose an origin from the ovarian stroma with luteinization of stromal tumor cells.

Key words: Sclerosing – Stromal tumor – Gonadal stromal tumor – Ovary

Sclerosing stromal tumor (SST) is a rare ovarian neoplasm first described by Charvardjian and Scully (1973). Since the original description few further studies have been reported (Damjanov et al. 1975; Scully 1977; Gee and Russell 1979). These tumors occur predominantly in young women and ultrastructural findings indicate that they are of ovarian stromal origin (Damjanov et al. 1975).

We describe 3 cases of SST studied by hormonal investigation, immunoperoxidase techniques and electron microscopy. This report attempts to define a more exact origin for these tumors and supports the concept that they may have hormonal activity.

Case reports

Case 1. A 15-year-old woman, gravida O-para O was examined in September 1979 because of amenorrhoea of 4 months duration. Menarche occurred at the age of 13 and her menses had been abnormal (hypomenorrhoea). Pelvic examination showed a tumor mass in the right ovary. A monolateral salpingo-oophorectomy was performed. The tumor, measuring 10 cm in diameter, almost entirely replaced the ovary. The external surface was smooth and showed some blood vessels in the capsule. Sectioning revealed a greyish-yellow soft-to-firm tumor surface. Small cysts filled with mucoid and serous fluid were also present as were focal haemor-

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rhages. Serum hormone analyses by radioimmunoassay techniques (Pelusi et al. 1979) showed a difference in the testosterone (T) and androstenedione (A) levels before (T: 0.69 ng/ml; A: 218 ng/100 ml) and after surgical removal of the tumor (T: 0.47 ng/ml; A: 60 ng/100 ml). After surgery the menses returned to normal and 3 years later the patient is still well.

Case 2. A 26-year-old-female, gravida O-para O was admitted to Policlinico S. Orsola in December 1980 because of a right adnexal mass found on a routine follow up examination for an episode of dysfunctional uterine bleeding and pelvic pain. Menstrual cycles had been regular since menarche at age 13. No differences in the serum hormone levels before and after monolateral salpingo-oophorectomy were observed. The tumor measured 6 cm in diameter and had aspects similar to those observed in case 1. After surgery, menses resumed spontaneously and were regular. Two years later the patient is still well and there is no clinical evidence of the disease.

Case 3. A 41-year-old-female, gravida 1-para 1, was admitted to the B. Trento, Verona, Hospital and underwent a hysterectomy and bilateral salpingo-oophorectomy for uterine fibromyomas. In the right ovary a tumor was discovered accidentally, having a diameter of 2 cm. No hormonal studies were done. The patient is still well 1 year after surgery.

Materials and methods

Tissues from all tumors were fixed in Carson, processed to paraffin, and cut at 5 μ. They were stained with haematoxylin and eosin, periodic acid-Schiff, Alcian blue, mucicarmine, Gomori's reticulum and Masson's trichrome.

Frozen sections were cut by cryostat and stained for lipids using Oil red 0 stain. An immunocytochemical study was performed according to the PAP method (Pileri et al. 1980). We used rabbit antiserum against the human testosterone, androsterone and 17-estradiol, diluted 1/300.

Samples from the first tumor were also taken for electron microscopic examination. These were fixed in glutaraldehyde, post-fixed in osmium tetroxide and embedded in araldite.

Ultrathin sections were stained with uranyl acetate and lead citrate.

Pathology

At light microscopy the morphological findings were similar in all cases, but the immunoperoxidase results differed. The most characteristic features were a pseudolobular pattern with cellular and well vascularized areas separated by oedematous or fibrous stroma (Fig. 1). The predominant cells were round or polygonal (Fig. 2) and some of these had a clear or vacuolated cytoplasm (Fig. 3). Spindle cells and occasional signet-ring cells were also seen. The nuclei were round and infrequently reniform. Mitotic figures were uncommon. Gomori's reticulum stain demonstrated abundant pericellular reticulin. Oil red 0 stain demonstrated the presence of lipid material in the vacuolated tumor cells. This material failed to stain positively with periodic acid-Schiff stain, Alcian blue and mucicarmine. Testosterone and androstenedione were identified by the PAP technique in the cytoplasm of 10–15% of the tumor cells in case 1 only (Fig. 4). The electron microscopic study showed tumor cells similar in appearance, in apposition to each other and closely related to the capillaries (Fig. 5). The cells were generally oval or polygonal with round nuclei occasionally displaying deep indentations. Their cytoplasm contained short cisternae of rough endoplasmic reticulum, abundant tubular or vesicular smooth endoplasmic reticulum (Fig. 6),

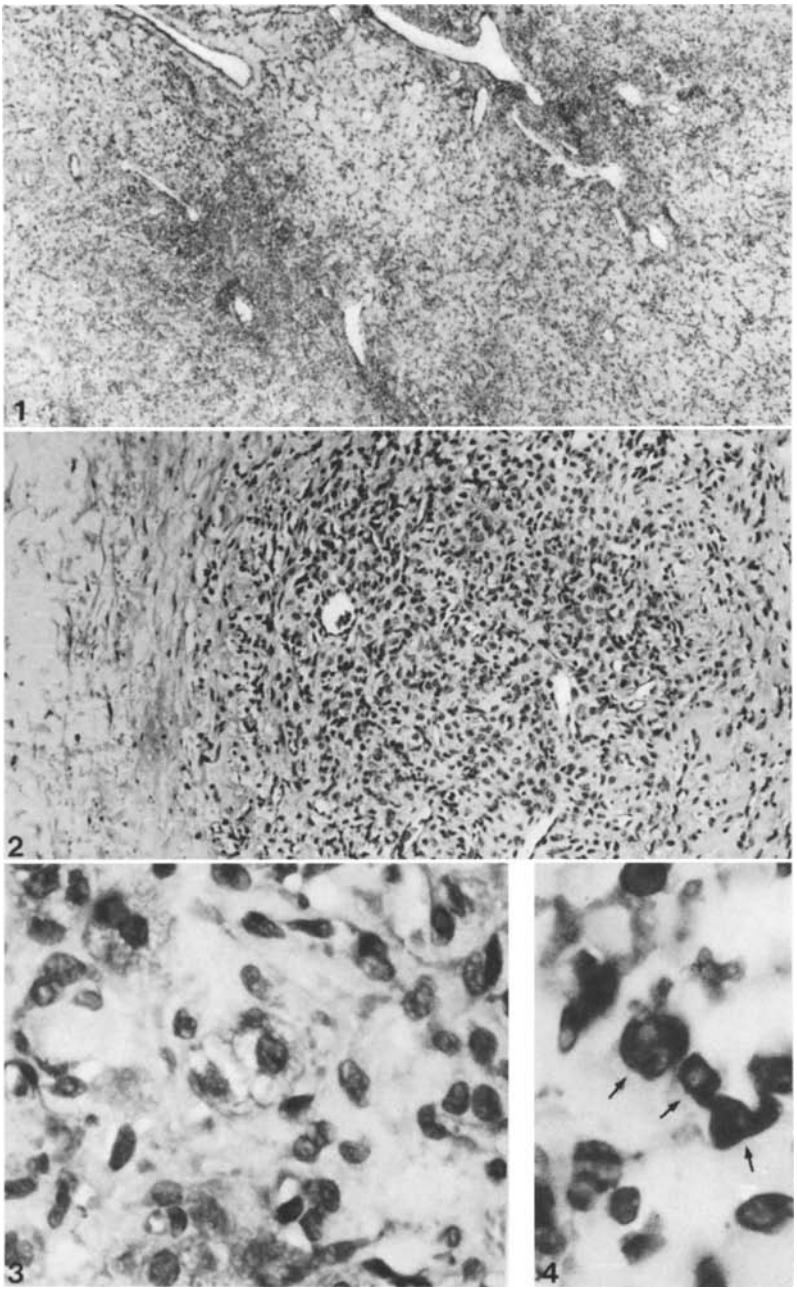

Fig. 1. Pseudolobular appearance produced by admixtures of cellular and oedematous background. H.E. × 26.4

Fig. 2. Cellular area alternating with oedematous or fibrotic zones. H.E. × 105.6

Fig. 3. Higher power of a cellular area showing elements with clear and finely vacuolated cytoplasm. H.E. × 422.4

Fig. 4. Intracytoplasmic localization of testosterone in some neoplastic cells (*arrows*). Peroxidase-antiperoxidase procedure × 1,000

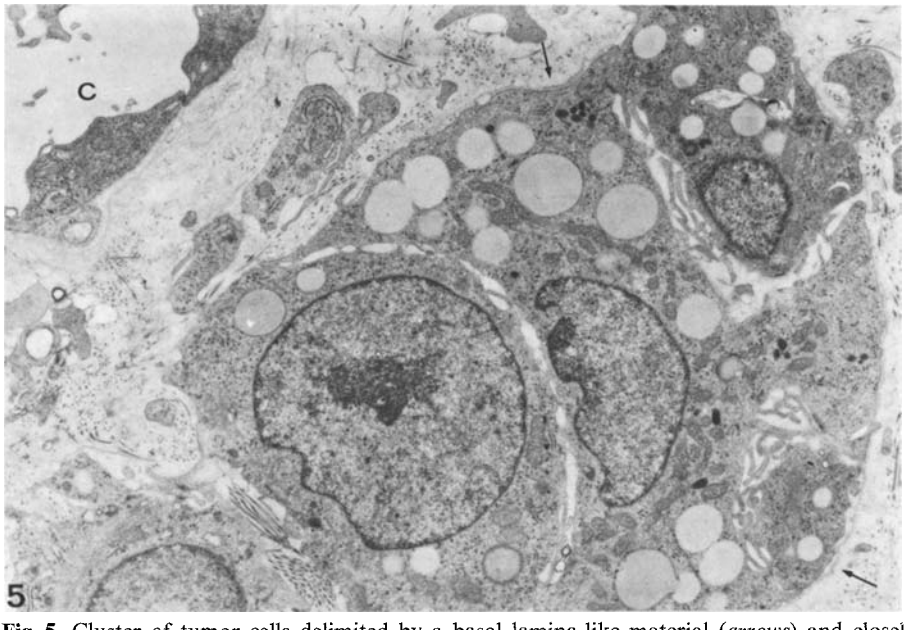

Fig. 5. Cluster of tumor cells delimited by a basal lamina-like material (*arrows*) and closely related to capillaries (*C*). Their cytoplasm shows rough endoplasmic reticulum cisternae, lipid droplets, mitochondria and primary lysosomes. Intercellular spaces contain interdigitating filopodial-like processes. × 3,900

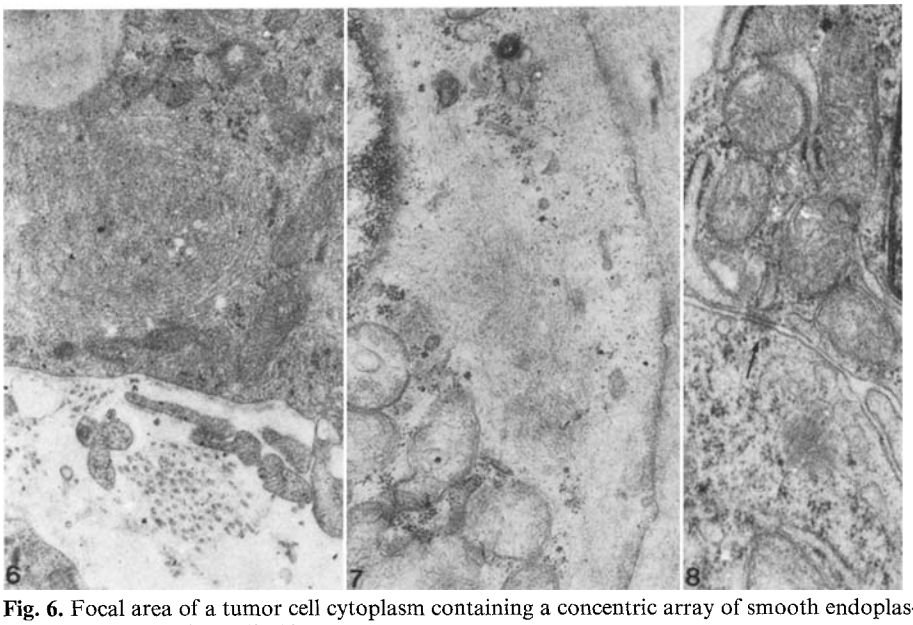

Fig. 6. Focal area of a tumor cell cytoplasm containing a concentric array of smooth endoplasmic reticulum tubules. × 7,830

Fig. 7. A bundle of intermediate filaments. × 18,570

Fig. 8. Plasma membranes of adjacent tumor cells joined by a desmosome-like structure (*arrow*). × 20,330

some primary lysosomes, numerous mitochondria with tubulo-vesicular cristae, many lipid vacuoles, dispersed Golgi apparatus, free lying polysomes and bundles of intermediate filaments (Fig. 7). In a few cells concentric membranous whorls similar to spironolactone-like bodies and pinocytotic vesicles were seen. The plasma membranes showed interdigitating processes projecting into the intercellular spaces; occasional immature desmosome-like junctions were found at the points of contact of adjacent cells (Fig. 8). A continuous deposition of basal lamina-like material surrounded clusters of neoplastic elements. The extracellular matrix contained collagen fibrils together with sparse fibroblastic-type cells.

Discussion

The light microscopic features of our cases are characteristic of a benign ovarian tumor first described by Chalvardjian and Scully with the descriptive term "sclerosing stromal tumor" (SST).

In SST the main microscopic appearance is the pseudolobular pattern produced by stromal oedema, sclerosis and cellular areas composed of round/polygonal/spindle cells. The cytoplasm of some cells may contain lipid droplets. Dilated vascular channels are seen in cellular areas, sometimes producing a haemangiopericytomatous aspect. These microscopic findings are peculiar and permit a differential diagnosis from other lesions such as signet-ring stromal tumor, ovarian myxoma, massive oedema and Krukenberg's tumor (Kalstone et al. 1969; Ramzy 1976; Majmudar et al. 1978; Roth et al. 1979; Holtz and Hart 1982). However, histological variations from the classical pattern towards either end of the thecoma-fibroma spectrum have been reported (Gee and Russel 1979).

As in our observations, SST generally occurs in patients under 30 years of age. Hormonal activity is considered unusual in these tumors, and detailed endocrinological plasma studies had not been performed on previously reported cases. Only our first case showed significant differences in the endocrine serum levels before and after surgical removal of the neoplasm, suggesting an androgenic activity clinically responsible for the amenorrhoea. The immunoperoxidase technique confirmed the hormonal function, and the recurrence of a normal cycle after surgery may be considered as additional proof.

Regarding the histogenesis, SST appears to derive from the ovarian stroma (Chalvardjian and Scully 1973; Damjanov et al. 1975). The electron microscopic appearance of our tumor supplies further evidence for stromal ovarian origin, showing, in addition, different features from those described by Damjanov et al. (1975). In fact, in our case the neoplastic elements were quite similar to each other and more often arranged in nests and closely related to the capillaries. Moreover the tumor cells showed desmosome-like structures, interdigitating cytoplasmic processes and basal lamina-like material. They had, in common with those of Damjanov's case, structures such as tubular mitochondrial cristae, abundant rough or smooth endoplasmic reticulum, lipid droplets, lysosomes and cytoplasmic intermediate filaments. Ultrastructural aspects similar to those observed by us can be seen in differ-

ent types of ovarian stromal tumors, such as Sertoli cell tumors (Murad et al. 1973; Ramzy and Bos 1976; Tavassoli and Norris 1980), granulosa cell tumors (Bjersing et al. 1973; Roth et al. 1979; Lack et al. 1981), hilus cell tumor (Paradisi et al. 1982), lipid ovarian stromal tumor (Kempson 1968; Ishida et al. 1977), luteoma (Garcia-Bunuel and Brandes 1976) and fibro-thecoma (Toker 1968; Amin et al. 1971). These ultrastructural similarities indicate that SST is of ovarian stromal origin. Nevertheless these findings are non-specific and do not fully identify the present tumor with any of the tumors reported above. Our case might be correlated more closely with lipid cell tumors and luteoma, both in the way the neoplastic cells are aggregated and by their cytological appearances, with cytoplasmic changes similar to those observed in the luteinized cells of the corpus luteum.

In conclusion, our studies support the view that SST may have endocrine activity as documented by clinical, immunohistochemical and laboratory data and by ultrastructural findings which reveal the presence of tubular mitochondria cristae, abundant tubular or vesicular smooth endoplasmic reticulum, lipid droplets and dispersed Golgi apparatus. They also confirm that this tumor has an ovarian stromal origin. We suggest an origin from the stroma with luteinization of stromal tumor cells. However, our ultrastructural results do not permit a definitive conclusion on the histogenesis of this tumor and are in agreement with Gee and Russel who maintain that "the sclerosing stromal tumor may not be as clearly defined an entity as originally suggested".

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