

Case report

Signet-ring stromal tumor of the ovary: a histochemical, immunohistochemical and ultrastructural study

Asunción Suárez, Jose Palacios, Emilio Burgos, Carlos Gamallo

Departamento de Anatomía Patológica, Hospital "La Paz", Paseo de la Castellana, 261, E-28046 Madrid, Spain

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Abstract. We report a signet-ring stromal tumour found in the ovary of a 50-year-old woman. The solid tumour was composed of spindle and round cells which stained with vimentin and some round cells were vacuolated and had the appearance of signet-ring cells. The vacuoles were negative with periodic acid-Schiff, with and without diastase digestion, with alcian blue, Sudan III, alpha-1-antitrypsin and alpha-fetoprotein stains. Ultrastructurally, they were membrane bound and contained scanty flocculent material. Some neoplastic cells contained intracytoplasmic eosinophilic globules which were positive with alpha-1-antitrypsin. Signet-ring stromal tumour is a benign, morphologically distinctive type of ovarian stromal tumour, which may present problems in differential diagnosis with other stromal and non stromal ovarian neoplasms.

Key words: Ovarian sex cord-stromal tumour – Signet-ring cells

Introduction

Signet-ring stromal tumour was the term proposed by Ramzy (1976) to designate an unusual benign ovarian neoplasm of probable stromal origin. It was characterized by the presence of signet-ring cells that did not stain for lipid or mucin. No further reports have been made since this initial description, although Young and Scully (1987) have observed a similar case in a 34-year-old woman. We report the histochemical, immunohistochemical and ultrastructural study of an ovarian tumour in a 50-year-old woman like the one reported by Ramzy (1976), and which also contained multiple eosinophilic intracytoplasmic globules.

Case report

A 50-year-old woman, gravida 2, para 2, who had undergone menopause 3 years before, presented with a history of abdominal pain. Pelvic examination revealed a palpable mass located at the left hemiabdomen and ultrasound demonstrated a solid left ovarian tumour. A simple left oophorectomy was performed. Twenty-six months after surgery, the patient remains well, with no evidence of the disease. The ovarian tumour was solid, egg-shaped and measured 9 × 6 × 5 cm. Its outer surface was grey, smooth and glistening. The cut surface was white, with irregular yellowish areas that were firm and fasciculated in appearance. No oedematous, cystic, haemorrhagic or necrotic areas were noted. A thin rim of ovarian parenchyma was present at the periphery of the tumour (Fig. 1A).

Microscopically the tumour was composed of an admixture of spindle and round cells. Some of the round cells showed a typical signet-ring appearance, and were irregularly scattered through the neoplasm (Fig. 1B). Spindle cells showed elongated nuclei, nonvacuolated cytoplasm and were arranged in fascicles. The round cells had a single clear vacuole which compressed the nucleus and/or single or multiple intracytoplasmic eosinophilic globules. Spindle and round cells were surrounded by reticulin fibres and, except for their vacuoles and eosinophilic globules, showed positive cytoplasmic immunostaining for vimentin (Dakopatts, Denmark; Fig. 2A), but were negative for cytokeratins (Lu-5, Roche, Switzerland), epithelial membrane antigen (Dakopatts), carcinoembryonic antigen (Lipshaw, USA), anti-alpha smooth muscle actin (Bio-Makor, Israel), desmin (Lipshaw), alpha-fetoprotein (Lipshaw), alpha-1-antitrypsin (Dakopatts), type IV collagen (Eurodiagnostic, The Netherlands), S-100 protein (Dakopatts) and testosterone (Biogenex, USA).

Clear vacuoles were negative for periodic acid-Schiff (PAS) stain with and without diastase digestion, alcian blue, and Sudan III. In addition, all immunohistochemical stains were negative. However, eosinophilic intracytoplasmic globules stained intensely with Masson trichrome, and very lightly with PAS, with or without diastase digestion, and showed intense immunoreactivity with alpha-1-antitrypsin (Fig. 2B). Ultrastructurally (Fig. 2C), clear vacuoles corresponded to optically empty intracytoplasmic spaces that were membrane bound but had no microvilli. Globules were small and varied in diameter; they were oval or round and their content was homogeneous, granular and electron dense. The globules were membrane bound and usually close to cisternae of rough endoplasmic reticulum. Globules were present in round cells with and without clear vacuoles.

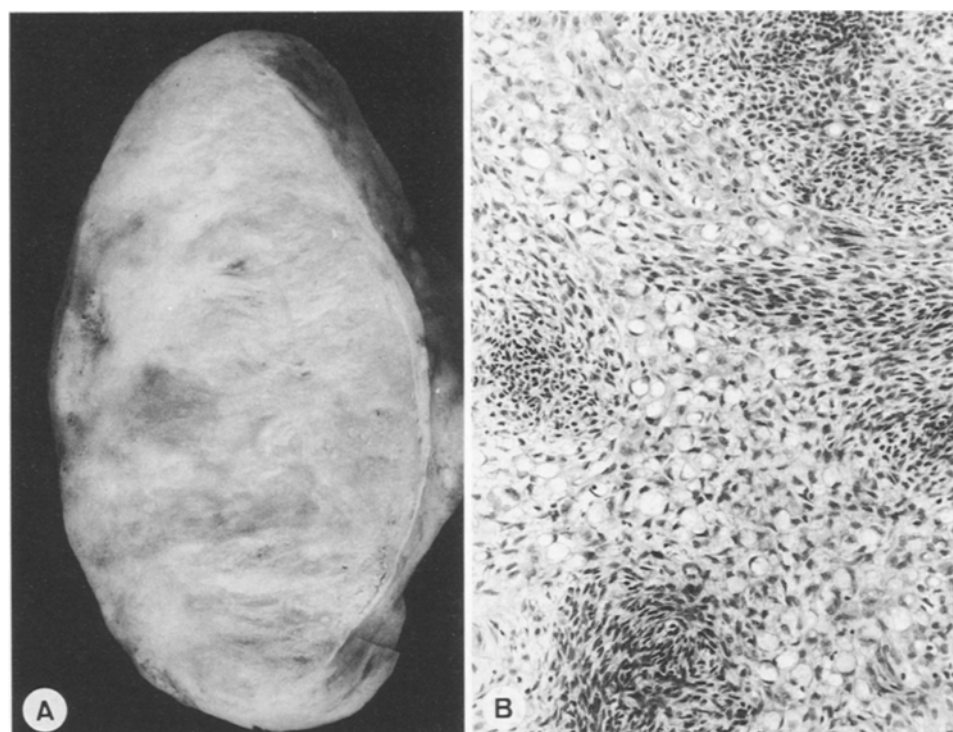


Fig. 1. **A** Sectioned surface of the tumour composed of solid, partially fasciculated tissue. **B** It is composed of bundles of fusiform cells and signet-ring cells arranged diffusely. H&E, $\times 120$

Table 1. Signet-ring stromal tumour of the ovary; histochemical and immunohistochemical differential diagnosis

	Clear vacuoles		Cytoplasm				Globules	
	PAS	Sudan III	Keratin	CEA	Vimentin	SMA	Alpha-1-antitrypsin	
Krükenberg's tumour	+	—	+	+	—	—	*	
Sclerosing stromal tumour	—	+	—	—	+	+	*	
Thecoma	—	+	—	—	+	—	*	
Signet-ring stromal tumour	—	—	—	—	+	—	+	

* Globules have not been described in these tumours

PAS, Periodic acid-Schiff; CEA, carcinoembryonic antigen; SMA, smooth muscle actin

Discussion

Because of the similar histological, histochemical and ultrastructural features of the signet-ring cells in both neoplasms, the present tumour is apparently the second reported case of the signet-ring stromal tumour described by Ramzy (1976). In addition, the results of our immunohistochemical study suggest that the neoplastic cells originated in the ovarian stroma and strongly support Ramzy's hypothesis on the histogenesis of this peculiar neoplasm.

Histologically the tumour is characterized by the admixture of spindle and round cells, some of which have the typical appearance of signet-ring cells. These features may be found in other ovarian neoplasms, mainly Krükenberg's tumour and the sclerosing stromal tumour (Young and Scully 1987, 1988) (Table 1). Signet-ring

cells in Krükenberg's tumour are PAS positive because of their mucin content and their nuclei look malignant, but the signet-ring cells in the present case do not stain with PAS and have monomorphic, mitotically inactive nuclei. The vacuolated cells in the sclerosing stromal tumour contain lipids which stain positively with fat stains. In the present tumour the absence of Sudan III staining in the clear vacuoles, as well as some other features such as pseudolobular pattern, sclerosis and rich vascularity in cellular areas (Chaldvarjian and Scully 1973; Saitoh et al. 1989), ruled out the diagnosis of sclerosing stromal tumour. Luteinized ovarian stromal tumours of the fibroma-thecoma group have polyhedral or round vacuolated cells against a background of predominantly spindle-shaped cells (Zhang et al. 1982) but the vacuolated appearance is due in part to the cellular lipid content. In the case under study clear vacuoles were

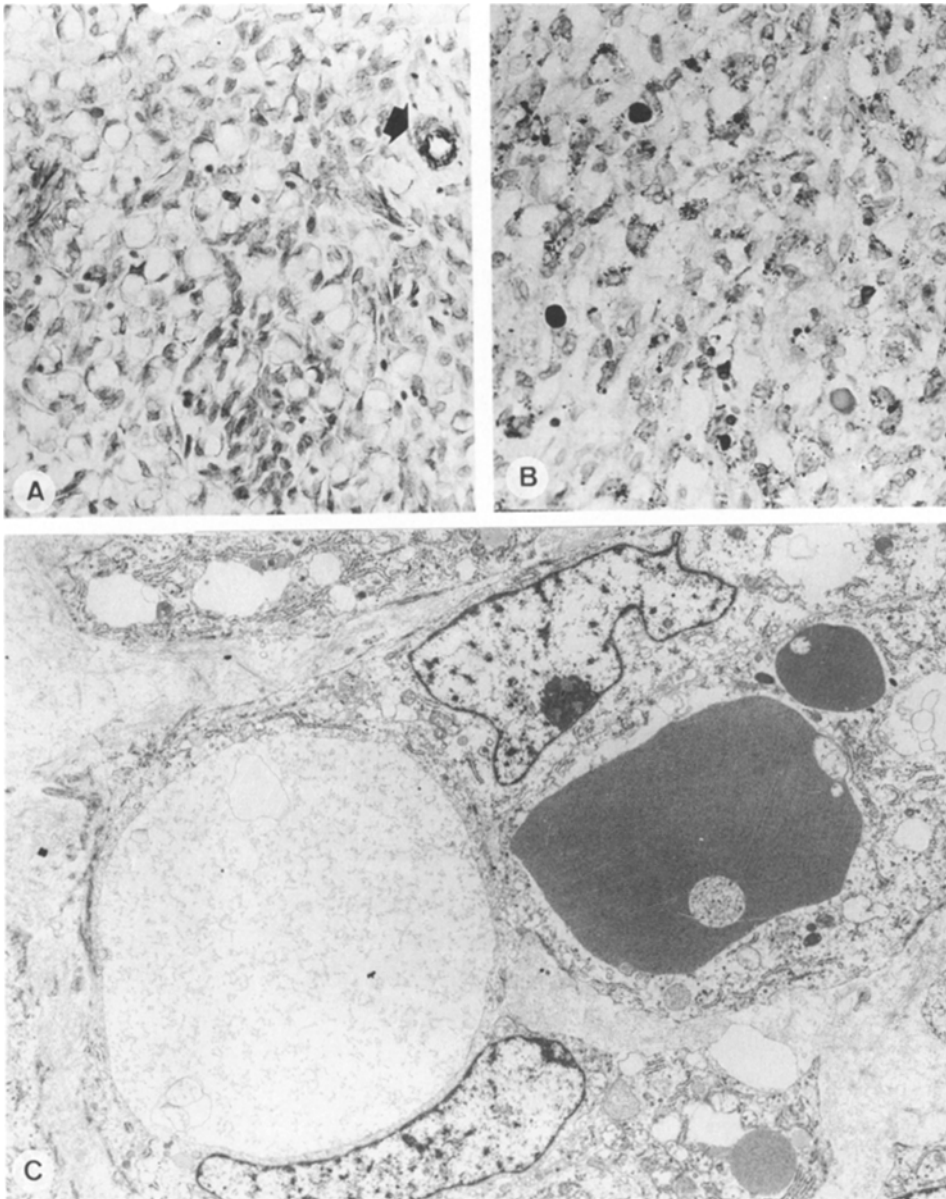


Fig. 2. **A** Signet ring cells show positive vimentin stain in their cytoplasmic borders. Note the endothelial immunoreactivity (*arrow*). Streptavidin-biotin-alkaline phosphatase, $\times 240$. **B** Positive globular staining with alpha-1-antitrypsin. Streptavidin-biotin-alkaline phosphatase, $\times 240$. **C** Two round cells, one containing a clear vacuole and the other a globule. Electron microscopy, $\times 2200$

negative with all the histochemical and immunohistochemical stains employed. Our lesion, like thecomas, did not stain with smooth muscle actin and desmin. These antibodies are useful in differentiating signet-ring stromal tumour and thecomas from sclerosing stromal tumours (Saitoh et al. 1989), and leiomyomas (Czernobilsky et al. 1989). The presence of clear cytoplasm with occasional hyaline globules has been reported in one case of ovarian leiomyoma (Matamala et al. 1988).

The presence of intracytoplasmic eosinophilic globules alpha-1-antitrypsin positive was not reported by Ramzy (1976). These globules have histological, histochemical, immunohistochemical and ultrastructural features similar to those reported in some epithelial, mesenchymal, and germ cell tumours, as well as in the hepatocytes of patients with alpha-1-antitrypsin deficiency (Scrogg et al. 1989). It has been postulated that this type of eosinophilic intracytoplasmic globule represents se-

cretory glycoprotein accumulated in the cytoplasm of tumour cells (Scrogg et al. 1989). Since globules were often associated with necrotic areas, Scrogg et al. (1989) suggested that ischaemic injury in tumour cells may be necessary for the development of these structures. However, in our case no necrosis was seen. The presence of cells with eosinophilic intracytoplasmic globules next to cells with clear vacuoles, as well as the presence of both globules and vacuoles within the same cell, suggest that these vacuoles may represent empty spaces after globule elimination.

In conclusion, signet-ring stromal tumour may be considered to be a morphologically distinctive type of benign ovarian stromal tumour, which may present problems in differential diagnosis with other stromal and non-stromal ovarian neoplasms. It seems that fibroblastic stromal cells differentiate into cells able to synthesize a glycoprotein product and to modify their morphology.

It remains to be established whether the acquisition of this secretory ability represents specific differentiation or whether it is a non-specific response of neoplastic stromal cells to an unknown injury.

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