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Giant Cell Tumor of the Ovary

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Summary. A 31 year old woman with primary sterility was found, at operation, to have endometriosis of the Fallopian tubes and a giant cell tumor of the ovary, histologically indistinguishable from giant cell tumor of bone. The tumor is considered to be primary and benign, with a follow-up period of $4^1/_2$ years and no signs of recurrence or malignancy.

Key words: Giant cell tumor – Ovary – Endometriosis of Fallopian tubes – Sterility.

Introduction

Giant cell tumors of bone are distinct neoplasms with a microscopic picture of proliferating round or spindle-shaped mononucleated stromal cells, regularly interspersed with multinucleated giant cells. The tumors are moderately or richly vascularized and are further characterized by lack of formation of intercellular substance (Dahlin 1967; Lichtenstein 1972). The tumors account for approximately 4% of all bone tumors in the series of Dahlin.

Extraosseous giant cell tumors with histological features similar to those occurring in bone are rare. The majority of these tumors have been described as arising in soft tissues from the subcutis, superficial or deep fascial structures and tendon sheaths, eventually involving skeletal muscle. They are reported in the series of Guccion and Enzinger (1972), Salm and Sissons (1971) and Carstens (1978).

Few cases of giant cell tumor arising in individual organs have been reported in the literature. Such extraosseous tumors have been found in the orbit (Abdalla and Hosni 1966), the larynx (Ribári et al. 1975), the thyroid (Silverberg 1973), the heart (Dorney 1967), the breast (Bässler 1978), the colon (Eshun-Wilson 1973), the pancreas (Rosai 1968) and the skin (Andreev et al. 1964). Four cases of giant cell tumors associated with mucinous cystadenoma or cystadenocarcinoma of the ovary have been published by Pucher (1909), Leschke (1951), Bettinger (1953), Veliath et al. (1975) and Kherdekar and Patoria (1976).

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The present report describes a giant cell tumor of the ovary, but in contrast to previously published cases there was no associated tumor.

Clinical History

A 31 year old woman, blood type B, Rh. positive, was first admitted in September 1975 complaining of primary sterility of two years duration. She had a previous history of appendectomy in 1961 and a skull fracture and contusion of the back in 1973. In 1972 a currettage due to functional bleeding had shown normal menstrual phase of the endometrium. Menarche occurred at the age of 15 years and the menstrual cycle had always been regular, apart from the above, with 4–5 days of bleeding every 26–28 days. There had been no vaginal discharge or abdominal pain. She employed P-pills[1] for contraception for a 2 year period from 1971 to 1973.

Physical examination showed an euthyroid woman with normal secondary sex characters. At gynecological examination, a firm, smooth, indolent but mobile tumor, the size of a hen's egg, was palpated in the left parametrium. Laboratory investigation showed normal blood status and normal serum electrolyte values, including Se-calcium, Se-phosphate and Se-alkaline phosphatase. The urine was found to be normal and the Wassermann and gonococcal reactions were negative.

As a uterine myoma was suspected, exploratory laparotomy was carried out and wide-spread peritoneal adhesions found. As a result, it was difficult to inspect and palpate the liver; both kidneys appeared normal. Fibrous adhesions were found in the pelvic area between the ileum, sigmoid colon, omentum and internal genital organs. There was no ascites or evidence of carcinomatosis. After the adhesions had been divided, approximately 8×5 cm left adnexae were found, consisting of a partly cystic enlarged ovary with a smaller bone-hard area and a sactosalpinx approximately 2 cm in diameter. The adnexae were attached to the posterior surface of the uterus and edge of the broad ligament. The right adnexa consisted of a normal sized ovary with a few small cysts on the surface and a thickened, swollen salpinx. The uterus was normal. The left adnexa was excised and a biopsy taken from the right ovary. The right salpinx was retained, despite the fact that a normal passage could not be established even after opening and attempted flushing with saline. After operation the patient attended several out-patient clinics and stated that she was in perfect health, with a normal menstrual cycle. However, vaginal examination in April 1979 disclosed an approximately 5×3 cm large non-mobile, hard but indolent mass in the left parametrium close to the uterus. The subsequent operation showed pronounced peritoneal adhesions between the colon, omentum and the upper left lateral angle of the uterus, but no signs of a tumor. A biopsy was taken from the right ovary and the right salpinx was resected.

In October 1979 the patient stated that she was in good health and had a regular menstrual cycle. On examination, there were no signs of tumor recurrence or metastases. Laboratory values of Se-calcium, Se-phosphate, Se-alkaline phosphatase activity and Se-alphafetoprotein were normal. Examination of the urine showed no abnormality. Roentgenological examination of the chest, spine, pelvis and extremities showed normal findings, except for a healed compression fracture of the first lumbar vertebra. The patient was last seen in February 1980 and was still in good health.

Pathology

Macroscopically the left adnexa consisted of an enlarged ovary measuring $8 \times 4 \times 4$ cm and an 8 cm long fibrous, thick-walled and moderately dilated Fallopian tube, adherent to the ovary by fibrous bands. The ovarian capsule was intact except for a small torn area, resulting from a peroperative biopsy. The major part of the ovary presented as a haemorrhagic cyst resembling a corpus luteum

[1] Neo-Gentrol

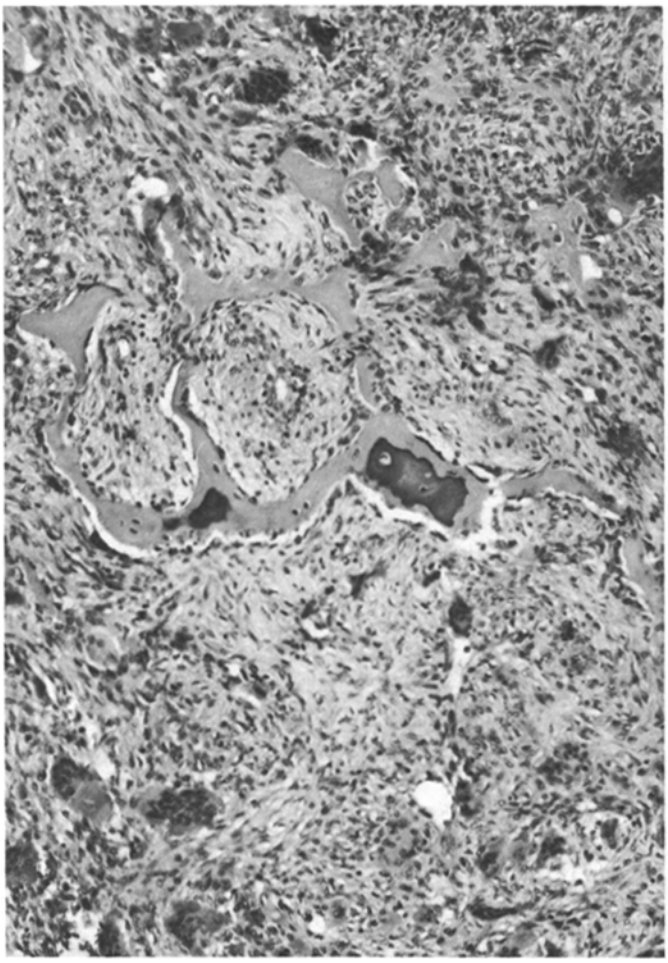

Fig. 1. Histological pattern of giant cell tumor composed of stromal cells and multinucleated giant cells. Note bone formation. H & E, ×130

cyst, but a circumscribed and firm part measuring approximately $3 \times 2 \times 2$ cm was also observed. The cut surface of the firm area was homogenous yellowish-brown.

Microscopical examination was performed on paraffin-embedded tissue. Sections of the cystic part of the ovary showed within a thickened fibrous capsule, a rim of compressed cortical stroma with normal follicles and simple cysts. Deeper portions of the tissue showed incomplete division by band-like fibrosis into areas with extensive haemorrhage and a dense inflammatory granulomatous reaction. A marked proliferation of histiocytic foamy cells was present, intermingled with fibroblasts, plasma cells and a smaller number of lymphocytes as well as haemosiderin-laden macrophages. Polymorphonuclear leukocytes, eventually amounting to microabscess formation, were also seen within the inflamma-

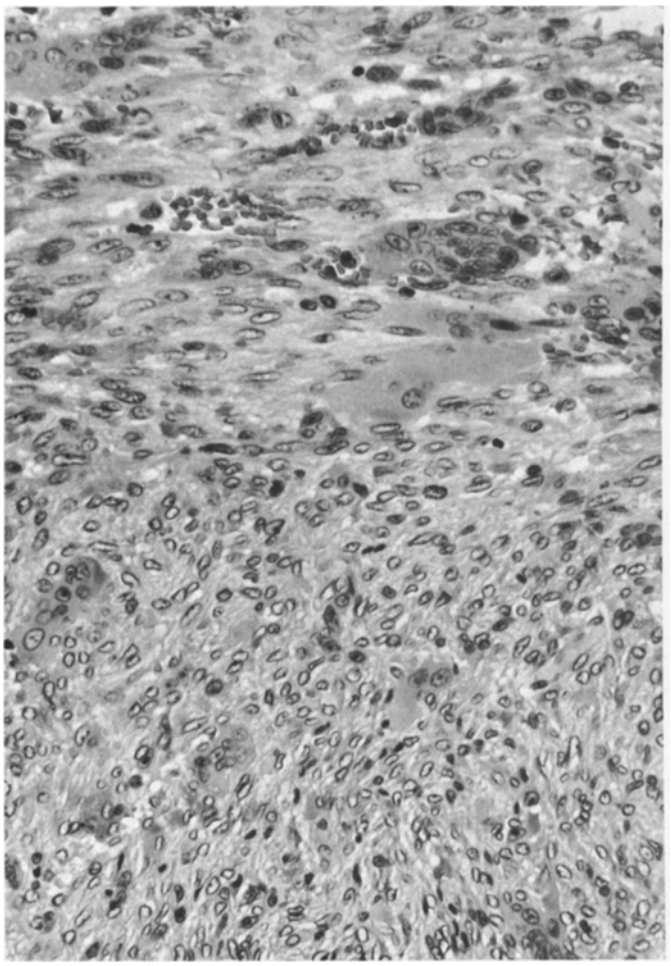

Fig. 2. Fascicular pattern of stromal cells interspersed with multinucleated giant cells. H & E, ×320

tory infiltrates. No remains of pre-existing follicle, corpus luteum or cystadenoma were identified within these areas. No signs of specific inflammation were found.

The solid part of the ovary showed quite a different histologic picture of a richly vascularized tumor composed of mononuclear stromal cells, regularly interspersed with multinucleated giant cells (Fig. 1). The stromal cells were medium-sized, ovoid or spindle-shaped and generally had round nuclei with moderate chromatin and often a centrally situated nucleolus. In places the cells were arranged in a fascicular pattern with slender cytoplasmic processes, indicating fibrogenic zones, but no features of sarcomatous differentiation were seen (Fig. 2). The giant cells were large, and had multiple nuclei, sometimes numbering 50–100. The nuclei which were mostly agglomerated towards the

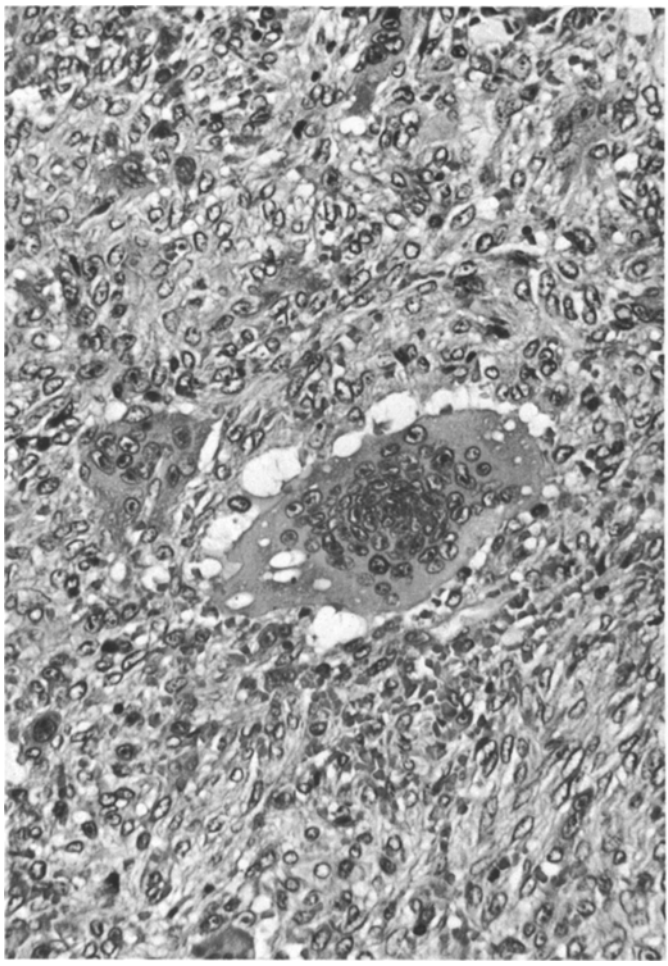

Fig. 3. Multinucleated giant cell with vacuolar degeneration of the cytoplasm. H & E, ×320

middle of the cells, were vesicular or oval and had distinct nucleoli, thus resembling the nuclei of the stromal cells. There was a considerable amount of cytoplasm which was eosinophilic, granular or vacuolated (Fig. 3).

Mitotic figures (up to 3–4 per high power field (×400)) were occasionally observed in the stromal cells, but on the whole the number of mitotic figures was small. No mitoses were found in the giant cells. Trabeculae of osteoid and bone were frequently observed, but no cartilagineous differentiation was present (Fig. 1). Tumor cells could be observed merging into areas with inflammatory reaction in the border zone of the cystic haemorrhagic part of the ovary (Fig. 4).

The cytoplasm of the giant cells stained either diffusely or in localized areas with periodic acid-Schiff, before and after diastase digestion, and moderately

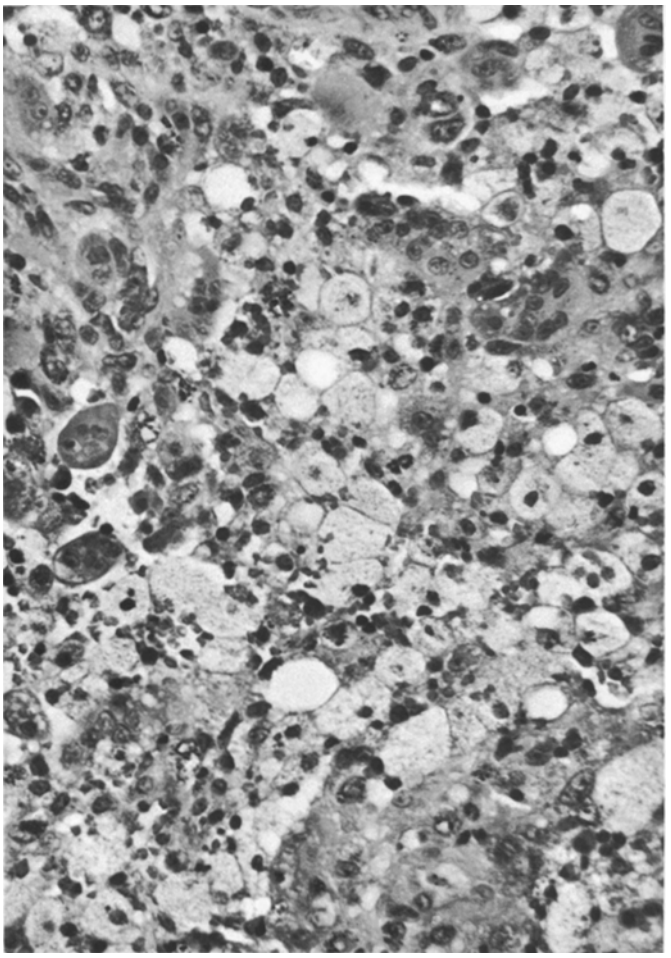

Fig. 4. Inflammatory reaction with leukocytes and foamy cells intermingled with small multinucleated giant cells. H & E, ×320

with Alcian blue but intensely with phosphotungstic acid-haematoxylin (PTAH). The stromal cells were negative for these stains. Sections stained with Sudan black B showed a negative reaction in stromal cells as well as in giant cells. Von Kossa staining for calcium was only positive in bony trabeculae. Gordon and Sweet's method for reticulin fibres showed abundance of reticulin fibres, often surrounding the individual stromal cells (Fig. 5).

Electron microscopy of the paraffin-embedded tissue proved unsuccessful.

Both Fallopian tubes (the right had been removed during the second operation) showed endometriosis and fibrosis on microscopical examination. Biopsies from the right ovary showed cortical tissue with normal or small cystic follicles.

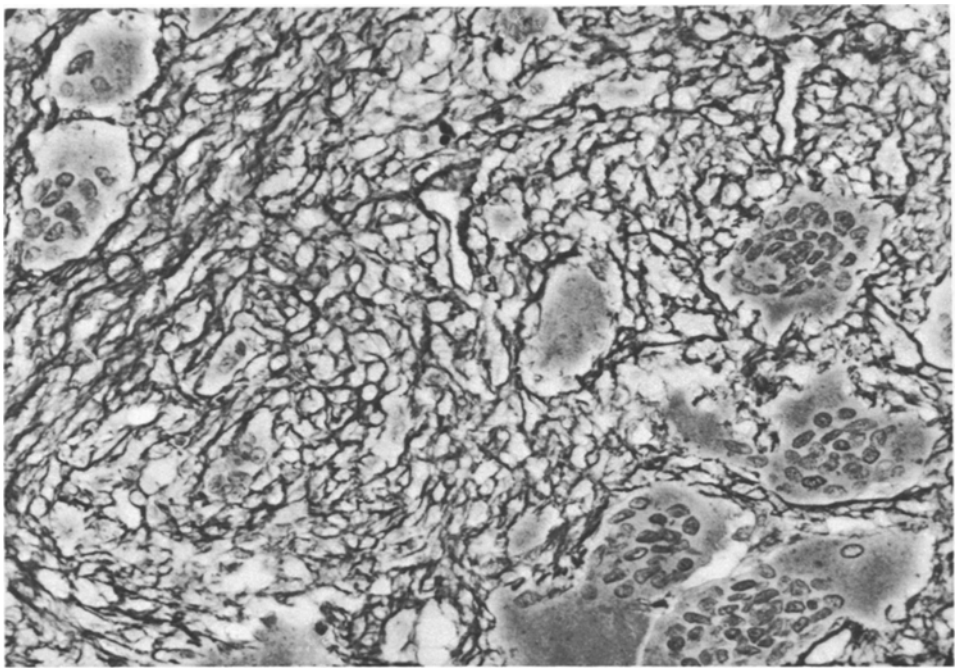

Fig. 5. Dense network of reticular fibres surrounding individual stromal cells and encircling the multinucleated giant cells. Reticulin × 320

Discussion

Giant cell tumors of bone have a characteristic histological appearance, composed of mononuclear stromal cells and a varying number of multinucleated giant cells. Despite the fact that uncertainty still exists as to the origin of the tumors, several authors suggest a mesenchymal origin and consider the stromal cell the principal cell of these tumors (Hanaoka et al. 1970; Lichtenstein 1972; Spjut et al. 1972; Steiner 1972). Giant cells are formed by fusion of mononuclear cells and have been found to be similar to normal osteoclasts by ultra-structural studies (Hanaoka et al. 1970; Sapp 1972), even though morphological differences have also been reported (Steiner 1972; Aparisi et al. 1979). Histochemical studies have demonstrated different properties in giant cells and stromal cells, but great resemblance in histochemical behaviour between giant cells and osteoclasts, indicating a close physiological and histogenetic relationship between the cells (Schajowicz 1961).

Primary extraosseous giant cell tumors of appearance similar to giant cell tumor of bone have been referred to by Schwinn (1976), in his extensive review of differential diagnosis of giant cell tumors of bone, but have been more thoroughly described in the series of Guccion and Enzinger (1972), Salm and Sissons (1972), Alguacil-Garcia et al. (1977) and Carstens (1978). The histogenesis of these tumors is uncertain and at present controversial. Electron-microscopical studies suggest a mesenchymal origin in many cases (van Haelst and de

Table 1. Clinical and pathological features of giant cell tumors of the ovary

Author	Patient age	Associated tumor	Size of giant cell lesion	Bone or osteoid formation	Follow-up
Pucher (1909)	44	Cystadenoma, mucinous? (Size of a man's head)	Nodules measuring 4×1 and 2.5×1 cm	No	Alive 2 years (operation for carcinoma mammae with lymph node metastases)
Leschke (1951)	36	Cystadenoma, mucinous (11 litres)	Not stated	No	No follow-up
Bettinger (1953)	19	Cystadenoma, mucinous (15 cm in diameter)	5×3 cm	Yes	No follow-up
Veliath et al. (1975)	25	Cystadenocarcinoma, mucinous (11×10 cm)	Not stated	No	Alive 8 months (No signs of recurrence or metastases)
Kherdekar and Patoria (1976)	55	Cystadenoma, mucinous (30 cm in diameter)	4×3 cm	No	Died 11th day (Atelectasis and pneumonia. No autopsy)
Lorentzen (1980)	31	None	$3 \times 2 \times 2$ cm	Yes	Alive $4^1/_2$ years (No signs of recurrence or metastases)

Haas van Dorsser 1976, Alguacil-Garcia et al. 1977; Carstens 1978) while other similar tumors in individual organs appear to be of epithelial origin (Gonzales-Licea 1967; Rosai 1968; Silverberg and DeGiorgi 1973).

This diagnosis of giant cell tumor of the ovary is considered primarily because no sign of another tumor could be found. It differs from other reports of ovarian giant cell tumors in-as-much as no co-existing tumor could be demonstrated. The histological picture is characteristic, with bone formation as in Bettinger's case, and, in addition a rather extensive inflammatory reaction with foam cell proliferation, the latter being a frequent finding in these tumors. The histochemical reactions of the present tumor were identical with those of Schajowicz (1961) in his study of giant cell tumors of bone. Although giant cell tumors are potentially malignant, and a benign histological appearance does not exclude secondary malignant transformation or metastatic spread (Dahlin 1967; Inoue et al. 1977; Carstens 1979), the present tumor has so far shown no signs of recurrence or metastatic spread after $4^1/_2$ years of follow-up.

The histogenesis of the present tumor is uncertain, but it is believed to be of mesenchymal origin. However, a teratomatous origin for giant cell tumors of the ovary, in connection with a co-existing mucinous cystadenoma or cystadenocarcinoma, was considered a possible explanation in the cases of Bettinger,

Veliath et al. and Kherdekar and Patoria. A number of authors have suggested that some cases of mucinous cystadenomas are of teratoid origin (Hughesdon and Symmers 1978; Novak and Woodruff, 1979). The clinical and pathological features of cases of giant cell tumor in the ovary, published in the literature are shown in Table 1.

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