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# Giant cell tumor of the ovary. Immunohistochemical evidence of origin from stromal ovarian cells

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**Summary.** Giant cell tumor (GCT) of the ovary is a rare condition, found almost invariably in the context of a mucinous tumor and presenting a microscopic picture indistinguishable from GCT of bone. We describe a case of GCT in the wall of a serous cyst of the ovary. An immunohistochemical study was performed using a panel of antibodies to epithelial, mesenchymal and leukocyte antigens. Mononuclear and giant tumor cells were positive for vimentin; CD 68 and LCA were found only in giant cells whereas actin was only found in mononuclear tumor cells. The immunophenotypic profile of the stromal cells of the residual ovary was identical to that of mononuclear tumor cells.

The presented data suggest that GCT of the ovary is probably a non-neoplastic lesion of the mesenchymal stromal cells that react against substances of the associated tumor or cyst.

**Key words:** Giant cell tumor, Immunohistochemistry, Ovary

## Introduction

Giant cell tumor (GCT) of bone is a well-defined neoplasia with a peculiar microscopic picture consisting of round or spindle-shaped mononucleated stromal cells admixed with multinucleated giant cells. Extra-osseous GCTs have been reported especially in soft tissue (Salon and Sisson, 1972) while they are relatively rare in individual organs (Ito et al., 1992). In the ovary a few cases have been previously described, all but one in the context of a mucinous tumor (Pucher, 1909, Leschke, 1951; Bettinger, 1953; Veliath et al., 1975; Kherderkar and Patoria, 1976; Lorentzen, 1980). The present report describes a GCT of the ovary, in which a detailed immunohistochemical study has been performed in order to understand the histogenesis of this lesion.

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## Materials and methods

A 42-year-old woman was admitted to the Hospital because of abdominal mass. The patient was nulligravida; her menstrual history was normal. Clinical examination showed a smooth, cystic movable mass of the right ovary. Laparatomy disclosed a large unilateral ovarian cystic tumor. The uterus and controlateral ovary were normal. The patient underwent right salpingo-oophorectomy. Post-operative clinical course was uneventful. Three years after the operation the patient was still in good health.

The specimens were fixed in buffered formalin. Tissue blocks were processed by conventional methods and embedded in paraffin; 5 µm sections were stained with haematoxylin-eosin, PAS, Giemsa, and Gomori.

Immunostaining was performed using the ABC method. The following antisera were utilized: keratin; EMA; vimentin; lysozyme; CD-68; S-100; LCA (CD-45); elastase; actin; desmin; factor VIII-related antigen; and proliferating cell nuclear antigen (PCNA).

## Results

The tumor was well circumscribed, firm and measured 3x2x1.5 cm. The cut surface was yellowish with brown areas of haemorrhage. A unilocular serous cyst, measuring 10 cm in maximum diameter, comprised the tumor and the remaining ovary (Fig. 1).

### *Light microscopy*

The tumor consisted of a loose network of oval to spindle-shaped mononucleated cells intermingled with numerous multinucleated osteoclast-like giant cells (Fig. 2). In some areas a variable proliferation of foamy histiocytes was present, admixed with fibroblasts, plasma cells and rare lymphocytes. Extensive areas of haemorrhage were also present as well as collections of haemosiderin-laden macrophages. The outer portions of the tumor, which contained a fibrous capsule, showed trabeculae of osteoid and mature bone formation. No

cartilagineous differentiation was observed. Mitotic figures were rare.

The cyst had a fibrous wall, lined by flattened or cuboidal serous epithelium. The remaining ovarian parenchyma had a normal microscopic appearance.

### *Immunohistochemistry*

Table 1 summarizes the immunohistochemical findings. The tumor cells showed strong positivity for vimentin both in stromal mononucleated and multinucleated giant cells (Fig. 3). Actin was found in stromal cells, but not in giant cells (Fig. 4). Giant cells showed positivity for CD-68 in the cytoplasm and for LCA in the membrane (Fig. 5); weak staining for lysozyme was also noted. Tumor cells were negative for the other antibodies. The stromal cells of the remaining ovary showed the same immunophenotype of the tumor mononucleated cells (positivity for actin, negativity for CD-68 and LCA).

**Table 1.** Immunohistochemical findings in mononuclear and giant tumor cell compared with stromal cells of the ovary.

| ANTIBODY | GIANT CELLS | MONONUCLEAR CELLS | STROMAL CELLS OF THE OVARY |
|---|---|---|---|
| Vimentin | +++ | +++ | +++ |
| Actin | - | +++ | +++ |
| Lysozime | + | - | - |
| S-100 protein | - | - | - |
| Keratin | - | - | - |
| EMA | - | - | - |
| Factor VIII-RA | - | - | - |
| CD-68 | ++ | - | - |
| LCA | ++ | - | - |
| PCNA | - | - | - |

## Discussion

GCT of bone is considered to be of uncertain origin (Liu Tze-Chun et al., 1989). The relationship between multinucleated giant cells and mononucleated stromal cells, the two components of the tumor, and their precise histogenesis have been widely investigated by means of ultrastructural (Luo Tienxi and Liu Tze-Chun, 1983; Roessner et al., 1984; Mellin et al., 1985) and immunohistochemical studies (Athanasou et al., 1985; Brecher et al., 1986; Doussis et al., 1992; Hasegawa et al., 1993), but remains controversial. The main hypotheses refer to monocytic-macrophage (Huang et al., 1993), and fibroblastic-histiocytic origin (Kindblom et al., 1982); histiocytic with occasional myofibroblastic and osteoblastic differentiation has also been noted (Hasegawa et al., 1993). In extraosseous sites, the term GCT comprises a wide range of lesions, occurring alone or in association with other epithelial or mesenchymal tumors for which a subdivision in groups has been proposed (Kenney et al., 1984). In the ovary, GCTs have

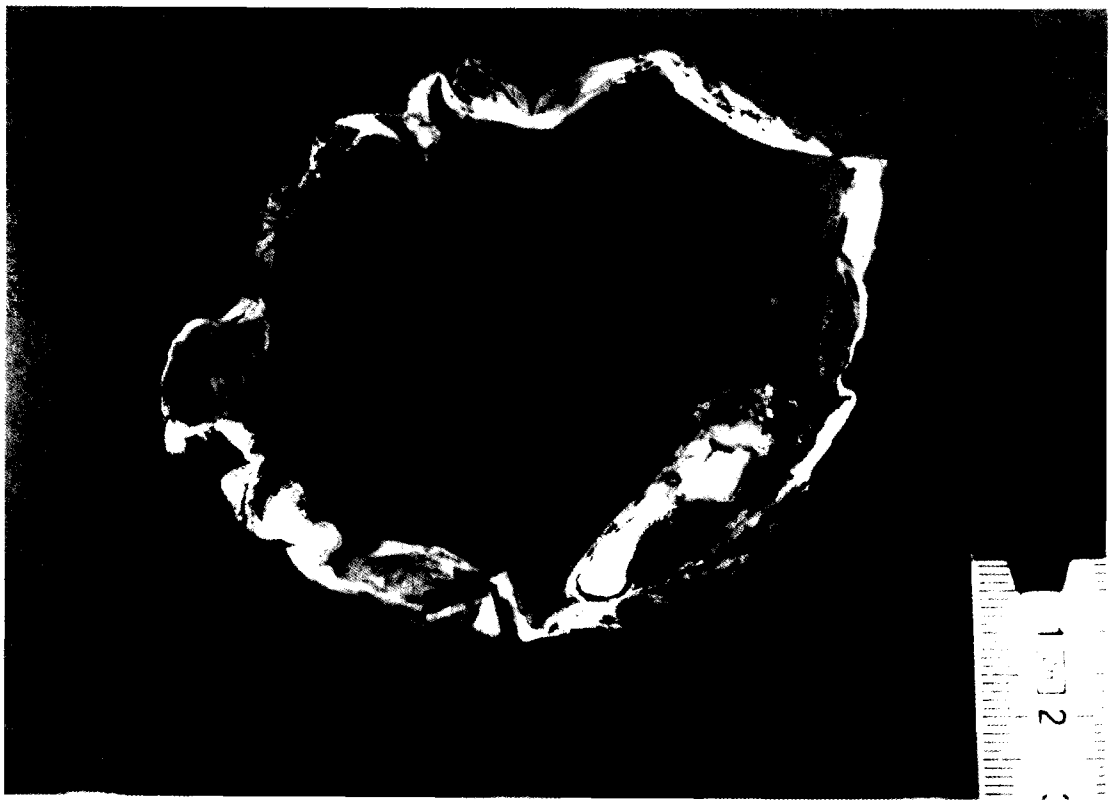

**Fig. 1.** Cross section of the tumor (arrow) demonstrating the origin from the cystic wall.

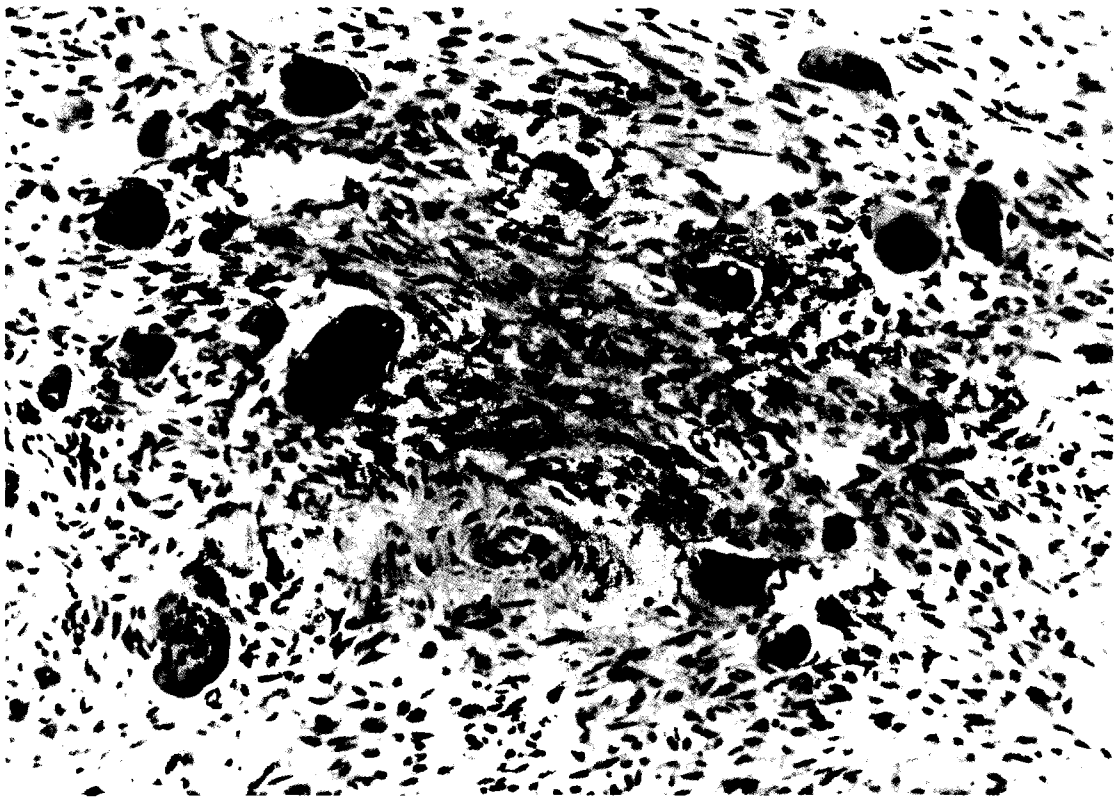

**Fig. 2.** The tumor consists of a mixture of spindle mononucleated and giant multinucleated cells. H&E, x 250

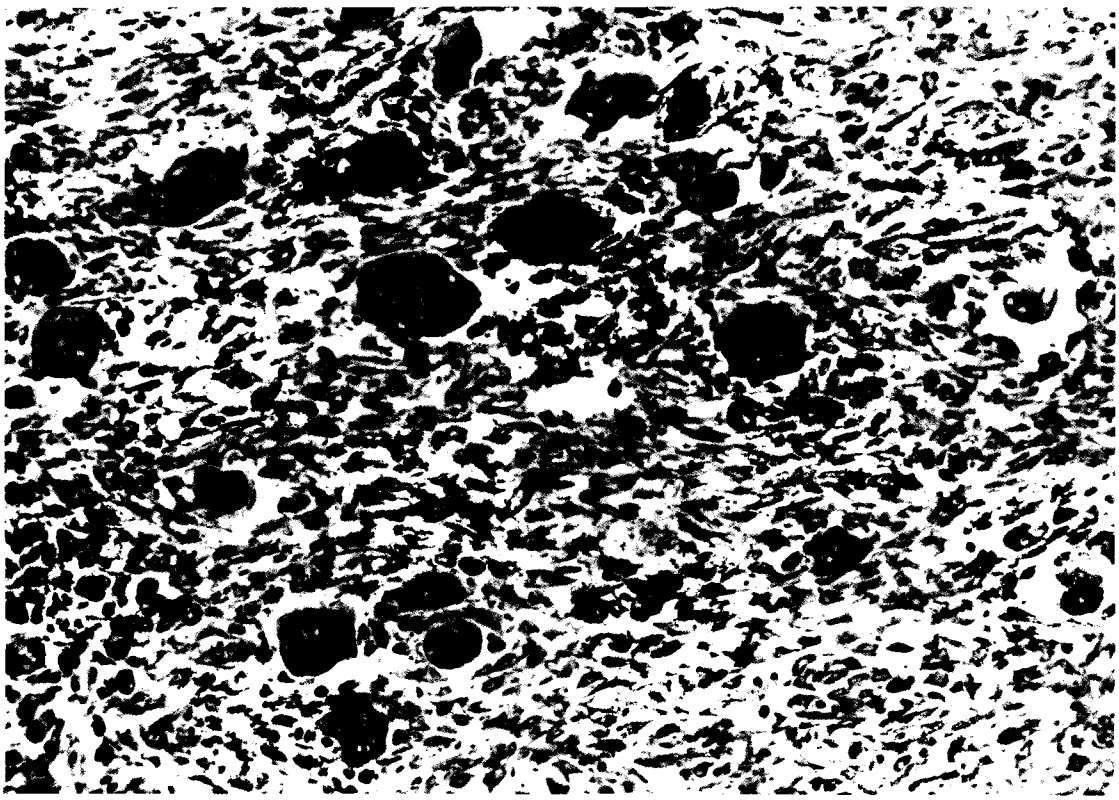

**Fig. 3.** Immunostaining for vimentin shows positivity in mononucleated and multinucleated tumor cells. ABC method, x 250

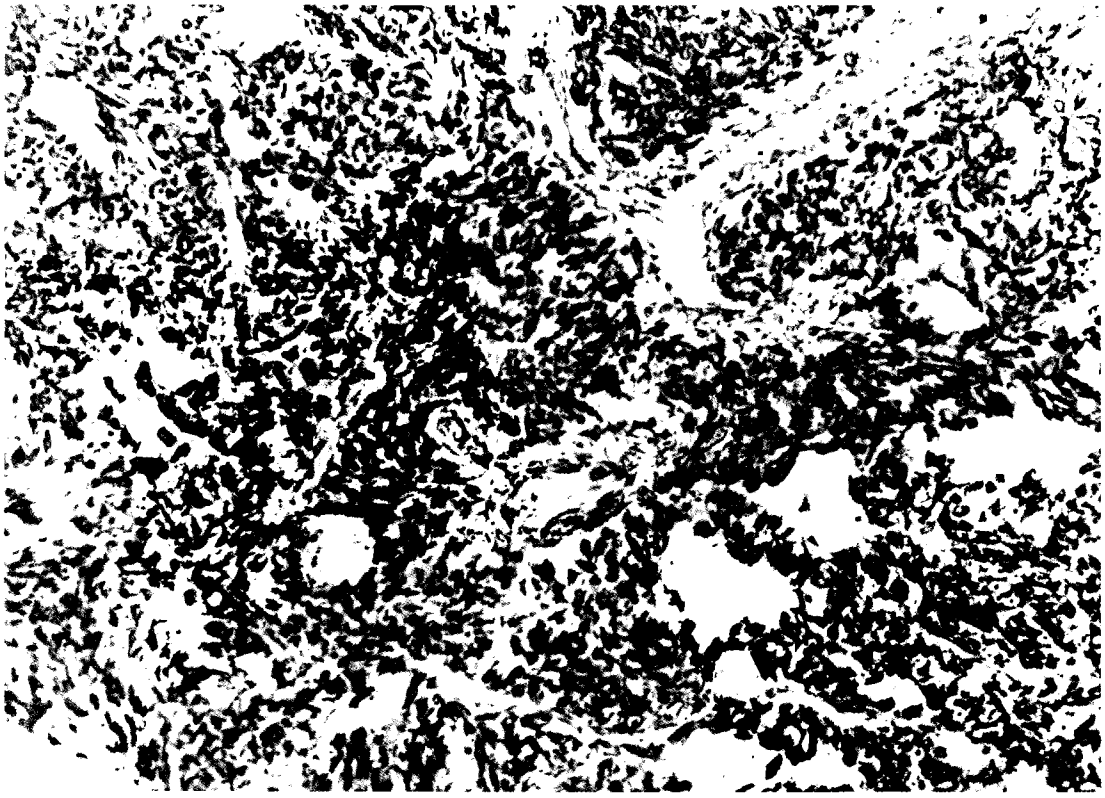

**Fig. 4.** Actin positivity is restricted to mononucleated cells. Multinucleated cells are negative. ABC method, x 250

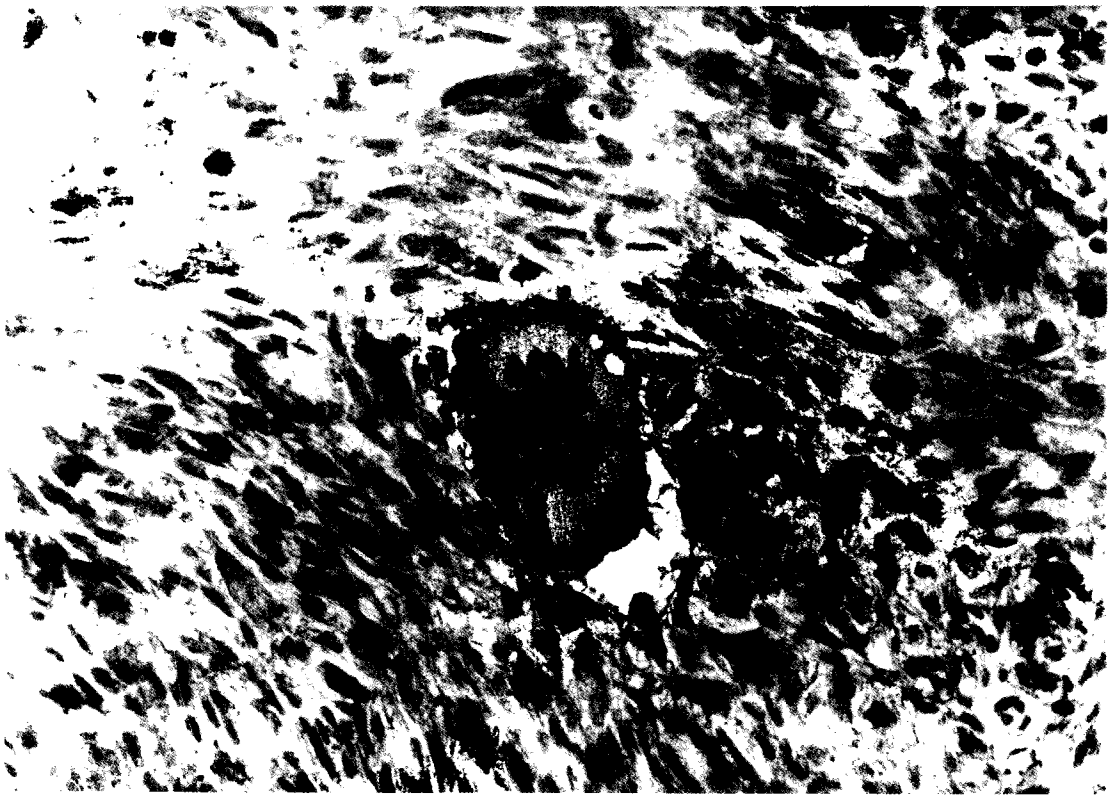

**Fig. 5.** Immunostaining for LCA demonstrates membrane positivity in multinucleated giant cell. ABC method, x 400

been previously described, most of them occurring together with mucinous tumor. The only GCT of the ovary not associated with a co-existing tumor was intimately connected with a large haemorrhagic cyst (Lorentzen, 1980).

GCT of the ovary displays similar histological features to those of spindle cell mural nodules associated to cystic mucinous tumor (Prat and Scully, 1979; Russell et al., 1981; Sondergaard and Kaspersen, 1991). GCT shows a mixture of fusiform mononuclear cells and giant osteoclast-like cells, with evidence of bone formation. The spindle cell mural nodules do not show bone trabeculae and the occasional giant cell component has an epithelial origin, as documented by immunohistochemical staining with keratin (Nichols et al., 1991). These differences suggest that the two entities have to be kept distinct.

Only a few convincing studies have been published about the origin of extraosseous GCTs. In particular, immunohistochemical studies have shown some similarities to GCT of bone (Amir and Rosenmann, 1990; Goldberg et al., 1991). In the ovary, the immunophenotype of GCT has never been studied. In our case, we compared the immunophenotypical expression of the mononucleated and giant tumor cells with that of the stromal non-neoplastic cells of the ovary. Our study shows that mononucleated cells of GCT react with actin but not with CD-68 and LCA; on the other hand, giant cells gave a positive reaction for LCA and CD-68, but not for actin. These data suggest that they are two different cellular populations. The comparison of the immunophenotype of mononucleated cells of GCT with that of the ovarian stromal cells shows a perfect identity between these two kinds of cells. Immunoreactivity for PCNA was not observed. In GCT of bone PCNA is restricted to mononucleated cells, suggesting that proliferating elements are stromal cells (Hasegawa et al., 1993).

Multinucleated giant cells, showing CD-68 and LCA positivity, reveal their histiocytic nature; their presence could be the expression of attraction due to mediators produced by proliferating cells. It is likely that GCT of the ovary represents a non-neoplastic reactive lesion of the mesenchymal ovarian stromal cells stimulated by substances contained in the associated tumor or cyst. An affirmation of this hypothetical reactive nature is also given by the finding of GCT in the wall of the cyst and the benign clinical course, without recurrence or metastasis.

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