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# Carcinosarcoma of the gallbladder

—Report of a case—

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## INTRODUCTION

Carcinosarcoma, often referred to as "malignant mixed tumor" is a rare neoplasm, but this tumor occurs in various organs, including the gallbladder. We report herein a carcinosarcoma of the gallbladder which consisted of adenocarcinomatous and undifferentiated sarcomatous ares, the latter differentiating towards abundant osteoid and calcified but nonlamellated bony trabeculae formation. There are 18 reported cases of this type tumor of the gallbladder in the literature[1,2].

## CASE REPORT

A 70-year-old korean woman was admitted to the hospital because of a week of intermittent right upper quadrant abdominal pain, radiating to the back. There was no chill, fever, jaundice or urinary abnormality. About 15 days prior to admission, she had noted a palpable right upper quadrant abdominal mass. Physical examination disclosed a smooth, round, firm, nontender, movable mass in the right upper quadrant of the abdomen.

Laboratory examinations revealed a hemoglobin of 11.2 mg/dl and a white cell count of 5,400/mm$^3$. Total bilirubin was 0.3 mg/dl. Alkaline phosphatase was 101 IU/dl, the glutamic oxalacetic transaminase 24 IU, the glutamic pyruvate transaminase 13 IU. Ultrasonogram revealed an enlarged gallbladder replaced by echogenic huge mass. Abdominal computed tomogram disclosed an intraluminal gallbladder mass without pericholecystic invasion. Upper gastrointestinal series were unremarkable. An electrocardiogram revealed possible left ventricular hypertrophy.

A diagnosis of gallbladder cancer was made preoperatively. At laparotomy, the gallbladder was found to be enlarged and firm. Liver, stomach, colon and other abdominal organs were within normal limits. No ascites was found. Cholecystectomy was performed. The post-operative course was uneventful and she discharged 16 days later.

## PATHOLOGIC FINDINGS

The gallbladder measured 13×4×3 cm and 95 gm. Its serosal surface revealed a focal, gray white, puckering site in the fundic portion. There was a huge, polypoid tumor, protruding into the cavity. The tumor arose from the fundic portion. It was 9.5×2.5×2.0 cm. Its cut surface was mostly spongy, friable with foci of necrosis and hemorrhage. There was an ill-defined, whitish, firm area in the base of the tumor (Fig. 1). The wall of the gallbladder away from the tumor was white granular. There was no gallstone within.

Microscopically the polypoid tumor consisted of an admixture of adenocarcinomatous and undifferentiated sarcomatous areas, the latter containing calcified or non-calcified osteoid tissue. Because of the rarity of such a lesion in the gallbladder, mapping of the entire gallbladder specimen, including

polypoid tumor was done and serially numbered blocks were prepared. The carcinomatous components predominated in the tumor base and also scattered in the polypoid body of tumor embedded in the sarcomatous stroma, where numerous neoplastic glands of varying sizes were lined by mostly stratified atypical epithelial cells with considerable erythrophagocytosis and atypical mitotic activities. The carcinomatous components were sharply delineated from the sarcomatous portion (Fig. 2, 3). Whereever they are seen together, both components are intimately mingled with each other (Fig. 4). Some dilated lymphatics are filled with clumps of carcinoma cells (Fig. 5). The musle coat and serosa of the tumor base was invaded by adenocarcinoma. The wall of the gallbladder away from the tumor revealed usual well differentiated adenocarcinoma with focal invasion to the muscularis and serosa

**Table 1.** Carcinosarcoma (Malignant Mixed Tumor) of the Gallbladder

| No. of case | Author | Year Reported | Age & Sex | Stones | Gross Appearance | Microscopic Findings | Diagnosis |
|---|---|---|---|---|---|---|---|
| 1 | Lazarevic[9] | 1942 | 43F | − | NS | ADC/Chondro-, myxo-, fibrosarcoma | Collision tumor |
| 2 | Klein[10] | 1961 | 56F | + | NS | ADC/Spindle-and giant cell stroma | Carcinosarcoma |
| 3 | Knorr[11] | 1963 | 73F | + | NS | ADC/SCC/Fibrosarcoma+giant cells | Carcinosarcoma |
| 4 | Edmondson[12] | 1967 | 68F | + | NS | ADC/focal SCC/SCS | Carcinosarcoma |
| 5 | Edmondson[12] | 1967 | NS | NS | NS | ADC/SCS/Cartilage | Malingnant mixed tumor |
| 6 | Sagi[13] | 1970 | 79F | + | NS | ADC/Fibro-, chondro-, myxosarcoma | Malignant mixed tumor |
| 7 | Wolfensberger[14] | 1971 | 74F | + | NS | ADC/Solid Ca, SCC, "pseudocartilage" | Carcinosarcoma |
| 8 | Mehrotra[7] | 1971 | 45F | + | Polypoid | ADC+Squamous metaplasia/SCS+osteoid | Carcinosarcoma |
| 9 | Roth[15] | 1972 | 83F | + | NS | SCC/Spindle-,round cell, myxosarcoma | Carcinosarcoma |
| 10 | Higgs[16] | 1973 | 77M | + | Extensive | ADC/SCS+osteoid, cartilage | Malignant mixed tumor |
| 11 | Stempinski[17] | 1974 | 69F | + | NS | ADC/SCC/Reticulum sarcoma | Carcinosarcoma |
| 12 | Mansori, Cho[18] | 1980 | 81M | + | Filled c̄ tumor | ADC/SCS+Cartilage | Malignant mixed tumor |
| 13 | Cardia[19] | 1981 | 63F | + | NS | Solid Ca, SCC, fibro-, lipo-, angiosarcoma | Carcinosarcoma |
| 14 | Von Kuster, Cohen[20] | 1982 | 91F | + | Polypoid | ADC/SCS, osteoid, cartilage | Malignant mixed tumor |
| 15 | Von Kuster, Cohen[20] | 1982 | 77F | + | Polypoid | ADC/SCS, Osteoid, cartilage, rhabdomyoblasts | Malignant mixed tumor |
| 16 | Aldovini[8] | 1982 | 75F | + | Filled c̄ tumor | ADC/SCS Osteoid | Malignant mixed tumor |
| 17 | Miyamoto[21] | 1983 | 61F | + | Polypoid | ADC/SCS, Osteoid, cartilage | Carcinoma |
| 18 | Inoshita[2] | 1986 | 53F | + | Polypoid | ADC/SCS, osteoid, cartilage, rhabdomyoblasts | Carcinosarcoma |
| 19 | Present case | 1986 | 70F | − | Polypoid | ADC/SCS Osteoid | |

Abbreviations: (ADC) adenocarcinoma, (SCC) Squamous cell carcinoma, (SCS) spindle cell sarcoma

(Fig. 6).

The undifferentiated sarcomatous components (Fig. 7) were made up of bizarre pleomorphic polyhedral or spindle cells with marked nuclear pleomorphism, erythrophagocytosis, and frequent atypical mitotic figures, admixed with heavy infiltrates of plasma cells and lymphocytes. These cells had abundant pericellular reticulin fibers (Fig. 3). The striking feature of the growth was the formation of osseous tissue, varying from relatively mature, nonlamellated, calcified bony trabeculae (Fig. 8) to barely identifiable osteoid tissue surrounded by atypical osteoblasts merging imperceptibly with pleomorphic cellular tissue (Fig. 9, 10). Nowhere was dystrophic calcification without ossification. There was, however, abundant osteoid tissue without calcification. The calcified bony trabeculae intermingled with uncalcified osteoid areas. In other areas, there was a myxomatous appearance (Fig. 11). Among the fascicular spindle cells, there were some multinucleated osteoclastlike giant cells which did not appear anaplastic (Fig. 12). There were large areas of necrosis and hemorrhage.

Immunoperoxidase stain with antibody for cytokeratin was strongly postivie in the cytoplasm of these tumor cells in the epithelial element, but negative in the stromal element.

## COMMENTS

Carcinosarcoma is a controversial tumor, particularly as to whether a true carcinosaroma really exists[3]. Sarcomatous metaplasia of a spindle cell or pleomorphic carcinoma and florid sarcomatous reaction in a carcinoma are somtimes confused[4]. Osteoid and cartilage, which appear to be malignant, may be present in a spindle or pleomorphic carcinoma in certain organs, such as the breast, esophagus, and larynx[5,6]. There are 18 reported cases of this type of tumor in the literature[1,2]. Present case is very similar to the reported case of carcinosarcoma of the gallbladder by Mehrotra et al[7] and Aldovini et al[8].

The clinical and pathological features of these 18 cases and our own are listed in Table 1. There are no substantial differences in the clinical and pathological aspects. They occurred in those over 40 and mostly in females. Gallstones are commonly associated with this type of tumor. It is unique but present case did not contain gallstone. It is of interest that 6 cases showed a polypoid growth in contrast to carcinoma which commonly grows diffusely in the wall. This polypoid or exophytic growth is also a hallmark of pseudosarcomatous carcinoma in the esophagus, bronchi, and larynx, which had more favorable outcome than the carcinoma[5,22]. Thirteen cases had heterologous components, such as cartilage and osteoid. Rhabdomyosarcomatous differentiation was documented in 2 cases.

The histologic diagnosis of carcinosarcoma may be open to question. Before the tumor in the present case can be accepted as a further example, the various histological appearances that can simulate a carcinosarcoma have to be ruled out[8]. The possibility to be considered are (a) an undifferentiated carcinoma growing in a sarcomatoid manner; (b) exuberant benign stromal reaction with osseous metaplasia in a carcinoma; (c) a sarcoma incorporating benign non-neoplastic epithelial structures as inclusion; and (d) collision of an adenocarcinoma with an independant osteosarcoma. In the present case the sarcomatous element consisited not only spindle and pleomorphic cells but had differentiated into neoplastic osteoid tissue and nonlamellar bony trabeculae, leaving little reason to doubt that a malignant mesenchymal component is present. In the present case, the epithelial element was frankly carcinomatous and invaded lymphatic channels. The possibility of a carcoma with benign epithelial inclusions can therefore be excluded. Calcification or even ossification of the gallbladder is not an uncommon sequel to chronic cholecystitis and may

also be found in association with a carcinoma. This possibility is excluded by the presence of neoplastic osteoid tissue and the complete absence of dystrophic calcification. In the present case carcinomatous element was found to be sharply delineated from the sarcomatous component. No transition is seen between the two types of tissue, so we can rule out an adenocarcinoma growing in the sarcomatoid manner. There was also intimate mingling of sarcomatous and carcinomatous tissues and the two elements were clearly distinguishable from each other. A collision tumor does not show widespread mixture of sarcomatous and carcinomatous elements.

It is interesting to note that the epithelium of urinary bladder and gallbladder has been found experimentally to act as a stimulus to heterotopic ossification. In view of the capacity of the epithelium of the gallbladder to induce bone formation, it is not surprising that a composite tumor with carcinomatous and osteosarcomatous elements should occur in this site[8].

Classification of those tumors that appear to contain tissue of endodermal (epithelial) and mesodermal origin is difficult. Tumors of this type have been reported as either malignant mixed tumors or carcinosarcomas. Proper designation of this type of tumor is open to discussion. The term carcinosarcoma is confusing and is loosely applied to heterologous groups, often synonymously to pseudosarcomatous carcinoma. The term malignant mixed tumor is usually used in case of uterus, where multipotential cells, probably of Müllerian origin are capable of differentiating to both epithelial and mesenchymal cells with heterologous elements, such as cartilage, bone and striated muscle[23]. However, because such primitive cells have not been seen in the gallbladder, "carcinosarcoma" seems to be self-explanatory, favorable term when restricted to a true carcinosarcoma appending the heterologous elements[2].

## SUMMARY

A case of carcinosarcoma of the gallbladder in 70-year-old korean woman is presented, the tumor consisting of adenocarcinomatous and undifferentiated sarcomatous elements, differentiating towards osteoid and calcified, but nonlamellar bone formations. The problem of the histologic diagnosis and terminology of carcinosarcoma is discussed and the literature is briefly reviewed.

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## ＝국문초록＝

### 담낭의 암육종 1예
—증례 보고—

계명대학교 의과대학 병리학교실

**김선영 · 이상숙 · 채종민 · 정재홍**

70세 한국여인의 담낭에서 생긴 암육종 1예를 보고하고자 한다. 본 암육종은 육안상 큰 용종형종괴로 담낭내부를 채우고 있었다. 담석은 발견되지 않았다. 현미경소견상 선암성분과 주로 방추세포들로 구성된 육종성분으로 구성되어 있었다. 육종성분내에는 다양한 유골과 일부 석회화된 골형성이 인지되었다. 본종괴에서 떨어진 주변의 점막에서 침윤성 선암이 관찰되었다.

저자들은 지금까지 문헌상 보고된 18예와 함께 담낭의 암육종의 특성을 분석하고 동시에 조직학적 진단할 때 문제점과 암육종의 명명에 대하여 문헌고찰과 함께 기술하였다.

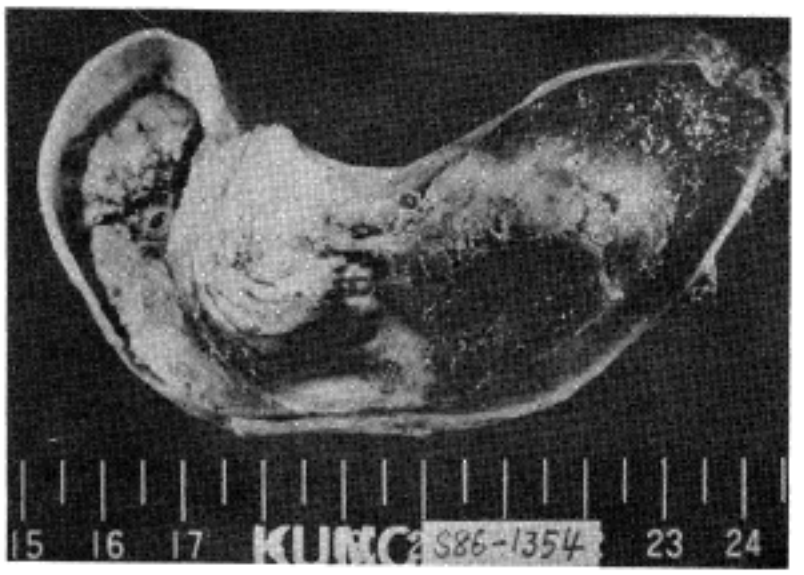


**Fig. 1.** Gallbladder showing a polypoid tumor arising from the fundus.

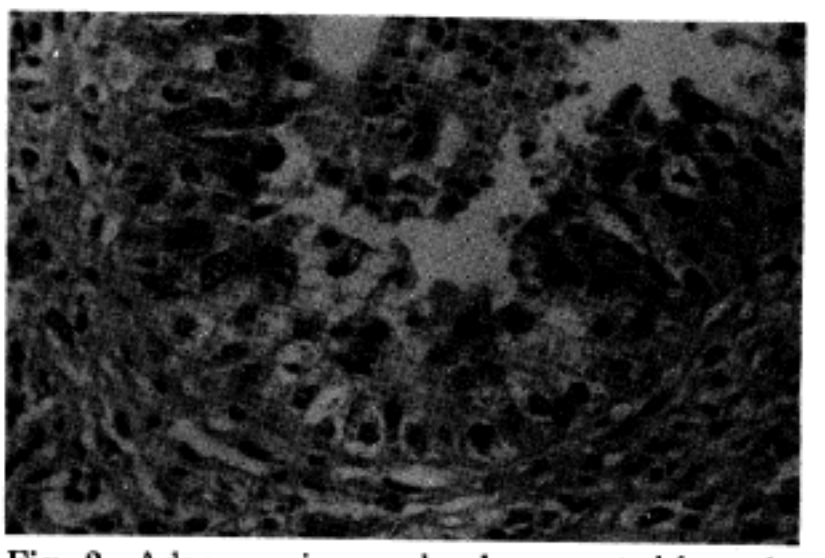

**Fig. 2.** Adenocarcinoma clearly seperated from the surroconding stromal element. (H&E, ×20)

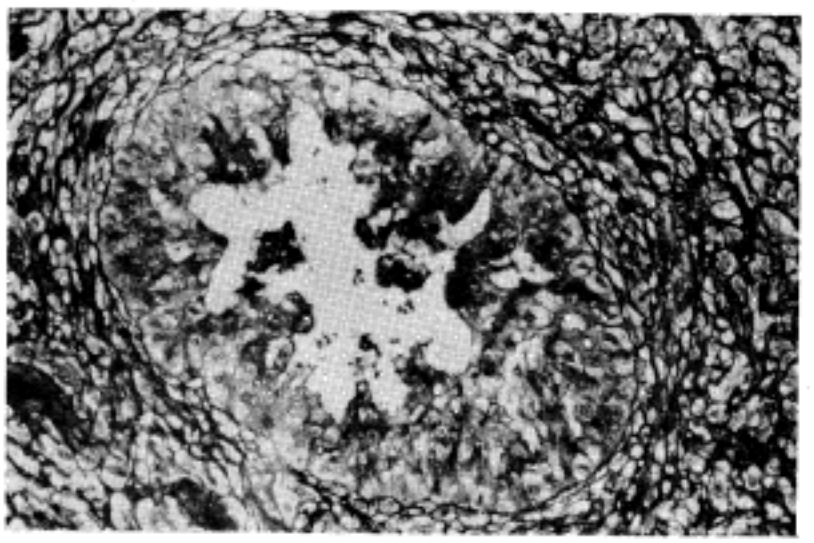

**Fig. 3.** Adenocarcinama clearly seperated from the surrounding stromal element, in which individual stromal cells are wrapped by reticulin fibers. (Reticulum, ×100)

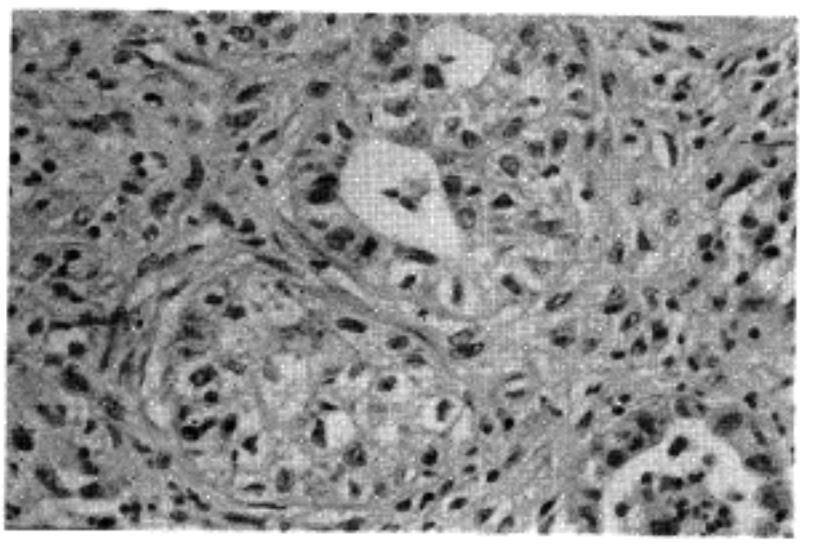

**Fig. 4.** Adenocarcinoma in small glandular pattern intermingled with the sarcomatous element. (H&E, ×100)

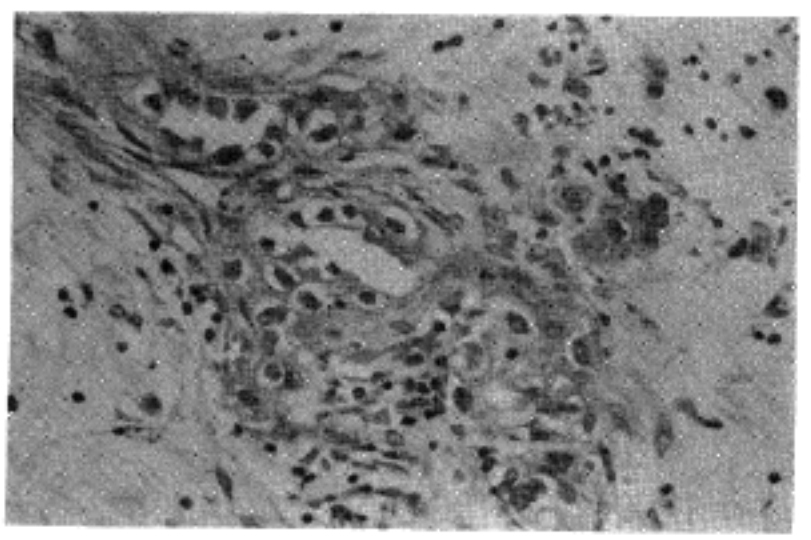

**Fig. 5.** Scattered tumor emboli by carcinoma cells in the base of tumor. (H&E, ×100)

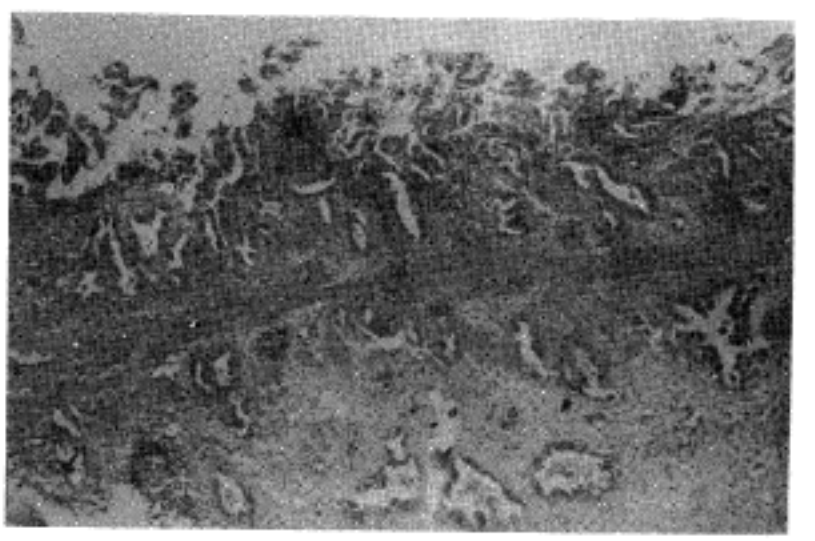

**Fig. 6.** Gallbladder wall away from the polypoid tumor showing infiltrating papillary adenocarcimoma. (H&E, ×20)

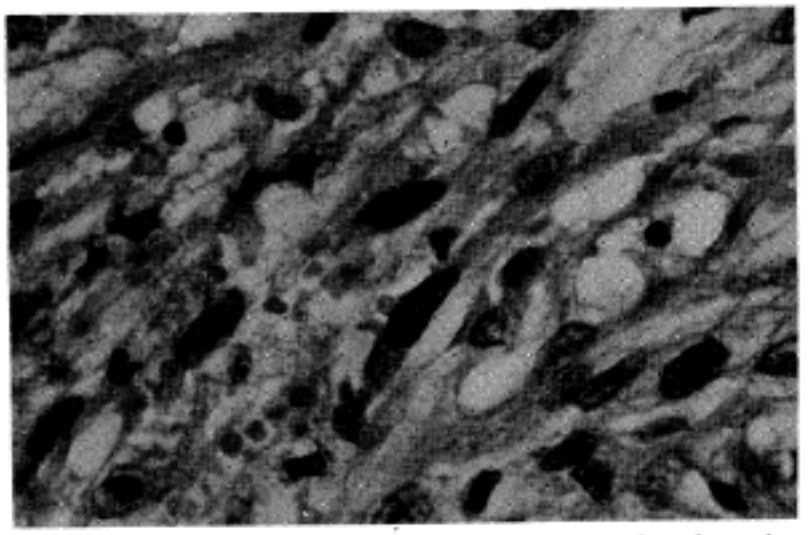

**Fig. 7.** Sarcomatous area showing anaplastic spindle cells with large hyperchromatic nuclei. (H&E, ×400)

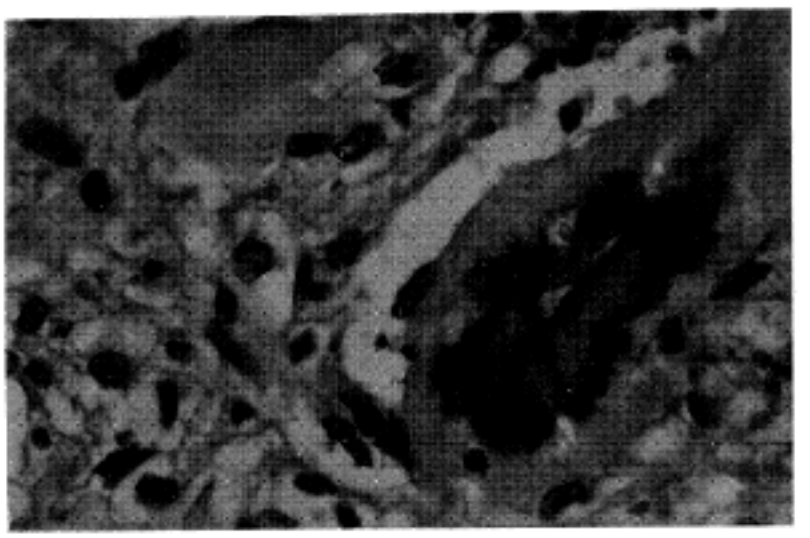

**Fig. 8.** Calcified bony and uncalcified osteoid trabeculae seperated by spindle cells. (H&E, ×400)

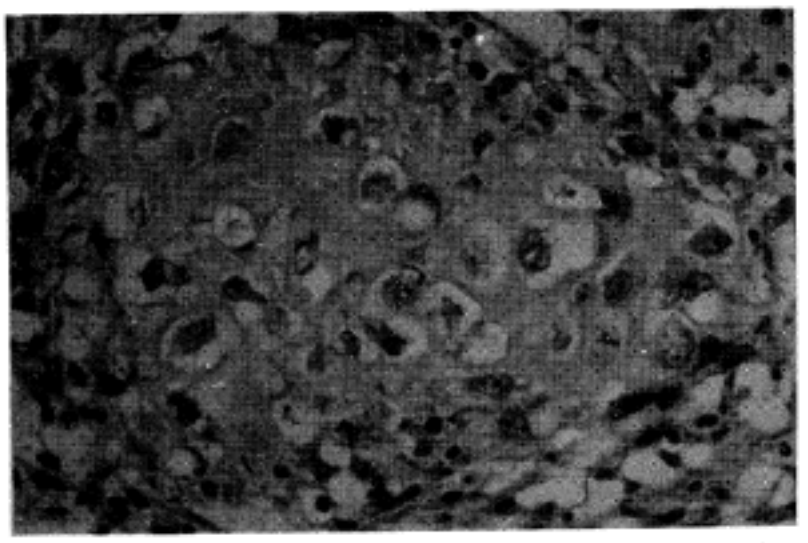

**Fig. 9.** Delicate osteoid formation and intervening atypical cells suggestive of chondroid differentiation. (H&E, ×400)

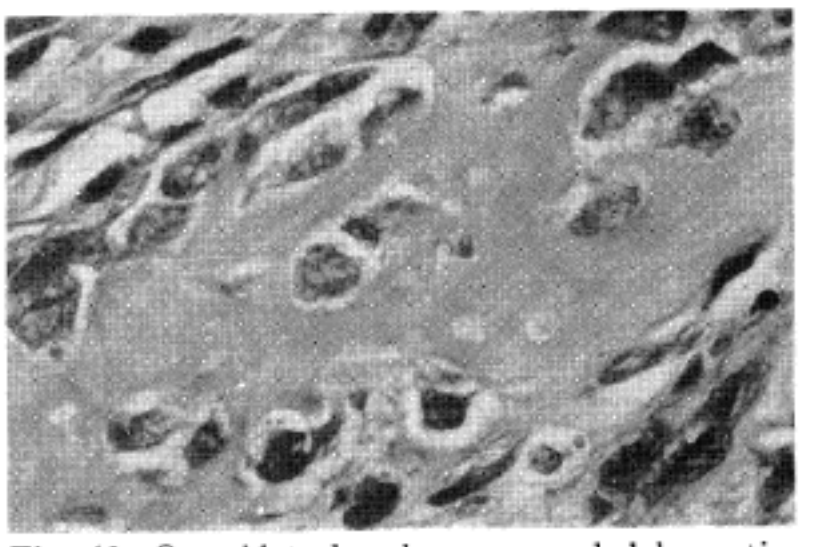

**Fig. 10.** Osteoid trabeculae surrounded by active osteoblasts and pleomorphic cellular tissue. (H&E, ×400)

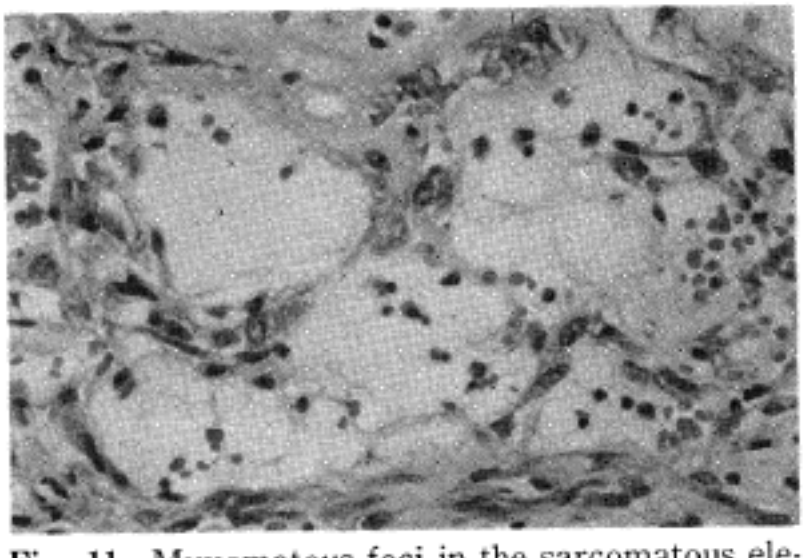

**Fig. 11.** Myxomatous foci in the sarcomatous element. (H&E, ×400)

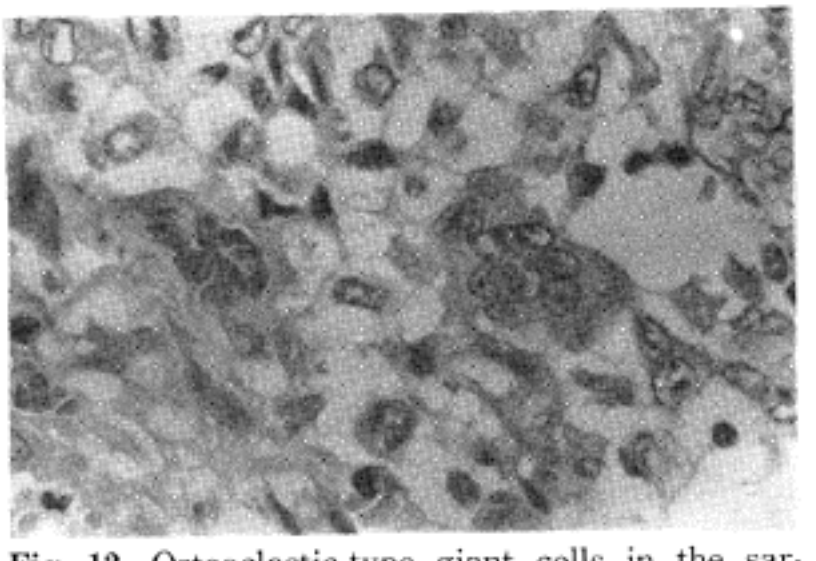

**Fig. 12.** Osteoclastic-type giant cells in the sarcomatous area. (H&E, ×400)