

CARCINOSARCOMA OF THE LUNG REPORT OF A CASE AND REVIEW OF THE LITERATURE

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Abstract

Pulmonary carcinosarcoma is a rare tumor composed of both carcinomatous and sarcomatous elements. Thirty cases of pulmonary carcinosarcoma have thus far been reported. An additional case in a 57 year old female with a carcinosarcoma in the left lung is reported. This case is unusual because it presented with multiple carcinomatous (squamous cell and adenocarcinoma) and sarcomatous (chondrosarcoma and undifferentiated sarcoma) components. In addition, this patient had a right pneumonectomy for an adenocarcinoma of the lung 7 years before. This is the first reported case of a second primary pulmonary carcinoma, associated with pulmonary carcinosarcoma.

From the analysis of published cases, it is apparent that there are two distinct types of pulmonary carcinosarcomas. In one type, the tumor is peripheral, and in the other type, the tumor is central endobronchial with a better prognosis. The clinical history and roentgenography are not particularly characteristic for this tumor. Pulmonary resection when feasible is the effective form of therapy.

Introduction

Carcinosarcomas (mixed malignant tumour) are rare malignant neoplasms that contain simu-tancosly intermixed elements of carcinoma and sarcoma. They have arisen, in decreasing order of frequency, in the uterus, hypopharynx, esophagus and lungs (Saphir and Vass, 1938). Since the original description of pulmonary carcinosarcoma by Kika (Bergmann 1951) in 1908, 30 cases have been reported.

The purpose of this paper is to report an additional case of pulmonary carcinosarcoma and to review in some detail the published experience in 30 cases of pulmonary carcinosarcoma.

Case Report

This patient, a 57 year old white female, was admitted to the Monmouth Medical Centre on September 27, 1974 because of progressively-increasing shortness of breath. In May, 1967 a right pneumonectomy had been performed at another hospital for carcinoma of the lung. Review of the slides confirmed the original histologic diagnosis of adenocarcinoma with anaplasia (Fig. 1).

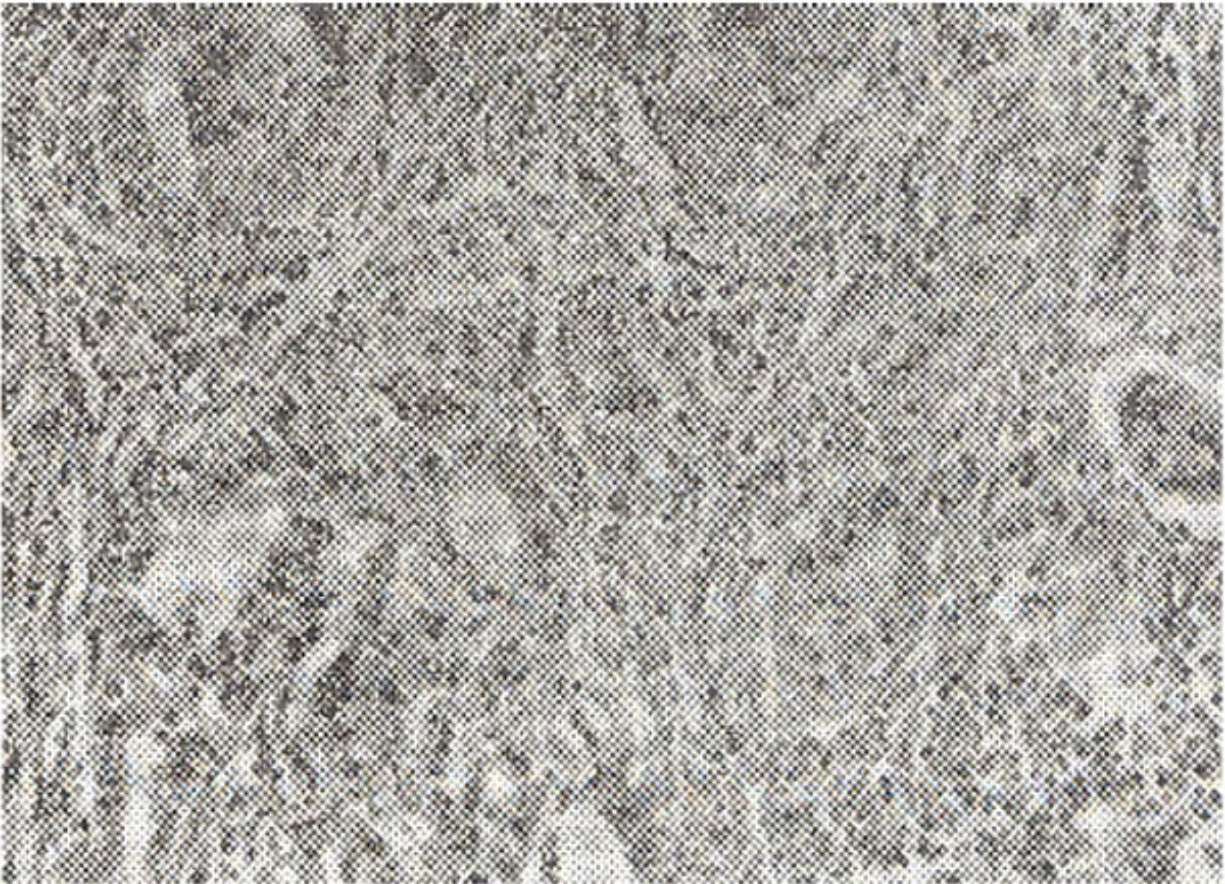


Fig 1: Photomicrograph of tumour removed from right lung in 1967, showing moderately differentiated adenocarcinoma (H.E.X 120)

In the slides reviewed, the lesion appeared to be moderately differentiated adenocarcinoma, and there was no evidence of a sarcomatous component. There were no metastases in hilar lymph nodes. She did not receive any radiation or chemotherapy at that time. In April, 1973 a routine x-ray of the chest revealed a left hilar mass which was thought to be recurrence and/or metastasis from the primary tumour removed in 1967. Radiation therapy to the left lung was begun. After the patient had received 1,000 rads, she refused to take further radiation therapy and was therefore placed on chemotherapy with Cytosin, Oncovin and Prednisone for 4 months without much improvement. During the last year she had several admissions to Monmouth Medical Centre for respiratory failure and congestive heart failure which was treated with Digitalis and Prednisone.

On physical examination the patient appeared chronically ill, she was drowsy and somewhat uncooperative. There was no rash or lymphadenopathy. Breath sounds were absent on the right side and were decreased on the left side with a few moist rales at the base. The heart was not enlarged. The liver edge was barely palpable, the spleen was not enlarged and there were no abdominal masses. Neurological examination was negative.

X-ray of the chest revealed a mass lesion extending from the right midline to the lateral chest wall on the left. An EKG showed changes of right ventricular hypertrophy.

The hematocrit was 45.8 per-cent; the white cell count was 12,000 with 85 per-cent neutrophils. The urea nitrogen was 15 mg/dl, the sodium was 139 meq/l; the potassium was 3.9 meq/l and the chloride

90 meq/l. The CO₂ content was 32.8 meq/l; the pH was 7.16 and the PCO₂ was 84 mm Hg. During her stay in the hospital, the patient was afebrile. She became increasingly unresponsive. She expired on the second hospital day in respiratory failure. An autopsy was performed.

Pathology

The left lung weighed 840 gms with a tumour mass in the upper lobe measuring 14 x 13 x 12 cm. The pleural surface of the lung was intact, there was no direct invasion of the chest wall or thoracic cage (Fig. 2).

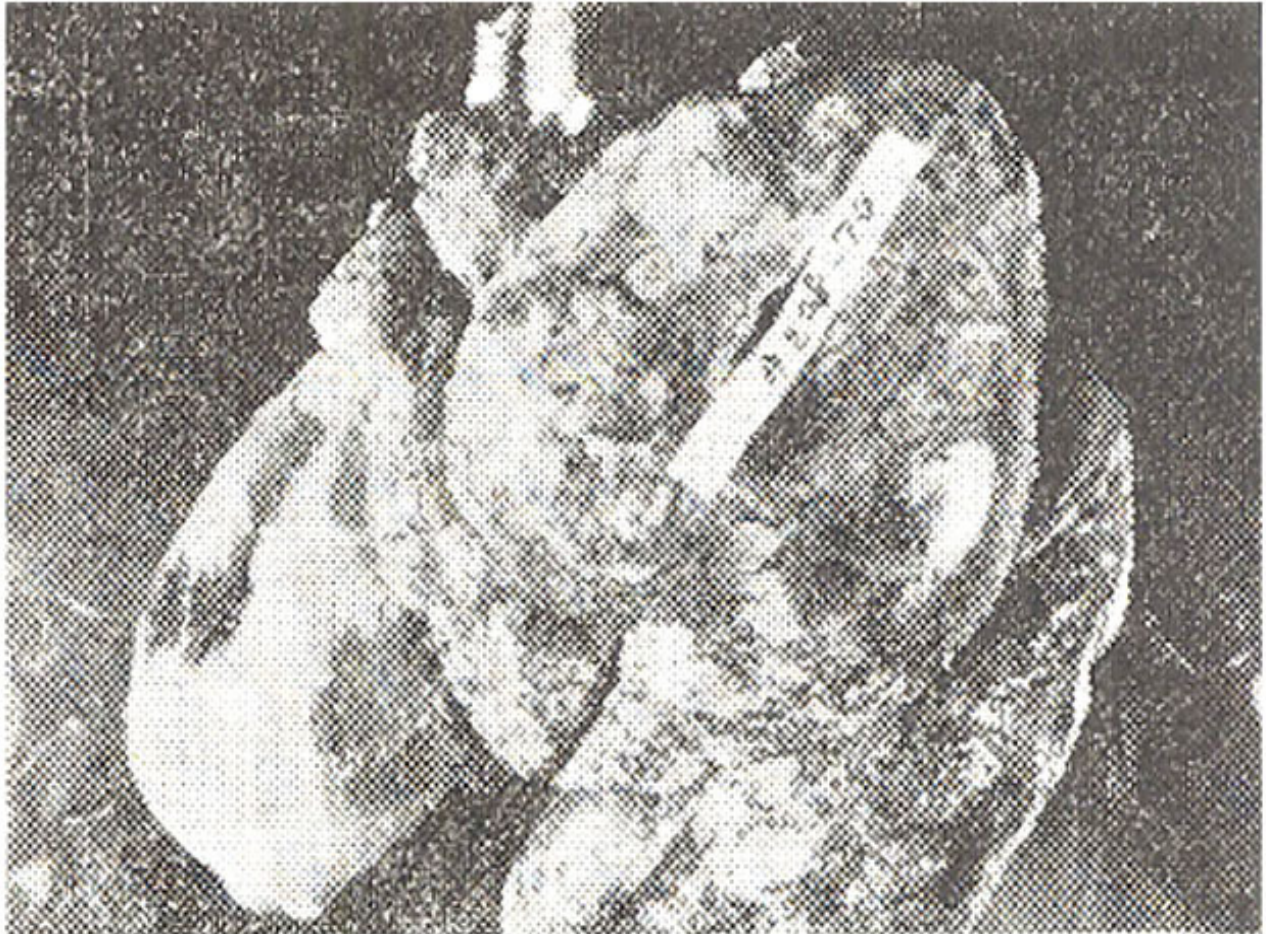


Fig. 2: Photograph of the left lung, showing a large tumour in the upper lobe. The pleural surface is intact.

The tumor had an endobronchial component in the form of finger-like projections growing in the lumen of the main stem bronchus (Fig. 3).

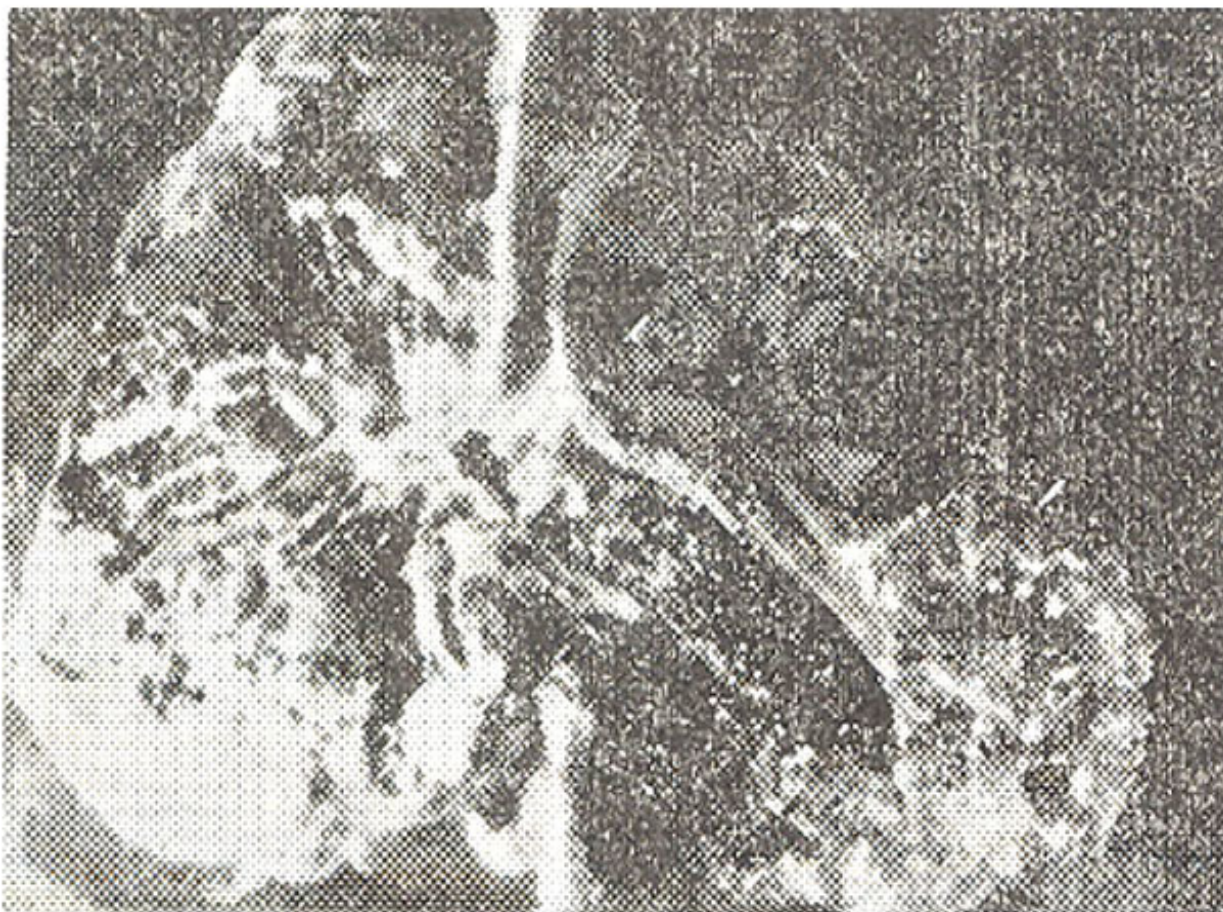


Fig. 3: Photograph showing fingerlike endobronchial growth in the left main bronchus.

The upper lobe was almost completely replaced by a firm tumor. When cut, there was a variegated appearance with areas of hemorrhagic necrosis in a tan parenchyma which contained small nodular, grey, glistening, firm areas (Fig. 4).

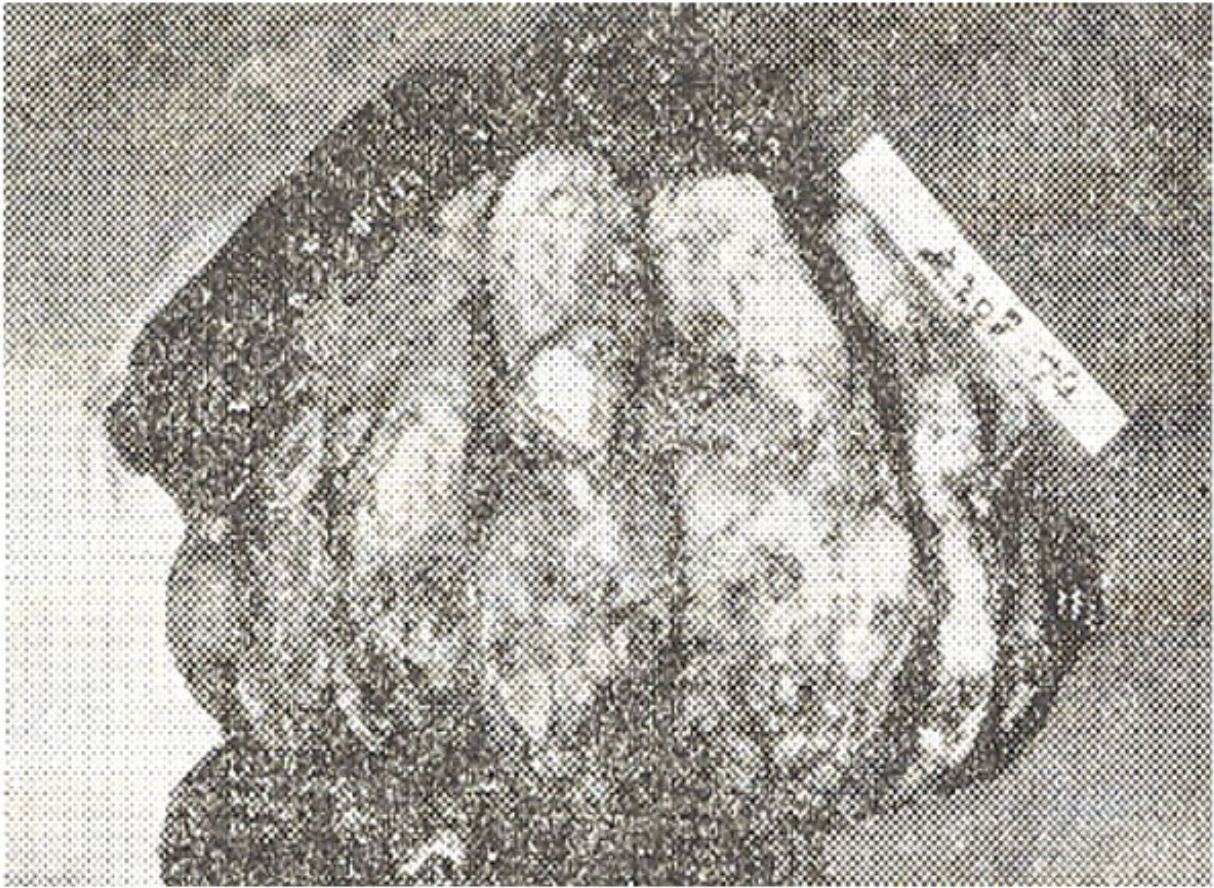


Fig. 4: Photograph of the cut surface of the tumor showing multinodular, grey, hemorrhagic variegated appearance. The tumour has almost completely replaced the left upper lobe.

Microscopically the bulk of the tumour was composed of round spindle shaped undifferentiated sarcoma (Fig. 5).

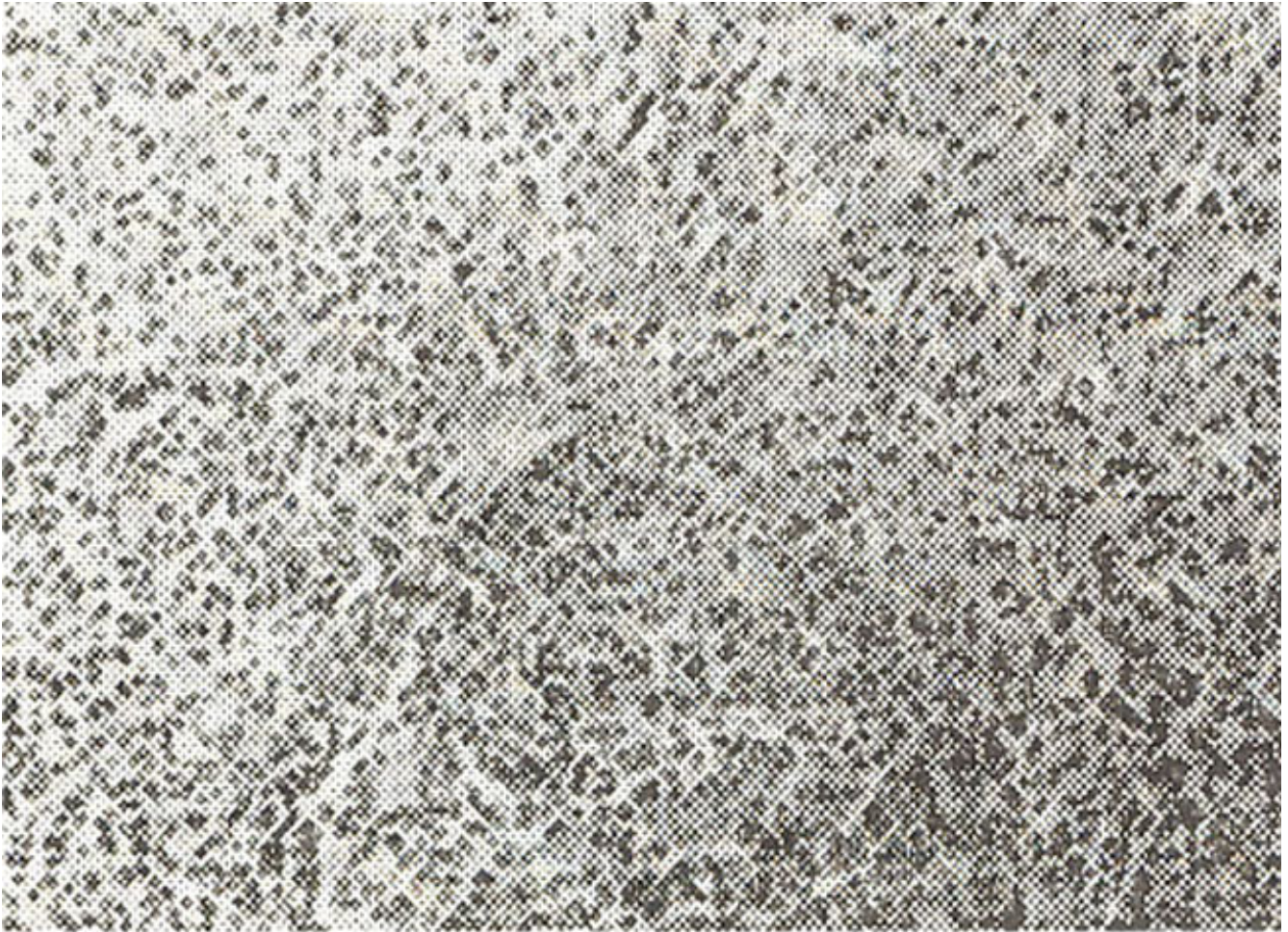


Fig. 5: An area of undifferentiated, round to spindle cell pleomorphic sarcoma (H.E.X 120)

Scattered in it were focal areas which had an organoid appearance reminiscent of carcinoid tumour (Fig. 6).

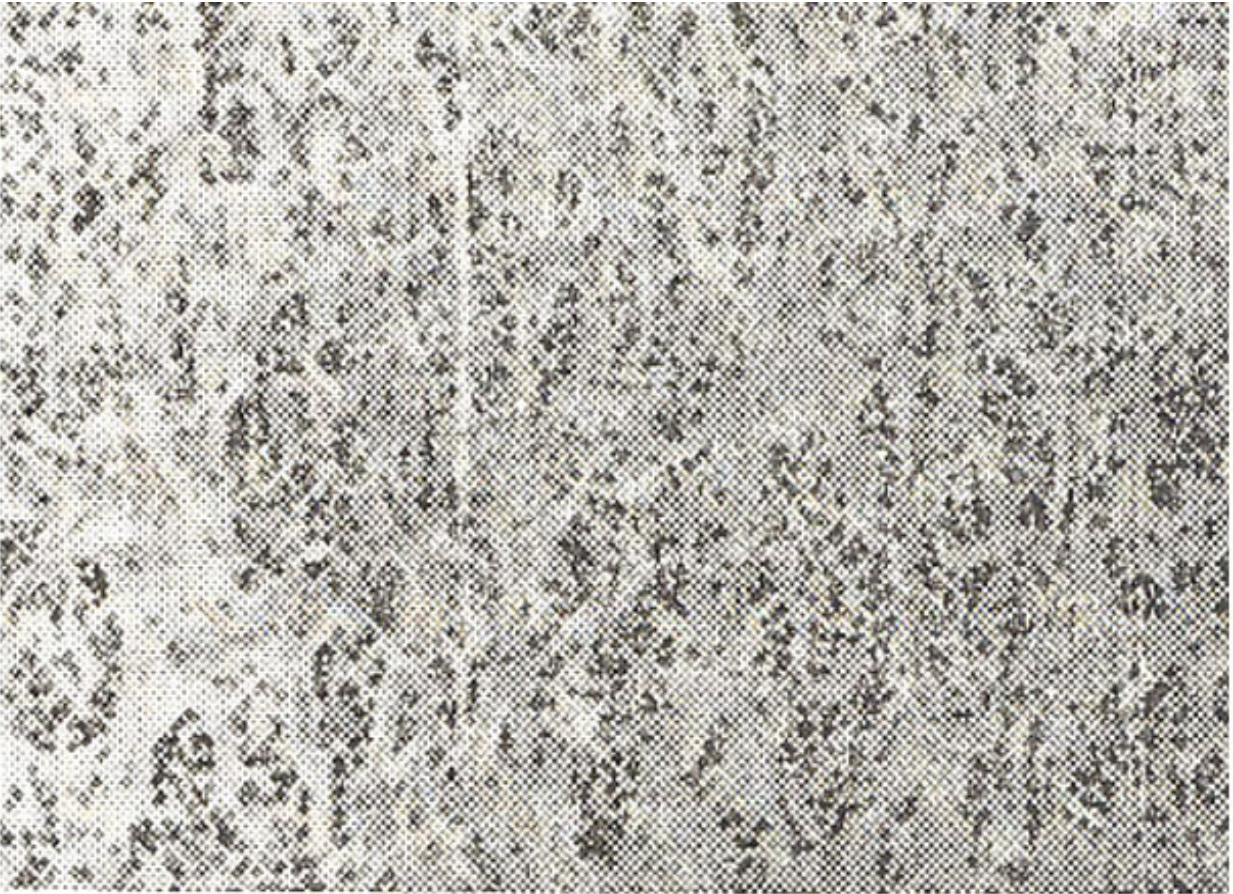


Fig.6: An area of round uniform cells arranged in nests and cords, separated by delicate fibrovascular connective tissue, reminiscent of carcinoid tumor (H.E.X 120)

Occasional multinucleated giant cells resembling rhabdomyoblasts were seen, but no cross striations could be demonstrated (Fig. 7).

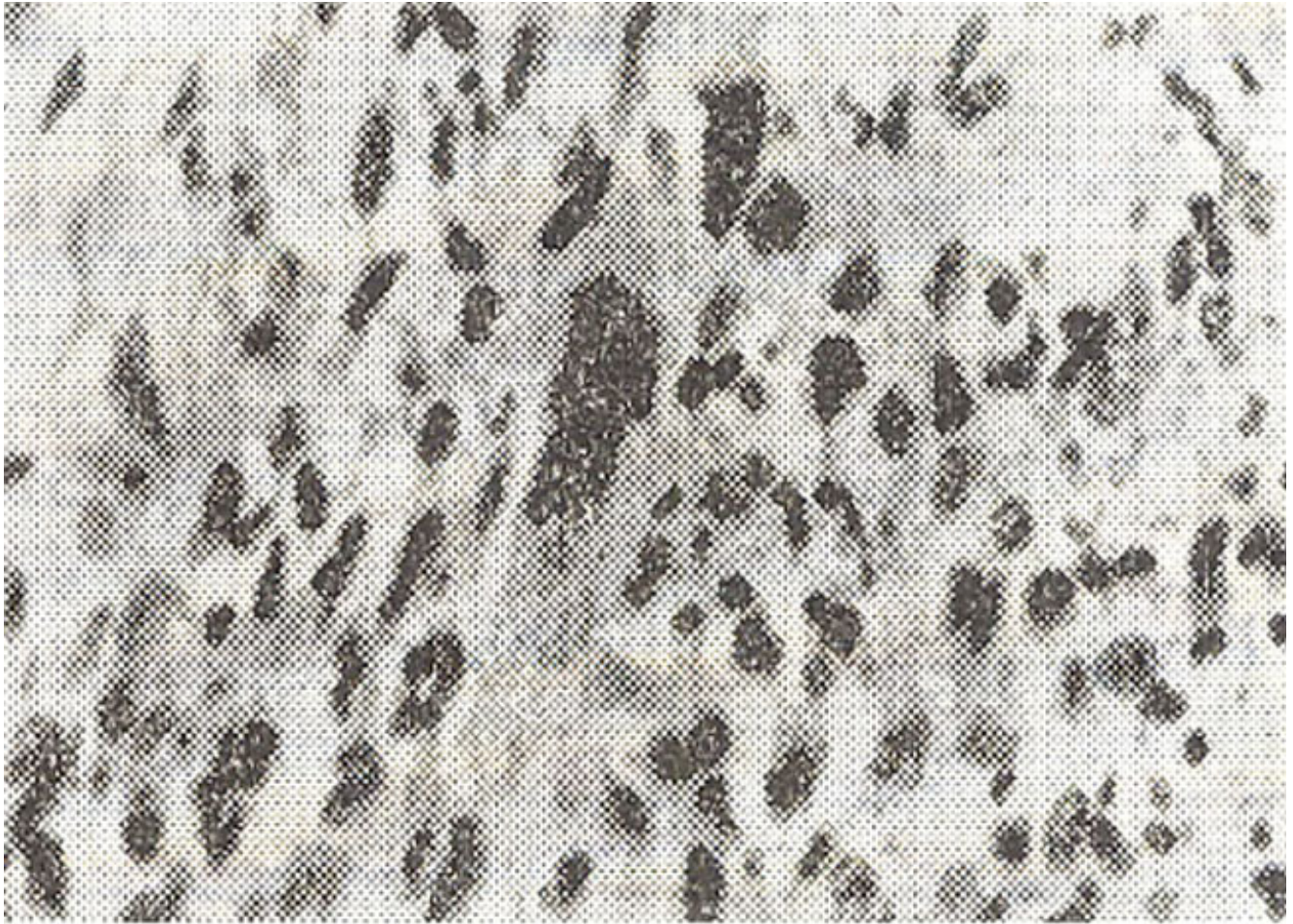


Fig. 7: Multinucleated giant cells resembling rhabdomyoblast (H.E. X 400)

Nodular masses of well to moderately chondrosarcoma was also present (Fig. 8 and 9).

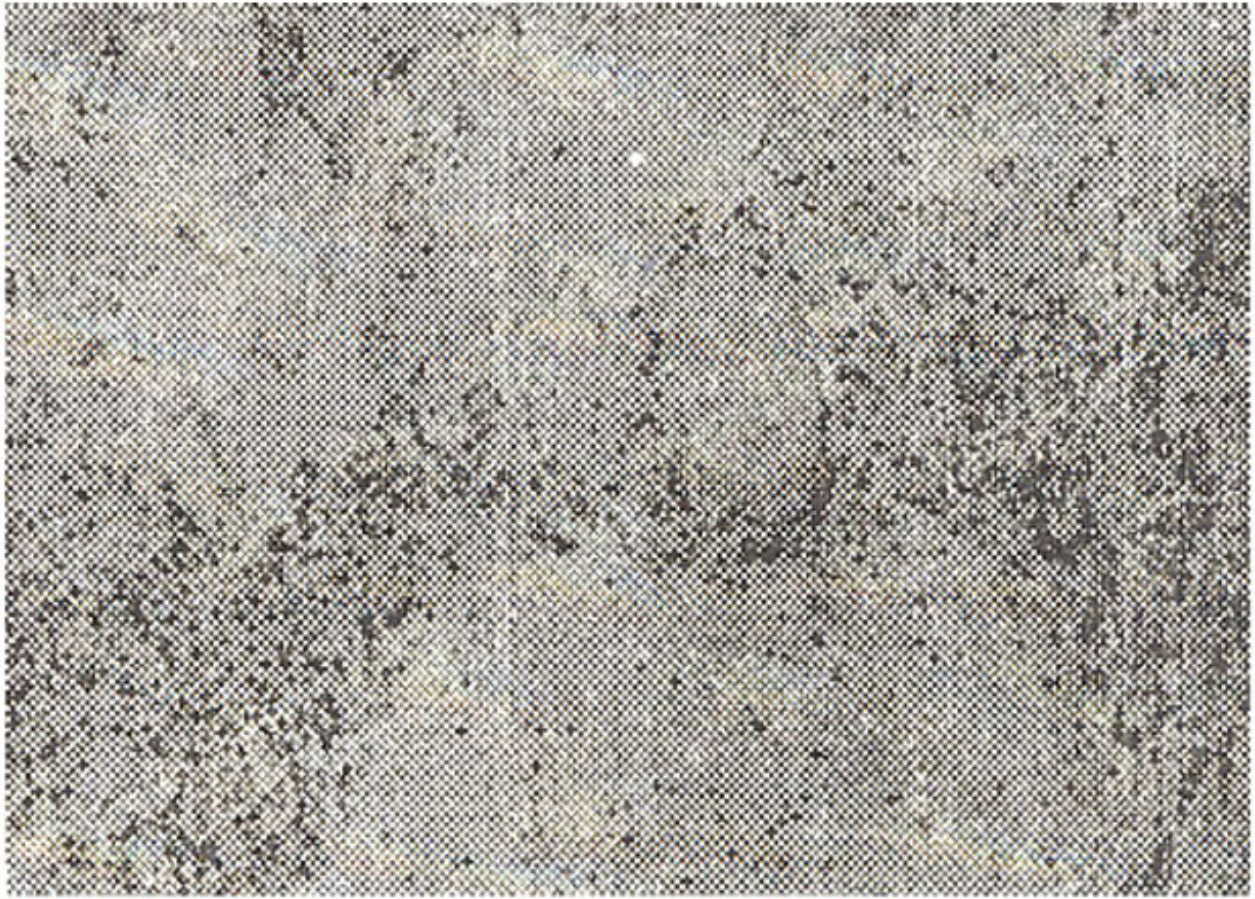


Fig. 8: Nodular masses of chondrosarcoma, surrounded by undifferentiated sarcoma (H.E.X 60)

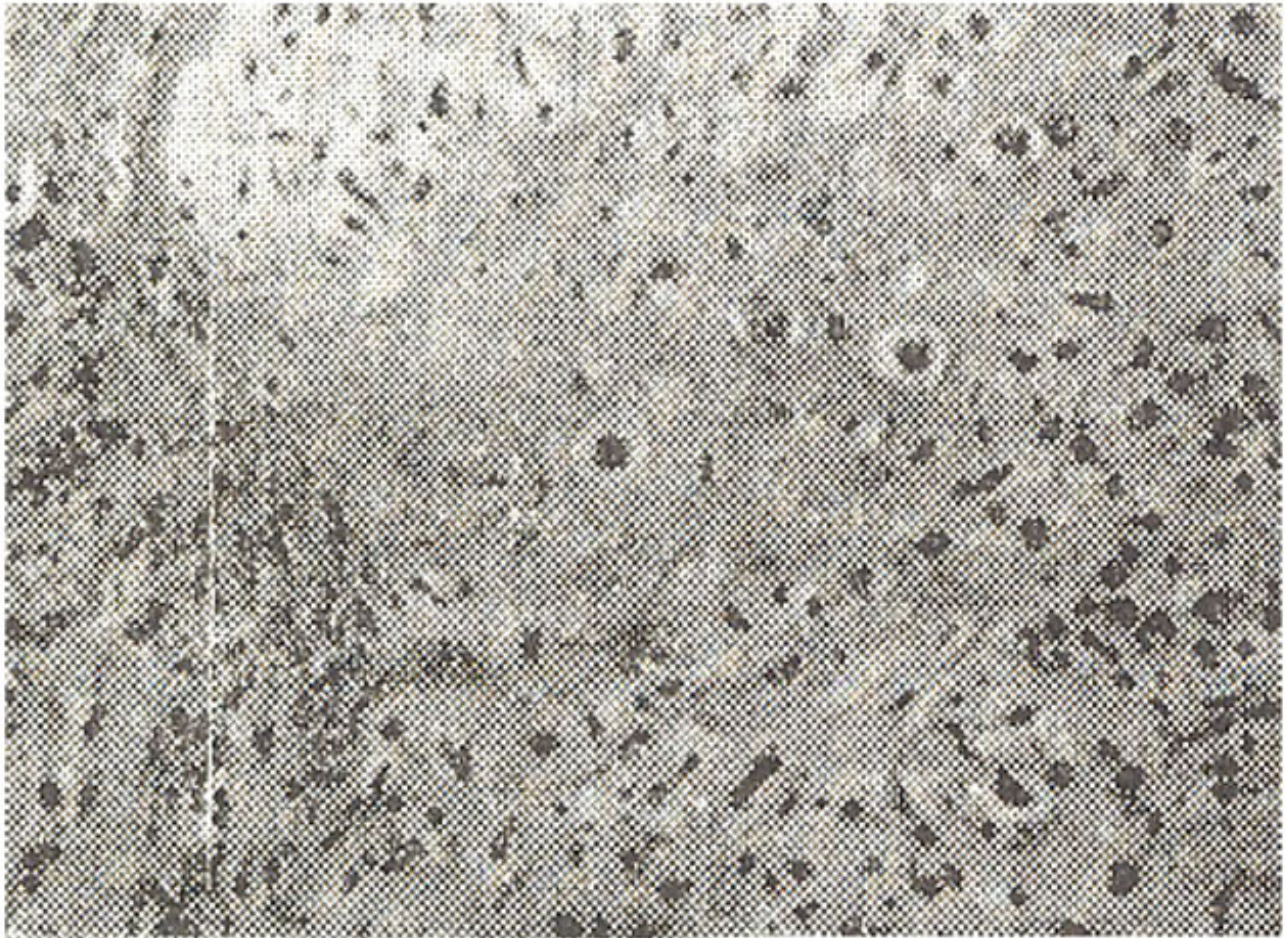


Fig.9: An area of chondrosarcoma showing malignant cells in lacunar spaces (H.E.X 400)

The carcinomatous element was composed of squamous cell carcinoma with keratin pearl formation (Fig. 10)

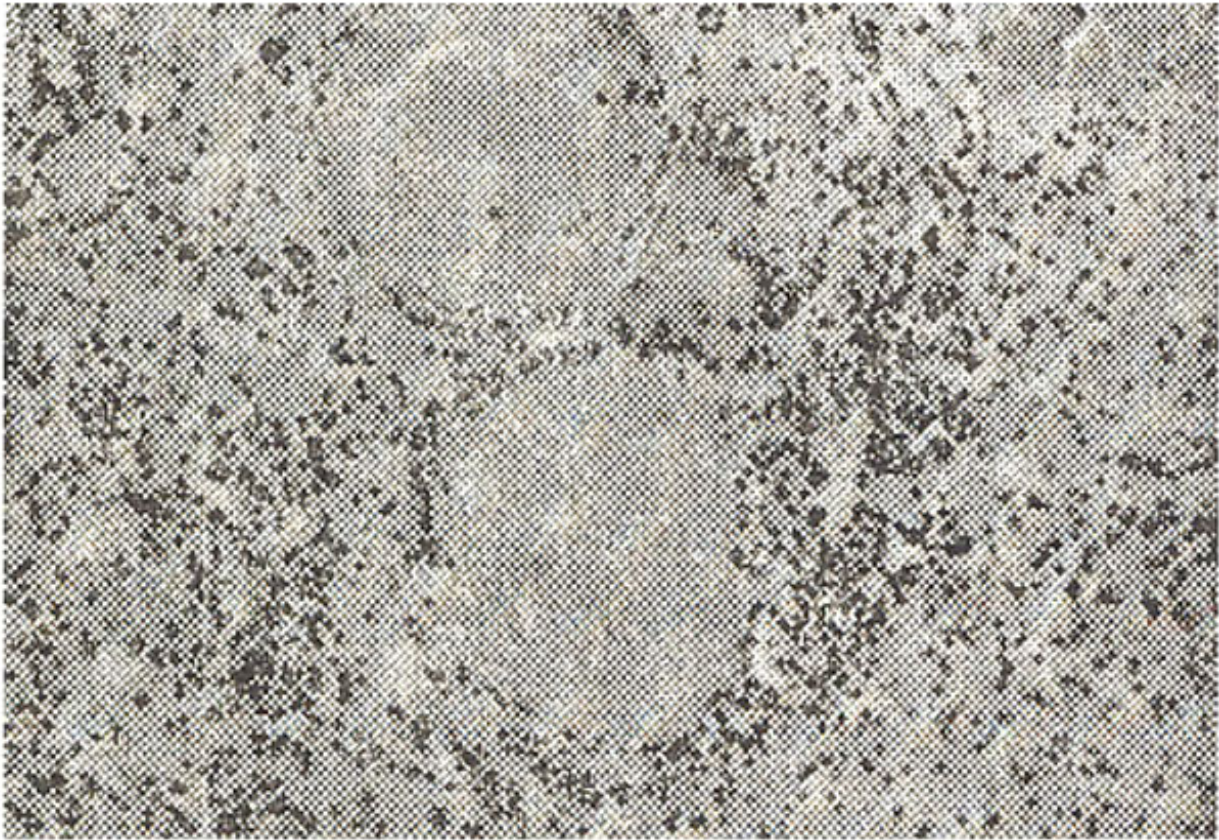


Fig. 10: Foci of well differentiated squamous cell carcinoma with keratin pearl formation. The surrounding stroma is rather loose and undifferentiated (H.E.X 120)

as well as foci of adenopapillary carcinoma (Fig. 11).



Fig. 11: Foci of papillary adenocarcinoma, surrounded by loose mesenchymal stroma (H.E.X 60)

There were no pleural, chest wall or distant metastases, but the tumor did show vascular (Fig. 12)

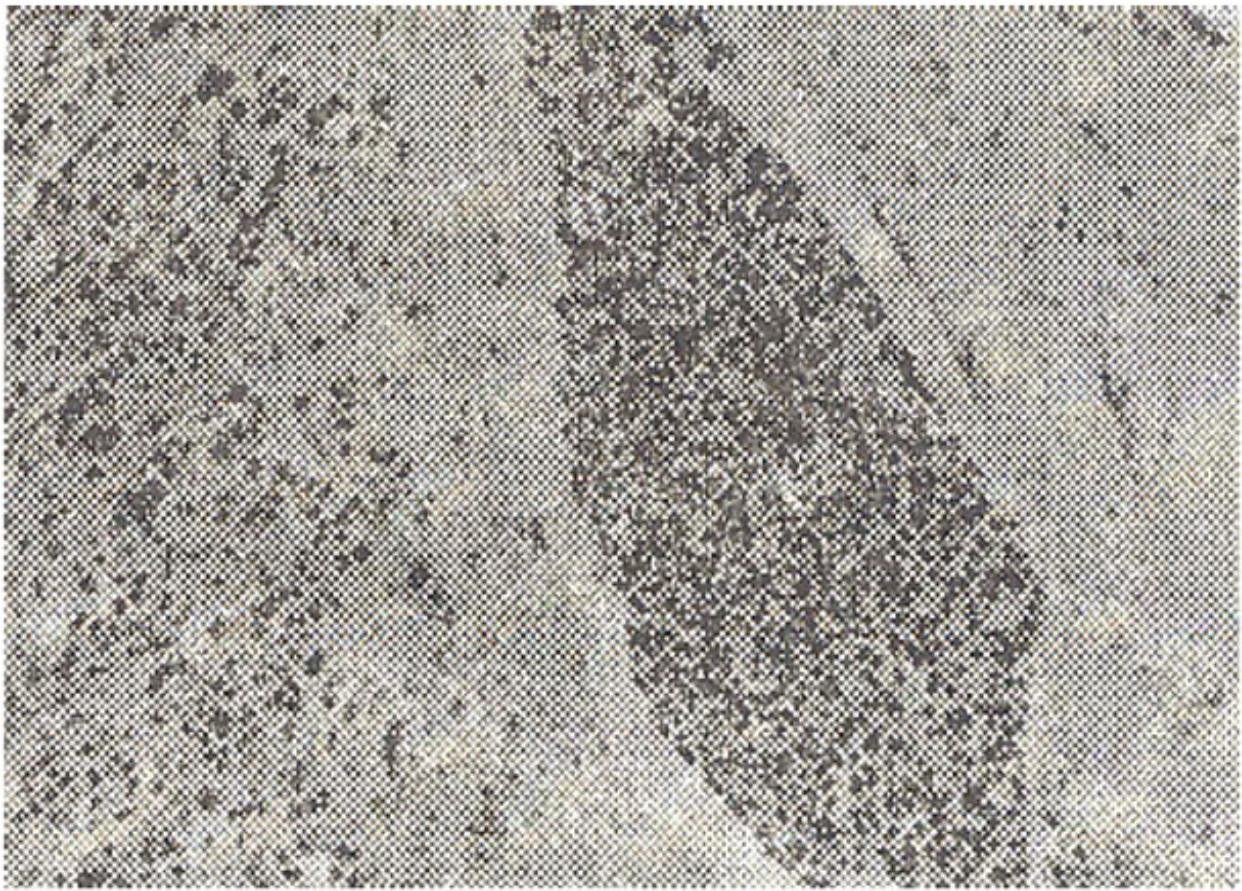


Fig.12: An area of vascular invasion (H.E. X120)

and perineural lymphatic invasion (Fig. 13).

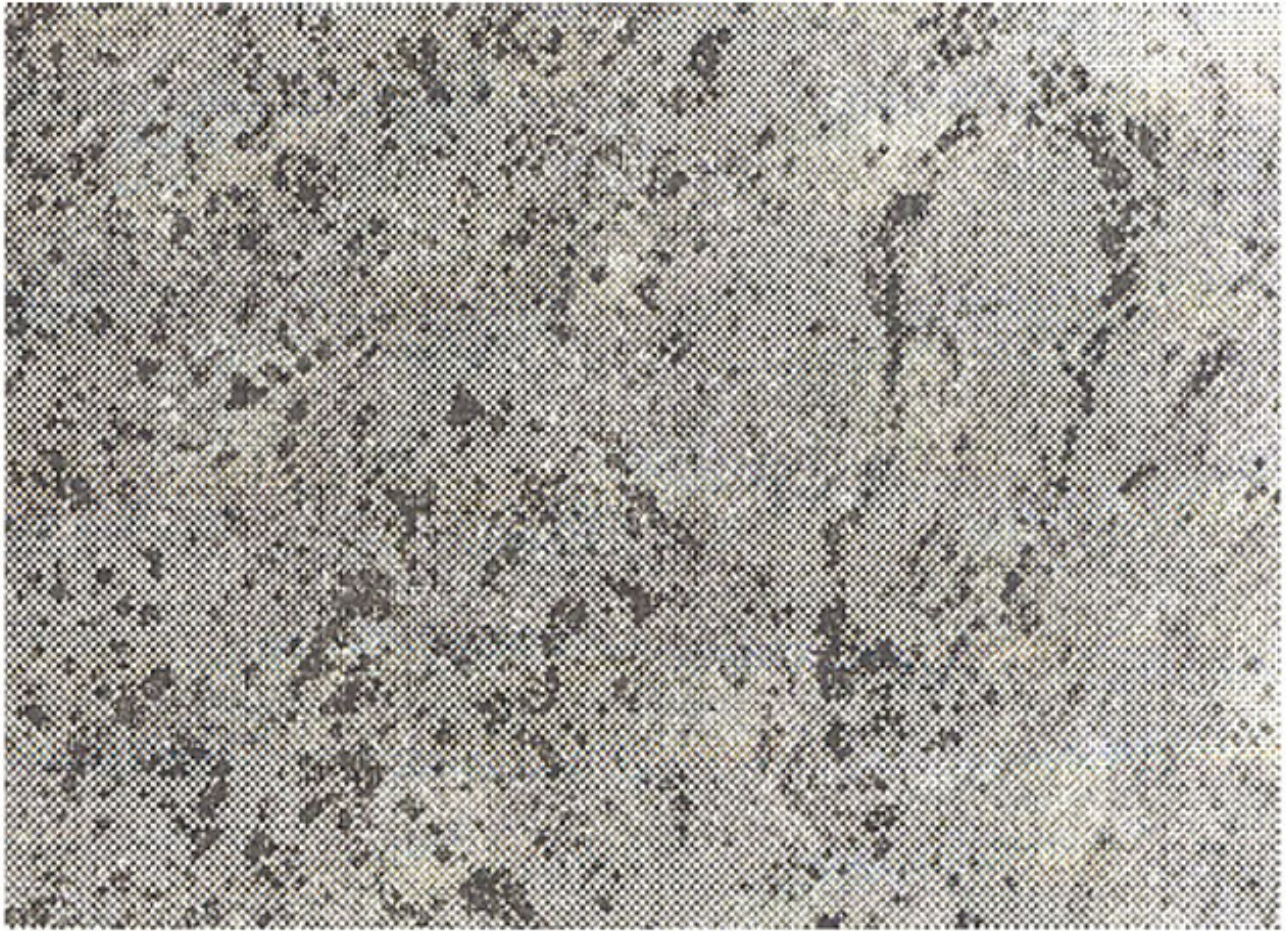


Fig.13: An area showing peri-neural lymphatic invasion (H.E.X 120)

REVIEW OF LITERATURE

A summary of 30 cases reported in literature is presented in the accompanying table.

Table: Showing Findings in 30 Reported Cases

| Case | Author and Year | Sex and Age Size and Location of Lesion | Microscopic | | Metastasis | Treatment | Follow-up |
|------|--------------------------|---|--|--|--|---|---|
| | | | Carcinoma | Sarcoma | | | |
| 1 | Saltykow, 1914 | F. 35 14 cm. rt. lower lobe | Undifferentiated | Spindle cell, pleomorphic | Yes: Chest wall invasion | — | (Autopsy) |
| 2 | Frank, 1915 | F. 45 10x8 cm. Lt. Lower lobe | Adenopapillary | Small spindle cell | Yes | — | (Autopsy) |
| 3 | Selye, 1928 | M.43 'Goose egg', rt. upper lobe with cavity | Epidermoid | Pleomorphic | Yes | — | (Autopsy) |
| 4 | Ogawa, 1929 | M.70 'Child's head' rt. upper lobe | Adenocarcinoma | Small spindle cell | Chest wall invasion | — | (Autopsy) |
| 5 | Fischer, 1938 | M.61 Replaced rt: upper lobe | Epidermoid | Large spindle cell and pleomorphic | Yes | — | (Autopsy) |
| 6 | Weber, 1939 | M.77 Replaced rt. upper lobe | Epidermoid, adenocarcinoma, and undifferentiated | Spindle cell | Yes | — | (Autopsy) |
| 7 | Hochberg et al. 1949 | F.55 11.5x10x5 cm. lt. upper lobe | Epidermoid | Fibrosarcoma | Yes: chest wall invasion | — | Died 17 Hr. post op. |
| 8 | Bergmann et al. 1951 | M.51 3x1.5 cm. rt. upper lobe | Epidermoid | Fibrosarcoma | No | Rt. pneumonectomy | Well 6 years |
| 9 | Bergmann et al. 1951 | M.56 3x1.5 cm. rt. upper lobe | Epidermoid | Fibrosarcoma | No | Rt. pneumonectomy | Well 19 months |
| 10 | Taylor and Rae, 1952 | M.69 4x1.5 cm. rt. main bronchus | Epidermoid | Fibrosarcoma | No | Rt. pneumonectomy | Well 3 years |
| 11 | Taylor and Rae, 1952 | M.57 2x1 cm. lt. main bronchus | Epidermoid | Fibrosarcoma | No | Bronchoscopy | Died 72 hours after admission |
| 12 | Peabody et al. 1958 | M.74 Lt. upper lobe | Adenocarcinoma | Fibrosarcoma | Yes: liver pancreas, kidney, adrenal, mesenteric lymph nodes | Lt. upper lobectomy | Died 4 months post op. |
| 13 | Drury and Stirling, 1959 | M.71 1 Cm. Lt. upper lobe bronchus with distal abscess | Epidermoid | Fibrosarcoma | No | — | Died of pneumonia, 6 months (Autopsy) |
| 14 | Drury and Stirling, 1959 | M.59 10 cm. rt. upper lobe | Epidermoid | Fibrosarcoma | No. | — | Died 6 weeks after admission (Autopsy) |
| 15 | Moore, 1961 | M.64 3 cm. rt. lower lobe with abscess | Epidermoid | Fibrosarcoma, chondrosarcoma, and osteosarcoma | No | Rt. lower lobectomy | Well 19 months |
| 16 | Prive et al. 1961 | M.46 2x1.5x1.5 cm. lt. upper lobe (multiple scattered nodules in lt. upper and lateral lobes) | Epidermoid | Chondrosarcoma and osteosarcoma | Yes | Lt. pneumonectomy | Well 18 months |
| 17 | Stackhouse et al. 1969 | F.73 Lt. upper and lower lobes and main bronchus | Squamous cell | Fibrosarcoma | Hilar and mediastinal nodes | Lt. pneumonectomy | Died 3 months |
| 18 | Stackhouse et al. 1969 | M.54 Size (?) polypoid in rt. upper and main bronchus: cavity in middle | Squamous cell | Fibrosarcoma | Rib and pelvis at 3 months | Bronchial biopsy external radiation | None after 3 months |
| 19 | Stackhouse et al. 1969 | M.74 6x5x5 cm. rt. upper lobe, polypoid | Squamous cell | Fibrosarcoma and osteogenic sarcoma | Hilar nodes (direct extension) | Rt. pneumonectomy | Died 6 months Myocardial infarction |
| 20 | Stackhouse et al. 1969 | F.60 6x5x3 cm. Lt. upper and polypoid | Adenocarcinoma undifferentiated | Fibrosarcoma | Mediastinum, humerus and lung | Lt. upper lobectomy and external radiation | Died 11 months |
| 21 | Stackhouse et al. 1969 | M.68 3x2.5x3 cm. lt. upper lobe, polypoid | Squamous cell | Fibrosarcoma | None | Lt. pneumonectomy | Died 6 days post op. |
| 22 | Stackhouse et al. 1969 | M.70 7x4.5x3 cm. rt. apex | Squamous cell and undifferentiated large cell | Fibrosarcoma and focal chondrosarcoma | Chest wall (direct) | Rt. upper lobectomy, Ex: radiation, Actinomycin D | Died 3 years 8 months. Autopsy: Residual tumor chest wall |
| 23 | Stackhouse et al. 1969 | M.52 3x4x3.5 cm. lt. upper lobe | Squamous cell | Fibrosarcoma and osteogenic sarcoma | Hilar nodes | Lt. upper lobectomy | Well 3 years 8 months |
| 24 | Stackhouse et al. 1969 | M.70 12.5x5.5x6 cm. and 4x2.5x2 rt. lower lobe | Adenocarcinoma | Fibrosarcoma | Hilar nodes | Rt. lower lobectomy and chest wall resection | Recurrence in lung 6 months |
| 25 | Stackhouse et al. 1970 | M.69 5x4x3 cm. lt. lower lobe | Adenocarcinoma | Fibrosarcoma | Hilar nodes | Lt. upper lobectomy | Died 2 months Clinical CNS |
| 26 | Razzuk et al. 1970 | M.61 Size (?) endobronchial, lt. upper main stem bronchus | Epidermoid | Spindle cell sarcoma | None | Lt. pneumonectomy | Died 21 months post op. |
| 27 | Razzuk et al. 1970 | F.66 3x2.5x2.5 cm. peripheral, lt. upper lobe | Adenocarcinoma, undifferentiated carcinoma | Spindle cell sarcoma | Hilar nodes | Lt. upper lobectomy | Died 10 months post op. |
| 28 | Chaudhuri, 1970 | M.65 10x10x6 cm. posterior and middle basal segments of lt. lower lobe | Squamous cell | Fibrosarcoma | Pleural, pericardial and chest wall (direct) | Lt. pneumonectomy | Died 3 months post op. |
| 29 | Chaudhuri, 1970 | M.69 1x1 cm. endobronchial Lt. upper bronchus | Squamous cell | Spindle cell sarcoma | None | Sleeve resection lt. upper lobe | Died 2 months post op. |
| 30 | Kakes et al. 1970 | M.72 Left lower lobe | Squamous cell | Myxoid Spindle cell sarcoma | None | Lt. lower lobectomy | 6 months post op.-well |

Note:—'Yes' in the column of metastasis indicates multiple distant metastases.

Clinical Features

Of the 30 cases with carcinosarcoma reported in the literature, there were 24 men and 6 women with M:F ratio of 4:1. The age ranged from 35 years to 77 years with the highest incidence in the sixth and

seventh decades. Twenty patients had symptoms referable to the respiratory tract. 16 patients complained of cough; 8 gave a history of hemoptysis; 8 of chest pain; 3 of dyspnea and 2 of hoarseness. Significant weight loss was observed in 8 patients. The case reported by Weber (Bergmann et al 1951) presented with anorexia, abdominal pain and vomiting. The clinical picture was explained by finding numerous gastrointestinal metastases. Ogawa's (Bergmann et al 1951) case presented with malaise and dull pain in the shoulder with radiation to the back. Three of the 9 cases reported by Stackhouse et al (1969) were asymptomatic; a mass was found on routine x-ray of the chest. X-ray evidence of bronchial obstruction with atelectasis was seen, in 8 cases. A mass was seen on x-ray in 18 cases. One case reported by Stackhouse et al (1969) had a lymphosarcoma nine years prior to pulmonary neoplasm and had been given radiation therapy.

Gross Pathology

The tumours varied in size; the smallest was 1 cm and the largest 14 cm in diameter (Bergmann et al., 1951). Three major forms of pulmonary carcinosarcomas were seen: (a) solely endobronchial; (b) solely peripheral or parenchymatous; (c) endobronchial with parenchymatous component. Of the 30 cases reported in literature, 10 were solely endobronchial; 13 were only parenchymatous (this includes 7 cases which were diagnosed at autopsy and were extensive with multiple distant metastases); 6 cases had both endobronchial and parenchymatous component.

Gross features of these tumours such as colour, and consistency were nonspecific and varied considerably. All extrabronchial masses were moderately firm, homogenous, multinodular circumscribed lesions which were pinkish or yellow-grey (Bergmann et al., 1951; Stackhouse et al., 1969). The intrabronchial components were polypoid and similar to the under-lying parenchymal component (Bergmann et al., 1951; Stackhouse et al., 1969).

Microscopic Description

A. Carcinoma

The most common carcinomatous element was epidermoid or squamous cell carcinoma which was seen in 20 cases. Adenocarcinoma was present in 5 cases. Adenocarcinoma with undifferentiated carcinoma was seen in 2 cases. Undifferentiated Carcinoma; squamous cell with undifferentiated carcinoma; and adenocarcinoma with squamous and undifferentiated components were observed in 1 case each.

B. Sarcoma

The most common sarcomatous component observed was a spindle cell or fibrosarcoma which was seen in 25 cases. In 1 case the sarcomatous element was composed of elements of fibrosarcoma, chondrosarcoma and osteosarcoma. Fibrosarcoma and osteosarcoma were seen in 2 cases. Chondrosarcoma and osteosarcoma; and fibrosarcoma and chondrosarcoma were found in one case each.

Metastases

Bergmann et al reviewed the literature in 1951 and found 7 examples of such lesions. All were diagnosed at autopsy. All except 1 showed distant metastases; the adrenals and the kidneys were the most common sites of metastases. Both malignant elements were present in 2 cases and the rest of the cases showed one malignant element. In Stackhouse's (1969) series, regional nodular metastases were noted in 5 of 8 patients who underwent operation. Both malignant elements were present in 3 patients; carcinoma only or sarcoma only was noted in 2 others by direct extension, and distant metastases were observed in 2 cases.

Survival

Known survival varied from 18 months to 6 years in 6 patients. These were patients last seen at 18 months (Prive et al., 1961); 19 months (2 patients) (Bergmann et al., 1951; Moore, 1961); 3 years (Taylor et al., 1952); 3 years 8 months (Stackhouse et al., 1969) and 6 years (Bergmann et al., 1951) without clinical evidence of recurrence. It is of note that predominantly endobronchial neoplasms were found in the survivors. The experience is similar to the pedunculated carcinosarcoma arising in the

esophagus and hypo-pharynx.

Discussion

The separate classification of carcinosarcoma in any organ system is a debated issue. Willis (1967) defines carcinosarcomas as a simultaneously malignant neoplasia in two distinct tissues; an epithelial tissue and a non-epithelial tissue; or a consequent sarcomatous change in the stroma of a carcinoma. The fortuitous development of two separate tumours, a carcinoma and a sarcoma in continuity ('collision tumour') should not be called carcinosarcoma. Saphir et al (1938) reviewed the subject and found 153 examples of carcinosarcomas of all sites. They accepted 3 or 4 cases as being carcinosarcomas and they expressed the opinion that all the other cases were in reality examples of morphological capabilities of one type of cell. In their analysis they found many complicating factors which played a role in the alteration of the fundamental histologic appearance of the tumour, such as: (a) variation of carcinoma cells, some of which can assume spindle shapes and may be interpreted as cells of spindle cell sarcoma, a feature which is particularly true of squamous cell carcinoma; (b) marked anaplasia of carcinoma cells; (c) chronic inflammation which either leads to morphologic change of tumour cells or provokes much connective tissue response which may be regarded as a part of malignant connective tissue tumour; (d) invasion of benign connective tissue tumour; and (e) sarcomas which had invaded normal or metaplastic epithelial structures.

However, carcinosarcoma, although rare, is a distinct pathologic entity. This is supported by experimental studies of transplants of mammary carcinoma in mice (Stewart et al., 1959). While transplanting pulmonary carcinoma subcutaneously, Stewart and associates noted the emergence first of carcinoma and then fibrosarcoma. On the basis of x-ray induced ovarian tumors in mice, Aykan (1956) concluded that the two kinds of elements undergo neoplastic transformation simultaneously and independently. There are various conditions which may simulate carcinosarcoma; most of which are merely carcinoma with an anaplastic epithelial component mimicking malignant mesodermal stroma. However, the presence of dense reticulin, malignant cartilage and bone is helpful in differentiating the two lesions. Sarcomatous development in a hamartoma can simulate carcinosarcoma. Cavin et al (1958) reported a case of leiomyosarcoma arising in a hamartoma. In none of the 31 cases including our own, was there any evidence of pre-existing hamartoma. Another suggestion that these tumours arise in teratomas is also acceptable; in a teratoma a variety of heterogeneous somatic elements are arranged in a more or less jumbled or haphazard fashion (Willis, 1967). This pattern is not seen in any of the carcinosarcomas of the lung. Pulmonary blastoma is a distinct entity and morphologically consists of well differentiated adenocarcinoma in a stroma of immature or undifferentiated sarcoma (Minken et al., 1968; Bauermeister et al., 1966).

From an analysis of 31 cases including our own, it is apparent that there are two distinct types of pulmonary carcinosarcomas. In one type the tumour is peripheral or parenchymatous. It may attain considerable size prior to detection and has a tendency towards direct invasion of the chest wall and mediastinal structures. There is also a tendency towards distant metastases and the prognosis is poor. The second type of tumour is more centrally located. It occurs as a pedunculated endobronchial growth. The prognosis with this type of tumor is surprisingly good. Pulmonary resection when feasible is the effective form of therapy.

The case reported in this paper has certain unusual features. The tumour presented with multiple carcinomatous (squamous cell and adenocarcinoma) and sarcomatous (chondrosarcoma and undifferentiated sarcoma) elements. As far as we know, there are 5 cases in the literature which presented in a similar fashion (Moore, 1961; Prive et al., 1961; Stackhouse et al., 1969). Another unusual feature of this case is the occurrence of an adenocarcinoma in the other lung 7 years before. The subject of two histologically different primary carcinomas of the lung has been reviewed by

Mobley and Martinez (1968). They found 33 such cases in the literature and reported an additional case. None of their cases were associated with carcinosarcoma. To our knowledge, this is the first reported case of carcinosarcoma associated with another histologically different primary carcinoma of the lung.

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