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Osteosarcoma of the Breast

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Summary. Osteosarcoma of the breast is an unusual neoplasm. The authors describe such a tumour found in a 38 year old woman. The neoplasm developed rapidly within 5 months of the patient's first observation. Histological study revealed extensive fibroadenomatous tissue with osteosarcomatous metaplastic foci. The tumor rapidly recurred and was then composed exclusively of sarcomatous tissue. The patient died 15 months after first recognition of the tumor probably from generalized metastases. The epithelial and mesenchymatous origin of osseous metaplasia within (phylloid) fibroadenoma is discussed.

Zusammenfassung. Fallbeschreibung eines primären osteogenen Sarkoms der Brustdrüse bei einer 38jährigen Frau, welches 5 Monate nach ersten klinischen Symptomen festgestellt wird. Kurze Zeit später tritt ein lokales Rezidiv auf. Exitus 10 Monate nach der ersten Excision bei wahrscheinlicher generalisierter Mestastasierung. — Histologisch handelt es sich zuerst um ein umfangreiches phylloides Fibroadenom mit eindeutig malignen osteoplastischen Herden. Später untersuchte Rezidive bestehen ausschließlich aus osteosarkomatösem Gewebe. — Die umstrittene Histogenese dieser seltenen Geschwulst wird diskutiert, wobei die Deutung der Knochenbildung als Metaplasie des mesenchymatösen Anteils des (phylloiden) Fibroadenoms am wahrscheinlichsten erscheint.

The rarity and controversial histogenesis of osteosarcoma of the breast prompt us to present a new observation on this subject.

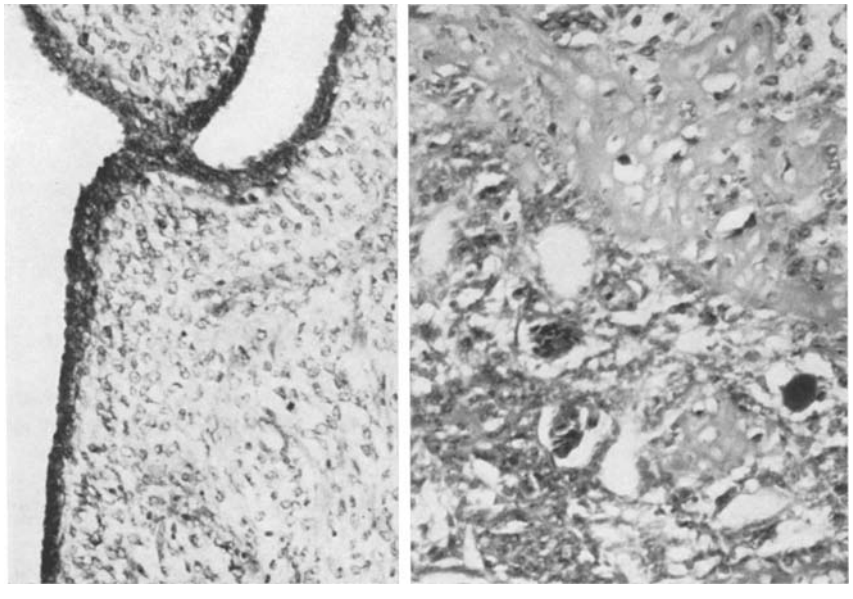
Case History

Five months before medical consultation, Mrs. Rosa C., 38 years old, fell at home, knocking her left breast against a stool. During the following days, a haematoma formed in that region, which disappeared. Four months after the accident, the young woman noticed a rapidly growing nodule in her left breast painful to the touch. Medical examination[1] revealed a firm induration in the supero-internal region of the left breast, about 6 cm in diameter, adhering to the deeper layers but not to the skin. No palpable axillary lymph nodes.

The mammography showed nodular shadows, partly calcified. From an extemporaneous biopsy we diagnosed a phylloid fibroadenoma with malignant osseous metaplasia. Radical mastectomy, according to Halsted, was performed only 6 weeks later. After two months, a tumoural invasion of the remaining external mammary and left axillary tissues was noticed and subsequent radiotherapy was carried out (5950 r). Seven months after the first diagnosis, two pulmonary metastases and pleural effusion were discovered. The patient returned to her native country where she died eleven months after tumour onset. There was no autopsy.

Macroscopy. 1. The extemporaneous biopsy (T 4320/70) consists of mammary tissue measuring 8 cm in its greatest dimension and contains a firm whitish nodule of $4 \times 2 \times 2$ cm, partially haemorrhagic with small beige foci grating under the knife.

1 The authors are grateful to Drs. A. Porchet and Ch. Perrin from Hôpital Pourtalès, Neuchâtel, for their clinical observations.



a b

Fig. 1a and b. C. Rosa, 38 years. Biopsy of left breast. T 4320/70, HE, 160:1. a (left): Phylloid fibroadenoma. Regular, hyperplastic epithelial wall. b (right): Area of malignant osseous metaplasia

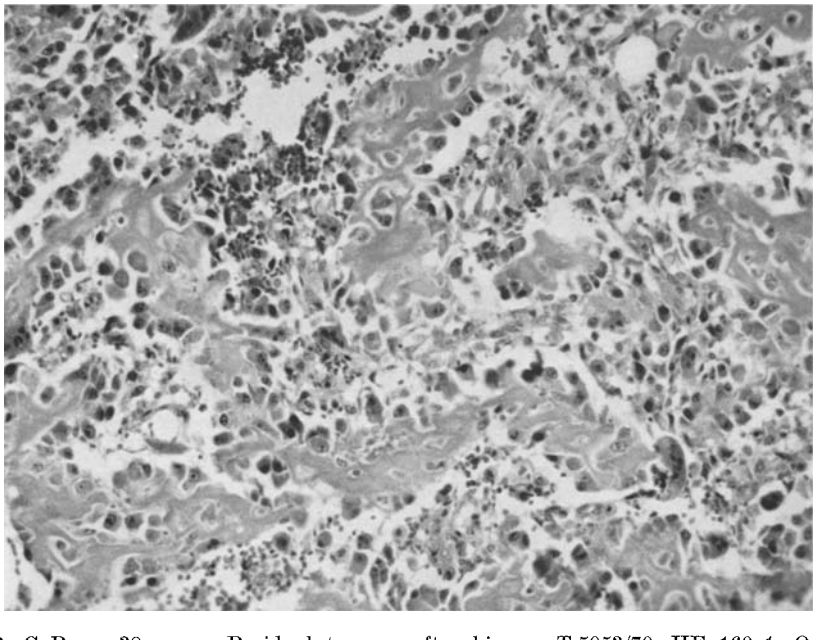


Fig. 2. C. Rosa, 38 years. Residual tumour after biopsy. T 5053/70, HE, 160:1. Osseous strands, partially calcified, marked nuclear and cellular atypia

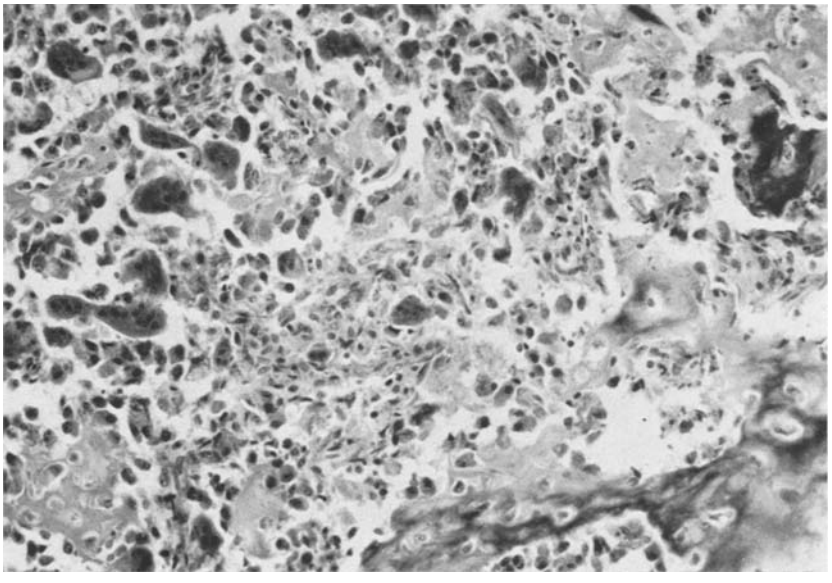


Fig. 3. C. Rosa, 38 years. Recurrent osteosarcoma, left mammary region. T 876/71. HE 160:1

2. In the removed breast (T 5053/70), we find a cavity filled with old blood bordered by haemorragic tissue in which we discover a second nodule of 1 cm resembling the first. The skeletal musculature is not invaded and no lymph nodes are found in the axillary fat tissue.

Microscopy. In several specimens, one notices a nodular tumoural proliferation, composed of a very cellular fibroblastic stroma, giving rise to fairly large digitations and arborisations. The mesenchymatous growth is traversed by elongated canalicular formations (Fig. 1a), lined with a single or multi-layered epithelium composed of hyperplastic cells with large basophilic nuclei without atypia. Several mitoses occur in the stroma. Adjacent to this tumour we find a large zone of hyaline degeneration and fibrosis corresponding to an "old" fibroadenoma. In several areas of the stroma, osseous metaplasia (Fig. 1b) has developed with thin reticular strands, occasionally calcified, surrounded by fusiform cells with marked nucleocytoplasmic atypia and mitoses; these elements resemble osteoblasts. Multinucleate osteoclasts bordering the strands and scattered throughout the stroma can be distinguished (Figs. 2 and 3).

Epicrisis

The tumour evolved rapidly in 15 months. From a well-defined nodule it became invasive, recurring in the operation scar and spreading to the lung. Histologically, the behaviour of the lesion changes, the fibroadenomatous tissue being entirely replaced by the osteosarcoma.

Discussion

Osteosarcoma is one of the rarest tumours of the breast. It represents about 0,25% of the sarcomas in this organ (Jernstrom *et al.*, 1963). In a literature survey, Jernstrom *et al.* (1963) discover 116 cases. Since then, it becomes difficult to compile valid statistic indications. The reason for this is that many authors hesitate to consider osteosarcoma of the breast as a well-defined entity because

this tumour belongs to the group of mesenchymatous neoplasms with variable osteoplastic properties, and there is, in the publications, no clear separation into benign and malignant types (Dyke, 1926; Haagensen, 1971; Norris *et al.*, 1967; Smith *et al.*, 1969).

Osteosarcoma of the breast occurs in advanced and middle age; it can grow slowly for a long time and, suddenly, evolve rapidly into a fatal outcome (Jernstrom *et al.*, 1963; Rottino *et al.*, 1945) with generalized haematogenic metastases, no ganglionar involvement being recorded as yet.

It has been proved that 40% of the cases of mammary osteosarcoma develop from a fibroadenoma (Gonzalez-Licea *et al.*, 1967; Jernstrom *et al.*, 1963; Willis, 1953), especially from phylloid type (Rottino *et al.*, 1945). The absence of diagnosis of fibroadenoma in a case of osteosarcoma does not mean that the former was not pre- or coexistant with the latter. Our case exemplifies this since the initial diagnosis of phylloid fibroadenoma with malignant osseous metaplasia changed to that of pure osteosarcoma. In order to simplify, the basic lesion may often not be quoted.

Even though it is two centuries since the discovery of osteogenic tumour of the breast, its histogenesis is still queried. One of the first explanations envisages the tumour as the product of a "dormant" bony inclusion originating from the clavicle which proliferates at a later date. This theory was quickly abandoned and replaced by another which considered the tumour a result of dystrophia in chronic inflammation. This type of lesion has been seen in the sheep, dog and cow (Dyke, 1926); according to Rottino *et al.* (1945), the tumour in these animals has no dystrophic origin.

The *teratogenous* theory has been advanced by several authors (Dyke, 1926; Geschickter, 1945; McIver, 1923; Rottino *et al.*, 1945; Sun, 1952). It envisages a proliferation of pluripotential embryonic cells enclosed in the mammary tissue. It is an attractive hypothesis which allows one to reconcile the presence of both epithelial and mesenchymatous elements. However, one would be dealing with a teratoma which selectively produces bony and cartilagineous tissue. Osteosarcoma of the breast would be one of those particular cases where malignant proliferation affects one single constituent of teratomatous tissue. Rottino *et al.* (1945) accept only one case of true breast teratoma in the literature.

According to numerous studies, mammary osteosarcoma arises from a *metaplasia* (Gonzalez-Licea *et al.*, 1967; Haagensen, 1971; Jernstrom *et al.*, 1963; Norris *et al.*, 1968; Rottino *et al.*, 1945; Smith *et al.*, 1969; Willis, 1967). The question is whether this metaplasia develops from the stroma (von Albertini, 1955; Allen, 1940; Dyke, 1926; Gonzalez-Licea *et al.*, 1967; Haagensen, 1971; Norris *et al.*, 1967; Rottino *et al.*, 1945; Willis, 1967) or from the glandular epithelium (von Albertini, 1955; Allen, 1940; Haagensen, 1971; McDivitt *et al.*, 1968; Smith *et al.*, 1969; Stewart, 1950).

It is acknowledged that most osteosarcomas of the breast originate from fibroadenoma of the phylloid type. The malignant transformation nearly always concerns the stroma; the epithelial cells remain regular (Gonzalez-Licea *et al.*, 1967; Hafner *et al.*, 1962; Notley *et al.*, 1965; Willis, 1953) even if they undergo certain modifications or sometimes are site of benign squamous metaplasia (Norris *et al.*, 1968; Willis, 1967). In 12 cases of malignant phylloid fibroadenoma

Hafner *et al.* (1962) notice no suspect epithelial transformation. According to Collins (1959), bone forms in the breast in an intramembraneous manner, therefore arising from the mesenchyme (Norris *et al.*, 1967). The tumour cells of mammary osteosarcoma produce collagen indicating a mesenchymatous origin (Gonzalez-Licea *et al.*, 1967). It is impossible to distinguish the undifferentiated tumour cells bordering the osseous strands from immature fibroblasts. The osteogenic cells (osteoblasts and osteoclasts) are often connected by desmosomes, and they bear no relation to the giant cells of foreign bodies.

The hypothesis of *epithelial* metaplasia is explained by vacuolisation of cubic carcinoma cells which become fusiform and take on a fibroblastic aspect. Gonzalez-Licea *et al.* (1967), after a searching study using optical and electron microscopy, state "the undifferentiated cells... showed desmosomes and an ability to produce collagen and ground substance. The authors believe that production of stroma and bone is not inconsistent with epithelial origin". Desmosomes can also be found between endothelial cells, cardiac muscle fibres and, especially, between normal osteoblasts.

We note in passing that a carcinoma may coexist with fibroadenoma (Norris *et al.*, 1967; Willis, 1967). The presence of two clearly distinct foci of carcinoma and osteosarcoma in the same breast has also been discovered (Wester *et al.*, 1960). The authors think that there is no connection between the two tumours.

We cannot adopt a definite position on the origin of metaplasia as a result of our histological observation. Nevertheless, we think that the tumour cells do not resemble epithelial cells since the latter do not seem to take part in the osteoplastic tumoural proliferation. It would appear more logical, and here we agree with the view of Norris *et al.* (1968), that a tumour which does not present any epithelial atypia in numerous histological samples and behaves clinically like a sarcoma, should not be considered as a carcinoma. The final evolution in our case in which the fibroadenoma becomes entirely replaced by the osteosarcomatous proliferation, could be an indication that we are dealing effectively with a particular tumour which may take its origin in a common breast tumour but subsequently develops as a typical osteosarcoma.

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