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Osteogenic sarcoma in the breast - Case report of a diagnostic dilemma

A O Oluwasola[1], C A Adebamowo[2], E R Ezeome[3], O Oduntan and [2]E E U Akang[1]

Departments of Pathology[1] and Surgery[2], University College Hospital, Ibadan; and Department of Surgery, University of Nigeria Teaching Hospital, Enugu, Nigeria.

Summary

Breast cancer is the leading cancer in females worldwide, the vast majority being carcinomas, and only 0.2-0.3% being sarcomas. Of the mammary sarcomas, extra-osseous osteogenic sarcomas constitute a small heterogeneous group. This communication reports a case of primary extra-osseous osteogenic sarcoma occurring in the breast of a 48-year-old female, and presents a literature review of this condition. A pre-requisite for the diagnosis of primary mammary osteogenic sarcoma is the exclusion of an osteogenic sarcoma arising from the underlying ribs or sternum. Like all other osteogenic sarcomas in general, these neoplasms are characterized by the direct formation of osteoid matrix by the tumour cells. Primary osteogenic sarcoma of the breast may arise from metaplastic sarcomatous transformation of neoplastic cells in a primary breast carcinoma, fibroadenoma, malignant phyllodes tumour, or may exceptionally represent a non-phyllodes sarcoma of the breast arising from the soft tissues of an otherwise normal or previously irradiated breast.

Keywords: *Breast,osteogenic sarcoma, pathology*

Résumé

Le cancer sein est le cancer le plus frequent chez les femmes dans le monde entier. La vaste majorite est carcinome et 0.2 – 0.3% est sarcome. Des sarcomes mammaires, les sarcomes extra-osseux osteogenique constituent un petit group heterogene. Cette étude ou communication reporte un cas primaire de sarcome extra-osseux osteogenique observé dans le sein di une femme de 48 ans et represente une literature de cette maladie. Un pre-requis pour le diagnostique du sarcome extra-osseux osteogenique primaire est l'exclusion d'un sarcome osteologique venant des cotes ou du stenum. Comme tous les sarcome osteogeniques en general, ces tumeurs sont characterises par la formation directe du matrix osteoid par les cellules cancerinogeniques. Le sarcome primaire osteogenique des seins peut venir de la transformation metaplastiques sarcomateux des cellules cancerigenes dans un carcinome primaire de sein, fibroadenome, cancer phillocles ou peut etre exceptionellement represente un non-phyllales sarcome de sein venant des tissues moux normaux ou des seins irradies au paravant.

Introduction

Breast cancer is now the most common malignant neoplasm seen in women in Ibadan, although the age-adjusted risk of developing breast cancer is still lower than in developed countries [1]. The vast majority of malignant breast neoplasms are essentially of ductal or lobular epithelial origin, and only a minority of cases are sarcomas. Breast sarcomas constitute only 0.2-0.3% of all breast malignancies [2,3].

Extra-osseous osteogenic sarcomas have been reported from such diverse locations as the thyroid gland, kidney, bladder and soft tissues, but are an exceptional finding in the breast, constituting a small heterogeneous group within the mammary sarcomas [4]. As at 1991, about 150 authenticated cases had been documented in the literature [5]. This is a report of a case of primary extra-osseous osteogenic sarcoma occurring in the breast. A literature review and the diagnostic dilemma posed by our case are discussed.

Case Report

A 48 year old female, Para 8^{+0} secondary school teacher was referred on 29 April 1997, with an 8 months history of progressively enlarging, hard left breast lump, which ulcerated 4 months prior to presentation. Examination of the left breast revealed an exophytic, ulcerated malignant tumour, with an offensive serous discharge. There were discrete, mobile axillary lymph node. The provisional diagnosis was carcinoma of the left breast stage III (T4N1M0).

Abdominal ultrasound on May 1997 revealed normal liver, gall bladder, kidneys, spleen and pancreatic bed, and the chest X-ray was normal, except for the tumour noted in the left breast shadow. There were no symptoms or signs referable to a skeletal problem. Fine needle aspiration biopsy of the breast on 6 May 1997 was reported as malignant (suggestive of invasive ductal carcinoma), and that of axillary lymph node as reactive hyperplasia.

She had modified radical mastectomy on 15 May 1997. Operative findings were a 17 x 12 cm. fungating left breast tumour fixed to pectoralis major muscle, but not the underlying ribs and multiple enlarged left axillary lymph nodes, up to level III. She made satisfactorily postoperative recovery and was commenced on a cycle of combination chemotherapy (cyclophosphamide, methotrexate and 5-fluorouracil) on 7 June 1997 while awaiting local chest wall radiation therapy and hormonal manipulation.

Examination of the surgical specimen revealed a large, fungating nodular tumour, which measured 15 x 8.5 x 11 cm. There were extensive areas of necrosis, hemorrhage and mucinous change. The medial margin of the tumour mass was incompletely excised. Nine enlarged axillary lymph nodes were dissected and sampled. Histological examination revealed a malignant connective tissue neoplasm composed of plemorphic bipolar cells (Figure 1). There was osteoid matrix formation by the tumour cells with focal neoplastic bone trabeculae (Figure 2). There were also prominent telangiectatic vascular channels in some areas of the tumour. The surrounding breast tissue appeared otherwise normal and did not show any evidence of ductal carcinoma. The

Correspondence: Dr C. A. Adebamowo, Department of Surgery, University College Hospital, P.M.B. 5116, Ibadan, Nigeria

lymph nodes showed reactive hyperplasia. The final histologic diagnosis was primary osteogenic sarcoma of the breast.

Upon receipt of the histology report, the adjuvant chemotherapy was stopped after the first course and the patient was advised to consider a doxorubicin-based regimen. She was placed on close monitoring for local recurrence and serial serum alkaline phosphatase assessment. She declined the proffered chemotherapy regime and defaulted from follow-up. In February 1999, she re-presented with complaints of a right hypochondrial mass and pain. On examination, she was found to be pale and had lost weight. There was no loco-regional recurrence but a ballottable right hypochondrial mass measuring 17 cm below the costal margin and extending across the midline was found. Ultrasound of the mass suggested that it was of renal origin and a Tru-Cut biopsy confirmed that it was metastatic osteogenic sarcoma.

She died two months after diagnosis due to disease progression.

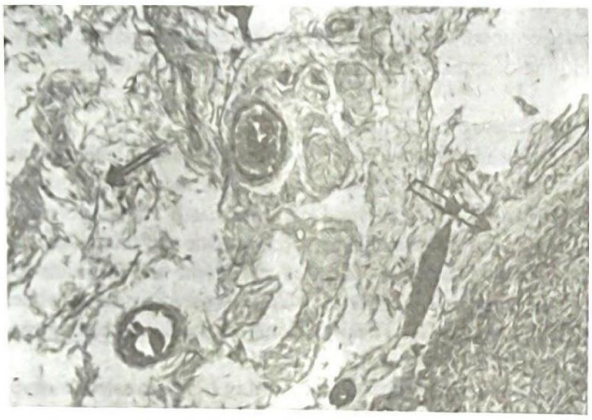

Fig. 1

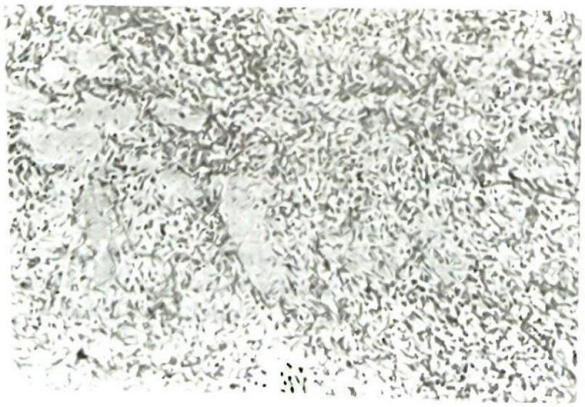

Fig. 2

Discussion

Primary osteogenic sarcoma of the breast is an extremely rare neoplasm [6]. This is especially true when this neoplasm occurs in its pure form. Several explanations for the histogenesis of this neoplasm have been suggested. An elementary pre-requisite for the diagnosis of primary mammary osteogenic sarcoma, as in this case is to exclude an osteogenic sarcoma arising from the underlying ribs or sternum. The tumor in this patient was completely free of the underlying bones at surgery, which was confirmed by chest X-ray examination. Secondly, the possibility of a primary breast carcinoma with extensive osseous metaplasia must be considered [7,8]. This possibility was excluded in our present case by the absence of focal carcinomatous foci in the surrounding breast tissues.

About thirty-one months after the initial presentation, our patient was diagnosed to have osteogenic sarcoma involving the kidney. This neoplasm was not present at the time of initial presentation, as determined by abdominal ultrasound examination, neither were there any symptoms or signs referable to other possible extraskeletal or skeletal primary lesions. Also against a primary renal origin for our patient's neoplasm is the absence of presenting symptoms suggestive of renal tumour, and the low likelihood of breast metastasis in patients with primary renal neoplasms. In a summary of eight cases of primary renal osteogenic sarcoma previously reported in the literature [9]. Half 50% of the patients each presented with haematuria and flank pain. None presented with breast metastasis, the most common metastatic sites being lungs, liver, and peritoneum.

Most osteogenic sarcomas are skeletal and they more commonly occur in patients between 10 and 25 years of age [10]. Although another peak age incidence occurs after 40 years, the tumour usually occurs in association with other disorders such as Paget's disease and radiation disorders [11], which were not present in this patient. Extraskeletal osteogenic sarcomas, by contrast, are rarely encountered in patients under 40 years of age [11]. Unfortunately the relatives of our patient did not consent to a post-mortem examination. This would have provided additional information on the pattern of disease progression in this patient, although it may not necessarily have ascertained the definitive primary site of our patient's osteogenic sarcoma at this advanced stage of the disease. However, we believe that this patient most probably had a primary osteogenic sarcoma of the breast, on the basis of the available clinical and pathological evidence.

Osteogenic sarcoma may also arise from pre-existing benign breast neoplasms, notably fibroadenoma. There have been several reports of osteogenic sarcoma associated with, and presumably arising from fibroadenoma [12,13,14]. Indeed, it has been contended that primary osteogenic sarcoma of the breast may not actually be a malignant tumour de novo, but one that develops by sarcomatous transformation of the connective tissue elements of a fibroadenoma [15]. Other benign breast neoplasms may be associated with osteogenic sarcoma. For example, osteogenic sarcoma has been reported following intraductal papilloma [2]. Again, in this case, no focus of benign neoplasia was seen.

Fourthly, osteogenic sarcoma may arise from metaplastic transformation in the stromal component of a malignant phyllodes tumour [3] In exceptional cases, osteogenic sarcoma might represent a non-phyllodes sarcoma of the breast arising from the soft tissues of a previously normal breast [16]. The case presented is probably an example of this last situation, having excluded primary osseous origin

and emanation from a pre-existing benign or malignant primary breast neoplasm.

The *sine qua non* for the histological diagnosis is the occurrence of sarcomatous elements directly laying down osteoid matrix. In the present case, there were focal prominent telangiectatic areas. In some osteogenic sarcomas, these telangiectatic foci may simulate a primary vasoformative neoplasm, but the presence of tumour osteoid formation assists in arriving at the correct diagnosis [17]. Histological diagnosis is further assisted by immunohistochemical studies, the tumour cells usually being strongly vimentin positive, focally positive for α-1 antitrypsin and cytokeratin-negative [7,8,15]. Ultrastructural examination further reveals the sarcomatous elements as osteoblastic, osteoclastic, histiocytic and undifferentiated cells.

Because of the rarity of these neoplasms, fine needle aspiration diagnosis may not be diagnostic, as in the present case. Features to recognize include the presence of extracellular osteoid material, and bizarre pleomorphic connective tissue cells [4,18]. The diagnosis may be suggested by the mammographic appearances such as the presence of homogenous dense calcific masses with threadlike spicules of bone radiating to the periphery [19]. A rarely reported clinical complication of these neoplasms is the occurrence of consumptive coagulopathy and tumour embolism [20].

There is no consensus as to the management of these tumours [5]. Surgical extirpation of the disease is associated with satisfactory long-term control. Where a pre-operative diagnosis has been made, axillary clearance is not necessary. Local chest wall radiation is useful for reduction of risk of local recurrence, as this event is common [19]. Controversy surrounds the indication for and choice of agents for adjuvant chemotherapy. Generally, osteosarcomas are chemo-resistant, but exceptional results have been reported with doxorubicin, cisplatin or ifosfamide based regimes in bone osteosarcomas [21]. The rarity of breast osteosarcomas has precluded investigation of the effectiveness or otherwise of these drugs and it is unclear whether extrapolation is justified. The issue is further complicated by the variable natural history of the disease.

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