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Malignant Phyllodes Tumor of the Breast Metastasizing to the Peritoneal Cavity

Suhair Khalifa Al Saad, CABS, FRCSI, CST* Sara Mathew George, MD, FRCPath**

A fifty-three year old Bahraini female presented with painless rapidly growing mass in the right breast of 3 months duration; no nipple discharge was found. Family history was positive for breast carcinoma in situ in her sister.

Lumpectomy was performed. Histopathology proved to be phyllodes tumor; therefore, mastectomy was performed to avoid local recurrence. The patient received local radiation to the mastectomy scar.

Four months after the initial surgery, she developed a nodule in the mastectomy scar, left breast lump in the upper outer quadrant and intra-abdominal mass.

A fine needle aspiration of the mass in the left breast showed spindle cells with focal atypia and a necrotic background. True-cut biopsy of the intra-abdominal mass showed the metastatic stromal component of the malignant phyllodes tumor with malignant spindle cells.

The patient condition worsened, developed bilateral pleural effusions. Adriamycin chemotherapy was planned, but the disease was aggressive enough to end her life within weeks.

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Phyllodes tumors are less than 1% of breast tumors and are fibroepithelial in origin. These tumors present with wide range of clinical behavior and represent a spectrum rather than a single disease entity[1].

Johannes Müller, in 1838, described in detail a large mammary tumor with a cystic appearance and leaf-like growth pattern. He named it 'Cystosarcoma phyllodes'[1]. Treves and Sutherland, in 1951, suggested a disease spectrum of benign, pre-malignant and malignant forms existed[1]. Lomonaco in 1960, proposed the name 'phyllodes', which was later adopted by the World Health Organization[1].

The aim of this presentation is to highlight that the malignant phyllodes could be an aggressive and fatal disease.

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* Assistant Professor Arabian Gulf University
Consultant Surgeon
**Consultant Pathologist
Salmaniya Medical Complex
Kingdom of Bahrain
Email: alsaadsuhair@gmail.com

THE CASE

A fifty-three year old Bahraini female presented to the breast clinic with painless rapidly growing mass in the right breast of 3 months duration; no nipple discharge was found. She had menarche at the age of 12 and was not on oral contraceptive pills or any hormonal therapy. She had her first delivery at the age of 25 years. She breast-fed all her four children. Past history was negligible. Family history was positive for breast carcinoma in situ in her sister.

On examination, the right breast was enlarged (double the size of the left breast). The overlying skin was stretched, glistening with dilated and congested veins. The mass measured 20 cm x 20 cm and it had soft and firm areas. There were no palpable axillary lymph nodes. Left breast was normal.

It was difficult to do a mammogram due to the large size and consistency of the mass. The US showed a huge, vascular, partly solid and partly cystic mass occupying almost the whole breast.

Fine needle aspiration cytology (FNAC) was bloody. The report was inconclusive. True-cut biopsy was not done because the tumor was vascular.

Because no histopathological diagnosis was achieved, the differential diagnosis was phyllodes tumor, most probably malignant and pseudo angiomatous stromal hyperplasia (PASH) which is a benign capsulated lesion and could attain a large size.

The patient had lumpectomy with safety margins. The tumor was capsulated weighing 1.8 kg and separated from the surrounding compressed breast tissue, vascular in nature and showing multiple feeding vessels. On gross examination showed an encapsulated mass 18 x 15 x 16 cm with whitish solid and cystic areas, see figure 1.

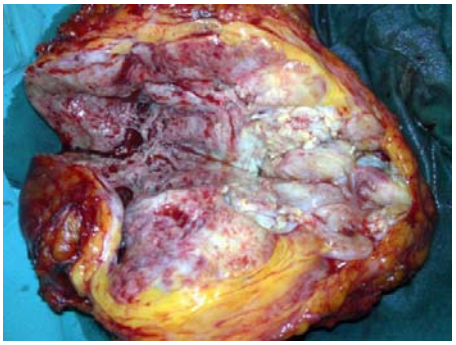

Figure 1: Gross Appearance of the Tumor after Resection. Open Tumor Was Fleshy, Cystic and Solid, Hemorrhage in the Cystic Spaces

Microscopy showed large leaf-like structures forming clefts lined by benign epithelial cells and areas filled with highly cellular spindle cell stroma, see figure 2.

The spindle cells showed hyperchromatic pleomorphic nuclei with mitotic count of 33/10 high power fields (each high power field is 0.45 mm), see figure 3.

Figure 2: Photomicrograph of Phyllodes Tumor Showing Large Leaf-Like Structures Forming Clefts Lined by Epithelial Cells

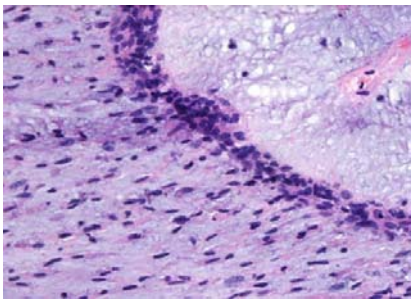

Figure 3: Photomicrograph of Phyllodes Tumor Showing the Benign Epithelium Covering the Leaf-Like Structures and the Spindle Stromal Cells

Hypocellular and necrotic areas were found. Adjacent breast tissue showed fibrocystic changes. Resected margins were free of tumor 1-2 cm except deep at the level of pectoralis major muscle, where it was 1 mm. The mastectomy was performed to avoid local recurrence, which is commonly seen with malignant phyllodes tumor. There was no residual tumor in the remaining breast on histopathological examination. CT scan of the chest, abdomen, pelvis and bones showed no metastasis.

The patient received local radiation to the mastectomy scar. Chemotherapy was not given due to the worldwide controversy.

Four months after the initial surgery, she developed a nodule in the mastectomy scar of about 2 x 1 cm^2 in size and left breast lump measuring 2 x 2 cm in the upper outer quadrant, which was confirmed with left mammogram, see figure 4.

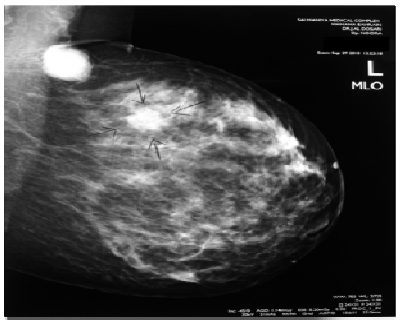

Figure 4: Mammogram Showing Two Masses in the Upper Outer Quadrant and Axilla of the Left Breast

She developed irritant productive cough. X-rays and CT scan of chest, abdomen and pelvis revealed multiple metastasis, a mass in the right mastectomy scar measuring 2.7 x 2.2 cm, two masses in the left breast and multiple nodules of varying sizes in both lungs; the largest 2.9 x 2.4 cm was in the right upper lobe with evidence of subpleural involvement, see figure 5. A mass was found in the peritoneal cavity measuring 7.7 x 6 cm closely related to medial aspect of hepatic flexure of the colon but separated from the liver and right colon, see figure 6.

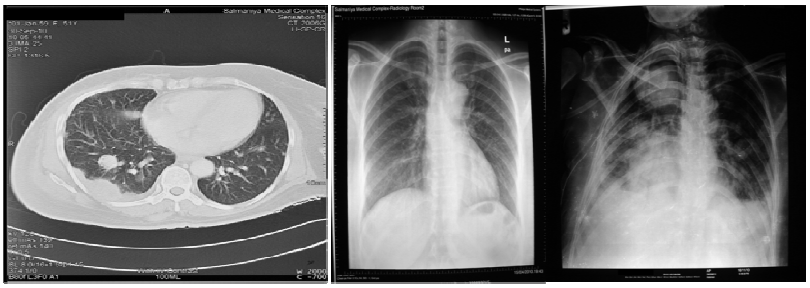

Figure 5 (A) **Figure 5 (B)** **Figure 5 (C)**

Figure 5: (A) CT scan of the Chest Showing Multiple Nodules of Varying Sizes in Both Lungs and Evidence of Subpleural Involvement. Chest X-Ray at First Presentation (B) and (C) after Systemic Metastasis

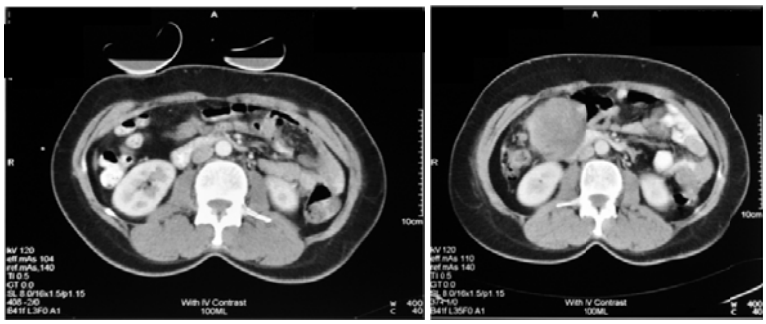

Figure 6 (A) **Figure 6 (B)**

Figure 6: CT Abdomen, (A) at Presentation (B) 5 Months Later, Showing a Mass Closely Related to Medial Aspect of Hepatic Flexure

A fine needle aspiration of the mass in the left breast showed spindle cells with focal atypia and a necrotic background. True-cut biopsy of the intra-abdominal mass showed the metastatic stromal

component of the malignant phyllodes tumor with malignant spindle cells and a mitotic count of 3/10 high power field, see figure 7. Immuno-histochemistry performed on both the primary right breast tumor and on the intra-abdominal tumor showed diffuse positivity for smooth muscle actin, desmin and focally for CD34. Cytokeratins (AE1/AE3, MNF116, CK7), S100, ER, PR, Bcl2 and CD31 were negative in the stromal cells. This indicated that the peritoneal mass was originating from the stromal part of the primary breast tumor.

The patient condition worsened, developed bilateral pleural effusions, which needed chest tubes. The oncologist planned to start Adriamycin but the disease was aggressive enough to end her life within weeks.

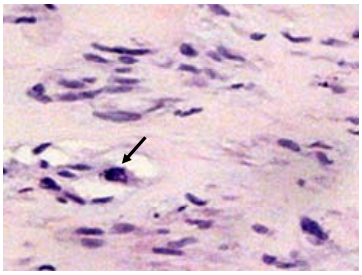

Figure 7: Core Biopsy from the Intra-Abdominal Mass Showing the Spindle Cells of the Metastatic Stromal Component with Mitosis

DISCUSSION

Phyllodes tumor is usually benign involving the female breast. Phyllodes is a Greek word derived from the sarcoma, meaning fleshy tumor and phyllo meaning leaf[1,2].

Although these tumors are benign but have an unpredictable nature and malignant potential[1]. The high-grade malignant phyllodes tumor (MPT) is an aggressive breast malignancy and accounts only for 25% of all phyllodes tumors[2].

Most phyllodes tumors occur in women between the ages of 35 and 55 years as the case in our patient. It is seen more in whites, mainly in Latina whites and East Asians.

The etiology is still unknown. Mangi et al observed an overlap between benign phyllodes tumor and fibroadenoma in 18% of their patients[3].

Phyllodes tumors are clinically similar to fibroadenomas and they have both mammographic and sonographic common characteristics. Ultrasound suggestive findings of these tumors were lobulated lumps in most cases. These lumps may have heterogeneous internal echoes and intramural cysts. Phyllodes tumor on mammography is described as a sharply defined round or oval mass with lobulation[4,5].

Unfortunately, clinical, radiologic and histologic examination results in low diagnostic accuracy in phyllodes tumors due to the overlapping characteristics with benign breast disease such as fibroadenoma[1]. Accurate diagnosis preoperatively is important for the appropriate surgical management[1,4,5].

Difficulties with diagnosis of phyllodes tumor by FNAC as we had in our case had been reported. Phyllodes tumor was diagnosed by FNAC in only 23% of cases. Core biopsy correctly diagnosed 65% of phyllodes tumors[6,7]. Most phyllodes are diagnosed retrospectively after excision biopsy.

Histologically, malignant phyllodes tumors are further divided into borderline, low-grade and high-grade, depending tumor borders, mitotic activity, stromal atypia and stromal overgrowth. Metastasis occurs through the spread of the stromal cells via the circulation. The malignant potential of the tumor is confirmed by the presence of stromal cells overgrowth[7].

Surgical resection is the definitive therapy for all phyllodes tumors, regardless of its histological type. It is recommended for small lesions (up to 3 cm) with safety margin of 1-2 cm. For larger lesions (over 3 cm), a segment resection also with safety margins is recommended. For even larger, borderline or malignant, mastectomy should be performed. Axillary lymph node dissection is not the routine procedure in treatment of phylloides. Phyllodes tumor spreads predominantly through the blood stream. It spreads to lymph nodes in only less than 10% of cases[8,9].

Radiotherapy role to the scar of mastectomy is still unclear[10]. A study suggested that adjuvant radiotherapy could improve the disease-free survival. Other studies only considered adjuvant radiotherapy for high-risk phyllodes tumors, for those more than 5 cm, with stromal overgrowth, with more than 10 mitoses/high-power field or with infiltrating margins[11].

Our patient had a tumor more than 5 cm with stromal overgrowth as well as more than 33/10 mitoses/high-power field.

Adjuvant chemotherapy in patients with stromal overgrowth and tumor size greater than 5 cm needs to be considered[10-12]. These patients are at risk of distant metastasis[12].

Chemotherapy regimens in malignant phyllodes tumors are still controversial. One regimen used Doxorubicin and Ifosfamide-based chemotherapies. This regimen proved to be beneficial in preventing local and systemic recurrence and in women who already had metastatic disease[10].

Local recurrence is approximately 26% (12-65%). It is more common with stromal overgrowth. If the tumor size was more than 10 cm, the prevalence of local recurrence was four times greater than smaller tumor[1,10,11,13]. This explains the early local recurrence in our patient, although she had complete resection and local radiotherapy.

Metastasis due to phyllodes tumors varied from 10% to 75%; hematogenous is the predominant route, and the most common sites were lung (66%), bone (28%) and viscerae (15%). The development of distant metastasis is fatal[9]. Metastasis to the peritoneal cavity without liver or visceral involvement as seen in our patient was not reported before. Metastasis to oral cavity, tongue and lips were reported and were suggested to be due to the excess of vascular blood supply[14].

The mortality rate in malignant phyllodes is up to 35%[14]. In metastatic phyllodes tumor, the prognosis is poor and the average survival is less than 2 years[1].

In our case, the disease was aggressive and had metastasized to the other breast, both lungs and to the peritoneal cavity without any visceral involvement.

Surgery, chemotherapy or even radiation therapy have no role in treating metastatic phyllodes; therefore, prognosis is generally poor and death usually occurs within the first two months after treatment[1,15,16].

CONCLUSION

High-grade malignant phyllodes tumor is an aggressive disease. Local recurrences and distant metastasis is associated with histopathological findings of stromal overgrowth, larger tumor size and involved margin. The prognosis is the worse with stromal overgrowth.

Treatment of phyllodes tumor requires complete removal of the tumor with safety margins. A combination of surgery, radiation therapy, chemotherapy and even hormonal therapy is controversial for malignant phyllodes tumor.

Metastasis to the peritoneal cavity without involving the surrounding organs was not reported before in the literature and indicates the aggressiveness of the disease.

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