ISSN: 2755-0141

Japan Journal of Clinical & Medical Research

SCIENTIFIC Research and Community

Case Report

Open Access

Malignant Phyllodes Tumor of the Right Breast with Sacral Bone Metastasis- A Clinical Case from our Practice with A Literature Review

Lena Marinova*, Nikolay Kahchiev, Vaska Vasileva and Katia Sergieva

Medical Oncology Clinic, Department of Radiation Oncology and Metabolic Brachytherapy, UMHAT "Queen Joanna" Sofia, Bulgaria

ABSTRACT

Phyllodes breast neoplasms are rarely diagnosed biphasic tumors that are benign, borderline, or malignant. We present a rare malignant phyllodes tumor in a 62-year-old woman with bone metastasis in the sacrum, presented 4 months after radical breast tumor surgery. Because of a severe pain syndrome, we performed intensity modulated radiotherapy with a high single dose of 8 Gy in two fractions, once a week.

In this article we emphasize the difficult histopathological diagnosis, as well as the differential diagnosis, requiring immunohistochemistry of the two tumor components / epithelial and stromal/, as well as the clinical and pathological characteristics determining the malignant nature of the disease. In the presence of a soft tissue component of the bone metastasis, a biopsy with immunohistochemistry is required to prove the histopathological diagnosis of the distant metastasis.

Distant metastases require complex treatment, including chemotherapy and palliative radiation therapy.

***Corresponding author**

Lena Marinova, Medical Oncology Clinic, Department of Radiation Oncology and Metabolic Brachytherapy, UMHAT "Queen Joanna" Sofia, Bulgaria.

Received: February 16, 2024; **Accepted:** February 23, 2024; **Published:** February 27, 2024

Keywords: Phyllodes Breast Tumor, Malignant Phyllodes Tumor, Immunohistochemistry, Bone Metastasis, Palliative Intensity Modulated Radiotherapy

Introduction

Phyllodes tumors (PTs) are rare fibroepithelial tumors accounting for less than 1 % of all breast neoplasms [1]. Based on histological and cytological findings, PTs are classified as benign, borderline, or malignant [2,3]. Malignant lesions occur in 2% to 45% of all cases with the stromal component of the tumor mainly responsible for metastasis [4]. Distant metastases through hematogenous dissemination are seen in 10%-20% of all cases [5]. Metastatic PTs mainly develop from 3 to 10 years after the inital therapy, but they can be delayed or occur as soon as synchronous presentation [6]. In this article we present a rare malignant phyllodes tumor in a 62-year-old woman with bone metastasis in the sacrum, presented 4 months after radical breast tumor surgery. We emphasize the difficult histopathological diagnosis, as well as the differential diagnosis, requiring immunohistochemistry of the two tumor components / epithelial and stromal/, as well as the clinical and pathological characteristics determining the malignant nature of the disease.

Clinical Case

It concerns a 61-year-old female patient who noticed a formation in the right mammary gland in July 2023. In the same month, an excisional biopsy of a tumor of approximately 30 mm in diameter was performed in the right breast, which pathohistologically proved a biphasic tumor

Histological Result

A tumor with two distinct morphological components united in a single nodule was observed. One shows an infiltrative growth pattern relative to the surrounding stroma with a rich vascular network represented by thin-walled hyperimitated vessels. The described part of the lesion grows in the form of swirling globular structures, reminiscent of plexiform structures, made up of cells with moderately pleomorphic nuclei of a spindle-shaped and oval shape with finely condensed chromatin and poorly represented bright eosinophilic cytoplasm. Up to 5 mitotic figures per 10 HPF are encountered in background artifacts. The second component is a solid growth involving glandular structures composed of cells with relatively small hyperchromic nuclei with visible nucleoli and sparse light eosinophilic cytoplasm. The second component grows infiltratively with 10 mitoses per 10 HPF. Stromal overgrowth was observed in a large part of the tumor.

Immunohistochemical Analysis

Tumor cells are positive for Vimentin, CKAE1/3 / punctate cytoplasmic staining mainly in the epithelial component, ER and PgR positive in 30% in the epithelial component and negative in the stromal cellular component. The tumor was negative for

CD99, Bcl, EMA, alfa SMA, SOX-10, CD 56, CK 5/6, p53 wild type, Desmin, Myo D1, CK 7, GATA 3, S100, CD 45, CD 68, Ki 67 - 8% in the epithelial component and 30% in the stromal cellular component.

Diagnosis

Malignant biphasic tumor with a heterologous component in the type of undifferentiated sarcoma. After one month, the patient underwent CT of the chest, abdomen and small pelvis with intravenous contrast - In the right mammary gland, a soft-tissue tumor formation with lobulated contours was visualized, with approximate axial dimensions of 44/33 mm. It reaches the skin, which is thickened. Rounded axillary lymph nodes are visualized bilaterally with preserved fatty hilus. The largest on the right has axillary dimensions of 20.5/9 mm. The remaining organs and structures in the chest, abdomen and small pelvis are without pathological changes.

Conclusion

CT data for tumor in the right mammary gland with CT data for axillary lymphadenopathy bilaterally (Figure 1). In September 2023, a right-sided mastectomy with axillary sentinel lymphadenectomy was performed.

Intraoperative Evaluation

The tumor is in the central and lower inner quadrant with a size of 8x5x5 cm. / When evaluated together with the previous excision, the diameter of the tumor is more than 10 cm (p T3); with clear stromal cellularity, stromal overgrowth present, mitotic ratio greater than 10/ 10 BBA / along with immunohistochemistry (IHC). Characteristics of the outer tumor border - focally infiltrative. Evaluation of the status of the surgical margin - No tumor infiltration within the surgical margin with the closest distance to it more than 2 cm. Total number of examined lymph nodes, including 1 sentinel - 3 that are without metastases. Malignant heterologous element not observed / along with IHC of MDM2, S100, SMA, Desmin, CD31. On immunohistochemical examination of the epithelial component, it was positive for PanCK and GATA3, and the stromal component was negative. The proliferation index Ki 67 is 70%.

Macroscopic

Mastectomy material measuring 23 x 19 x 8 cm. Sections showed nodular tumor tissue measuring 8 x 5 x 5 cm, beginning under the skin of the lower inner quadrant and extending up to 2 cm at the base closest to the surgical margin. The tumor has a nodular characteristic with regular outer borders.

Diagnosis- Malignant phyllodes tumor / pT3 N0 / AJCC -2016

In January 2024, MRI and CT revealed a large metastasis in the sacrum with a soft tissue component (Figure 2), from which a biopsy was taken, the immunohistochemistry of which proved a metastasis from a malignant phyllodes tumor of the breast (Figure 3A, B). Due to a severe pain syndrome, unresponsive to pain medication, the patient was referred for palliative radiation therapy. In view of the severe pain causing immobilization of the patient, we performed intensity modulated radiotherapy (IMRT) using the VMAT method with a high single dose of 8 Gy in two fractions once a week (Figure 4 and Figure 5). We achieved significant pain relief and referred the patient to fellow chemotherapists for assessment of the required chemotherapy regimen.

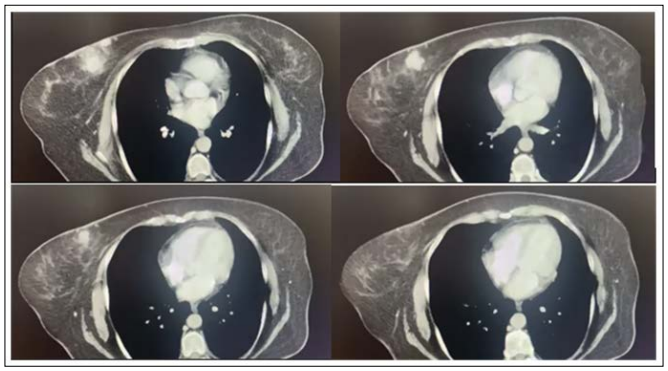

Figure 1: CT of the Chest with Intravenous Contrast

In the right mammary gland, a soft-tissue tumor with lobulated contours was visualized, with approximate axial dimensions of 44/33 mm. It reaches the skin, which is thickened.

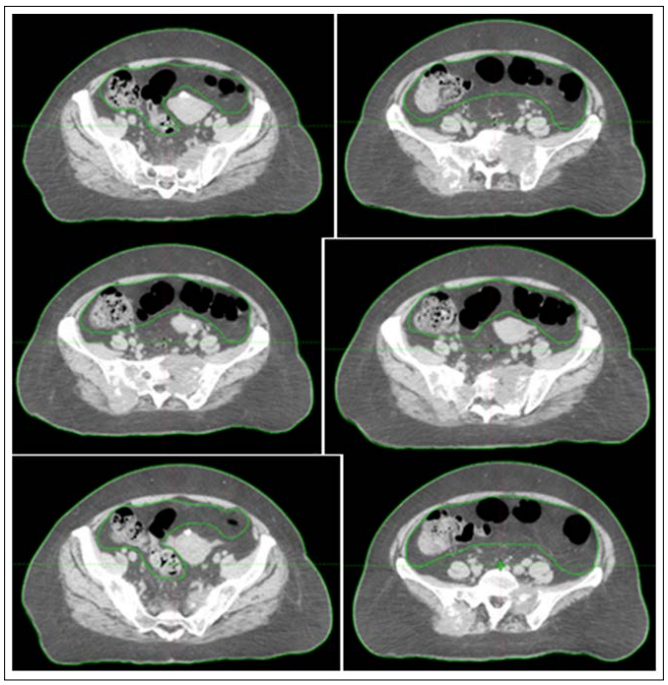

Figure 2: CT of Sacral Bone Metastasis

with a large soft tissue component

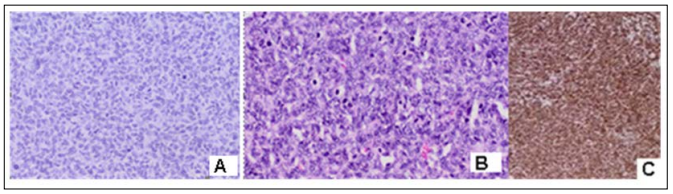

Figure 3A: Immunohistochemistry of the Soft Tissue Component of the Bone Metastasis

A/ Cytokeratin negative reaction in the sarcomatoid tumor component; B/ High mitotic index in the sarcomatoid tumor component; C/ Diffuse positive Vimentin reaction in metastatic tumor cells.

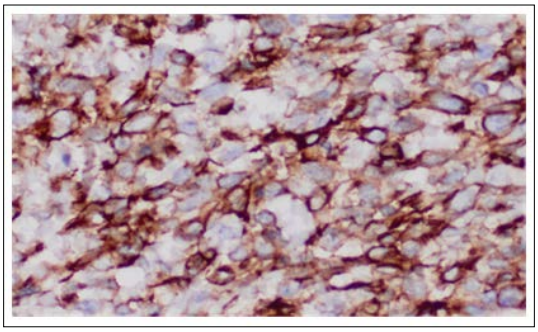

Figure 3B: CD10 Positive IHC Reaction in Metastatic Tumor Cells

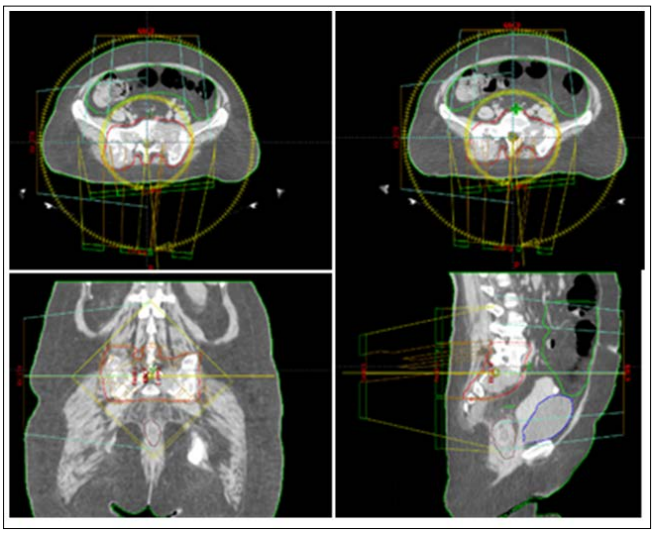

Figure 4: Intensity Modulated Radiotherapy
with a high single dose of 8 Gy in two fractions, once a week.

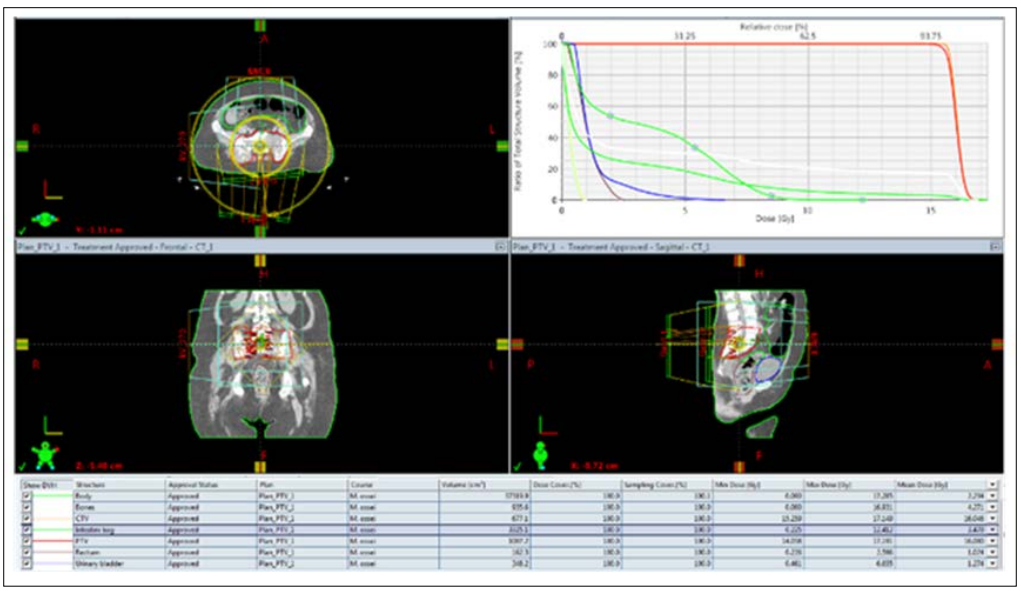

Figure 5: Intensity Modulated Radiotherapy

using the VMAT method with dose distribution in the target volume/ the sacral bone metastasis with the soft tissue component/ and in the critical normal tissues and organs.

Discussion

There are numerous histological grading systems for PTs, with most being 3-tiered – "benign, borderline, or malignant" or "low, intermediate, or high grade" – and use the same histological parameters (with varying cutoffs): margin characteristics, cellular atypia, stromal overgrowth, stromal cellularity, and mitotic rate [7]. PTs are subdivided into benign (60%-75%), borderline (15%-20%), or malignant (10%-20%), based on the assessment of 5 features: the degree of stromal cellular atypia; the mitotic activity per 10 high-power fields (HPFs); infiltrative or circumscribed tumor margins; the presence or absence of stromal overgrowth (ie, the presence of pure stroma devoid of epithelium); and the nature of the tumor border [8]. They are rapidly growing tumors that originate from the periductal stroma and are comprised of both epithelial and stromal histological tissues [2]. Histological examination showed a biphasic proliferation characterized by a double layered epithelial component arranged in clefts surrounded by an hipercellular fibrosarcomatous component organized in leaf-like structures [9]. In our clinical case, two cellular components /epithelial and stromal/ composed of atypical cells with the presence of atypical mitoses, are observed. In the one cell component, plexiform structures, made up of cells with moderately pleomorphic nuclei of a spindle-shaped and oval shape with finely condensed chromatin and poorly represented bright eosinophilic cytoplasm are considered. The other cellular componentis a solid growth involving glandular structures composed of cells with relatively small hyperchromic nuclei with visible nucleoli and sparse light eosinophilic cytoplasm. Stromal overgrowth was observed in a large part of the tumor. This histopathological finding proved a biphasic malignant breast tumor, which was confirmed as a phylloid tumor with immunohistochemistry showing a positive finding for CKAE1/3 in the epithelial component and positive activity for Vimentin in the stromal component. Stromal overgrowth as a predictor of PT metastasis was supported by 5 studies [10-12]. Histologic criteria such as tumor margins, stromal cellularity, mitotic rate and nuclear pleomorphism are helpful in predicting malignancy [4]. The metastatic potential of the tumor is determined by its stromal component, although metastases are thought to occur in less than 20% of malignant cases [13]. Distinguishing this subset of malignant phyllodes tumor is paramount [14]. The most reliable predictive factors for development of distant metastases are stromal overgrowth, nuclear pleomorphism and high mitotic activity [6,15]. In the excised tumor material up to 30% Ki 67 proliferation index was found, while in the surgical material after the mastectomy, the tumor doubled in size from 4 cm to 8 cm in one month, and its proliferation index was already 70%. This indicates an extremely aggressive tumor with high malignancy, and the presence of a well-vascularized tumor for the high risk of hematogenous spread. Most likely, the performed excisional biopsy with resection through the tumor cells is the main reason for the rapid aggressive local tumor growth. The Singapore nomogram "AMOS" uses the degree of stromal atypia, mitotic count, overgrowth and surgical margin status to predict the clinical behaviour of breast PT [16,17]. Due to the rarity of malignant PT and its related metastasis, it is difficult to make a presumptive diagnosis, particularly when it presents at a distant site and at a time distant from the initial presentation and surgery [4]. Koh et al. showed that a combination of large tumor size (≥90 mm) and the presence of malignant heterologous elements had a statistically significant association with the development of distant metastasis [18]. In Figure 2, CT of the pelvis visualizes a large sacrum metastasis with adjacent soft tissue infiltration, representing the soft tissue metastatic component. Although in the presented clinical case a bone metastasis developed in the sacrum 4 months after the performed mastectomy, for the purpose of differential diagnosis we performed a biopsy from the metastatic soft tissue component. This biopsy after immunohistochemistry proved the diagnosis of metastasis from a malignant phyllodes tumor. As presented in Figure 3A, immunohistochemical analysis showed a typical metastasis from a phylloid tumor of the breast with Vimentin positive reaction in the tumor cells, negative for Cytokeratin in the sarcomatous cells, which had a high mitotic index and positive reaction for CD 10 (Figure 3B), which has been shown to be a predictive factor in aggressive breast tumors. The patients whose tumors contained CD10-positive stromal cells had a shorter metastasis-free interval (P=0.0008). CD10 was the single significant prognostic factor for overall survival in the univariate analysis (P=0.0021) [19]. Al-Masry et al. have shown that the expression of CD10 can be used to predict the occurrence of distant metastasis [20].

The main treatment for phyllodes tumors of the breast is surgery with a resection line of 1 cm in healthy [21-23]. Survival after metastatic disease is poor, with various case series reporting median survival ranging from 4 to 17 months, with large variability based on the site of metastatic disease [24]. Although the radiosensitivity is not not fully understood, both radiotherapy and chemotherapy are recommended in metastatic patients [25,26]. Due to the strong pain syndrome causing immobilization of the patient, we conducted IMRT using the VMAT technique with a high single dose of 8 Gy in two fractions once a week (Figure 4 and Figure 5).

Conclusion

Malignant phyllodes tumors of the breast are a rare aggressive disease. Differential diagnosis requires histopathological examination performed by an experienced pathologist combined with immunohistochemical analysis elucidating the biphasic cellular characteristic of the disease. The main treatment for phyllodes breast tumors are a wide resection with 1 cm of healthy surrounding tissue. Non-radical surgery for the malignant variant of the phyllodes tumor leads to rapid aggressive local spread, as well as to distant hematogenous metastases. In the presence of a soft tissue component of the bone metastasis, a biopsy is required to prove the disease. Although the radiosensitivity of malignant phyllodes breast tumors is not yet fully understood, palliative radiotherapy for bone metastases induces complete resolution of the pain syndrome.

References

1. Parker S, Harries SA (2001) Phyllodes tumours. Postgrad Med J 77: 428-435.
2. Lindquist K, Van Heerden J, Weiland L, Martin J (1982) Recurrent and metastatic cystosarcoma phyllodes. Am J Surg 144: 341-343.
3. Kim S, Kim J, Kim D, Jung W, Koo J, et al. (2013) Analysis of phyllodes tumor recurrence according to the histologic grade. Breast Cancer Res Treat 141: 353-363.
4. Nguyen BD (2006) Imaging of pelvic bone metastasis from malignant phyllodes breast tumor. Radiology Case Report 1: 15.
5. Hlavin ML, Kaminski HJ, Cohen M, Abdul-Karim FW, Ganz E (1993) Central nervous system complications of cystosarcoma phyllodes. Cancer 72: 126-130.
6. Kapiris I, Nasiri N, A'Hern R, V Healy, G P Gui (2001) Outcome and predictive factors of local recurrence and distant metastases following primary surgical treatment of high-grade malignant phyllodes tumours of the breast. Eur J Surg Oncol

27: 723-730.

7. Hassouna J, Damak T, Gamoudi A, Riadh Chargui, Fethi Khomsi, et al. (2006) Phyllodes tumors of the breast: a case series of 106 patients. Am J Surg 192: 141-147.
8. Lakhani SR, Ellis IO, Schnitt SJ (2012) World Health Organization classification of tumours of the breast. International Agency for Research on Cancer (IARC); Lyon: 2012.
9. Mohamed Reda El Ochi, Mehdi Toreis, Mohamed Benchekroun, Zineb Benkerroum, Mohamed Allaoui, et al. (2016) Bone metastasis from malignant phyllodes breast tumor: report of two cases. BMC Clin Pathol 16: 4.
10. Chen W, Cheng S, Tzen C, Tsen-Long Yang, Kuo-Shyang Jeng, et al. (2005) Surgical treatment of phyllodes tumors of the breast: retrospective review of 172 cases. J Surg Oncol 91: 185-194.
11. Chaney A, Pollack A, McNeese M, Zagars GK, Pisters PW, et al. (2000) Primary treatment of cystosarcoma phyllodes of the breast. Cancer 89: 1502-1511.
12. Asoglu O, Ugurlu M, Blanchard K, Clive S Grant, Carol Reynolds, et al. (2004) Risk factors for recurrence and death after primary surgical treatment of malignant phyllodes tumors. Ann Surg Oncol 11: 1011-1017.
13. Gatalica Z, Vranic S, Ghazalpour A, Joanne Xiu,1 Idris Tolgay Ocal, et al. (2016) Multiplatform molecular profiling identifies potentially targetable biomarkers in malignant phyllodes tumors of the breast. Oncotarget 7: 1707-1716.
14. Roberts N, Runk DM (2015) Aggressive malignant phyllodes tumor. Int J Surg Case Rep 8C: 161-165.
15. Carter BA, Page DL (2004) Phyllodes tumor of the breast: local recurrence versus metastatic capacity. Hum Pathol 35: 1051-1052.
16. Tan PH, Thike AA, Tan WJ, Minn Minn Myint Thu, Inny Busmanis, et al. (2012) Predicting clinical behaviour of breast phyllodes tumours: a nomogram based on histological criteria and surgical margins. J Clin Pathol 65: 69-76.
17. Chng TW, Lee JYH, Lee CS, HuiHua Li, Min-Han Tan, et al. (2016) Validation of the Singapore nomogram for outcome prediction in breast phyllodes tumours: An Australian cohort. J Clin Pathol 69: 1124-1126.
18. Koh VCY, Thike AA, Nasir NDM, George Wai Cheong Yip, Boon Huat Bay, et al. (2018) Size and heterologous elements predict metastases in malignant phyllodes tumours of the breast. Virchows Arch 472: 615-621.
19. Keiichi Iwaya, Hitoshi Ogawa, Miki Izumi, Masahiko Kuroda, Kiyoshi Mukai (2002) Stromal expression of CD10 in invasive breast carcinoma: a new predictor of clinical outcome. Virchows Archs 440: 589-593.
20. Al-Masri M, Darwazeh G, Sawalhi S, Ayman Mughrabi, Maher Sughayer, et al. (2012) Phyllodes tumor of the breast: role of CD10 in predicting metastasis. Ann Surg Oncol 19: 1181-1184.
21. Chaney AW, Pollack A, McNeese MD (2000) Primary treatment of cystosarcoma phyllodes of the breast. Cancer 89: 1502-1511.
22. Asoglu O, Ugurlu M, Blanchard K, Clive S Grant, Carol Reynolds, et al. (2004) Risk factors for recurrence and death after primary surgical treatment of malignant phyllodes tumors. Ann Surg Oncol 11: 1011-1017.
23. Adesoye T, Neuman HB, Wilke LG, Jessica R Schumacher, Jennifer Steiman, et al. (2016) Current Trends in the Management of Phyllodes Tumors of the Breast. Ann Surg Oncol 23: 3199-3205.
24. McGregor G, Knowling M, Este F (1994) Sarcoma and cystosarcoma phyllodes tumors of the breast – a retrospective review of 58 cases. Am J Surg 167: 477-480.
25. Eich PD, Diederich S, Eich HT, O Micke, W Wagner (2000) Diagnosis radiation oncology: malignant cystosarcoma phyllodes. Strahlenther Onkol 176: 192-195.
26. Asoglu O, Karanlik H, Barbaros U, Hakan Yanar, Yersu Kapran, et al. (2006) Malignant phyllodes tumor metastatic to the duodenum. World J Gastroenterol 12: 1649-1651.