



## **Pancreatic Metastasis from Malignant Phyllodes Tumor of the Breast: A Rare Case Report and Literature Review**

**M. Shahimin<sup>1\*</sup>, P. B. C. Pang<sup>2</sup>, N. Hidayah<sup>1</sup>, H. R. Aznim<sup>3</sup>, A. Awang<sup>4</sup>, J. Sidhu<sup>2</sup> and Sadhana Mahamad<sup>1</sup>**

<sup>1</sup>*Breast and Endocrine Unit, Department of Surgery, Hospital Putrajaya, Malaysia.*

<sup>2</sup>*Gastroenterology Unit, Department of Medicine, Hospital Kuala Lumpur, Malaysia.*

<sup>3</sup>*Department of Pathology, Hospital Putrajaya, Malaysia.*

<sup>4</sup>*Department of Pathology, Hospital Kuala Lumpur, Malaysia.*

### **Authors' contributions**

*This work was carried out in collaboration among all authors. Author MS designed the study, wrote the protocol and wrote the first draft of the manuscript. Author NH managed the literature searches.*

*Authors PBCP and JS performed and provided the Endoscopic Ultrasound and Endoscopic Retrograde Cholangiography findings. Authors HRA and AA prepared the interpretation and slides for histopathology. Author SM managed the writing-reviewing and supervision. All authors read and approved the final manuscript.*

### **Article Information**

#### Editor(s):

(1) Dr. Ashish Anand, GV Montgomery Veteran Affairs Medical Center, USA.

#### Reviewers:

(1) Vikrant Rai, Western University of Health Sciences, USA.

(2) Neeraj Bokde, Aarhus University, Denmark.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/66113>

**Received 25 January 2021**

**Accepted 30 March 2021**

**Published 05 April 2021**

**Case Study**

### **ABSTRACT**

Phyllodes tumors (PTs) are defined as a fibroepithelial neoplasm of the breast. Although most of the Phyllodes tumors are benign, malignant cases do uncommonly occur. Pancreatic metastasis from malignant Phyllodes tumor is extremely rare, and only 5 cases have been reported in the literature. We presented a case of a pancreatic metastasis in a patient diagnosed with a malignant phyllodes tumor who had completed her treatment two years ago. Our objective is to draw the readers' attention to the possibility of pancreatic metastases from malignant phyllodes tumor in patients who had remission of malignant phyllodes and presented with signs and symptoms of primary pancreatic carcinoma.

*Keywords: Malignant phyllodes tumor; rare pancreatic metastasis.*

\*Corresponding author: E-mail: shahimin89@gmail.com;

## 1. INTRODUCTION

Phyllodes tumors (PTs) are fibroepithelial tumors composing of two components; epithelial and cellular stromal. Phyllodes tumor is a rare tumor of the breast. It constitutes about 0.3% to 1% of female breast neoplasm, in which the peak of affected women are aged 35 to 55 years old [1]. They are rarely found in adolescents and the elderly. Phyllodes tumor can be further classified as benign, borderline, or malignant depending on histological features. The majority of the tumors are benign, constituting about 35% - 65%, while the remainder is divided between borderline and malignant subtypes [2]. Benign Phyllodes tumor is often indistinguishable from fibroadenoma in terms of clinical, radiological, and cytological, and is usually cured by surgical resection. On the other hand, Malignant Phyllodes tumor shows infiltrating behavior and an increased risk of distant metastases [3]. Distant metastases, mainly to lungs and bone, are seen in 10% to 20% of patients with malignant Phyllodes tumors [4]. Whereas the pancreas is an uncommon site for metastasis, only a few cases have been reported. From our literature review, only 5 cases of pancreatic metastases from malignant Phyllodes tumor have been described so far. Hence, we reported a case of malignant Phyllodes tumor that has been metastasized to the pancreas.

## 2. CASE REPORT

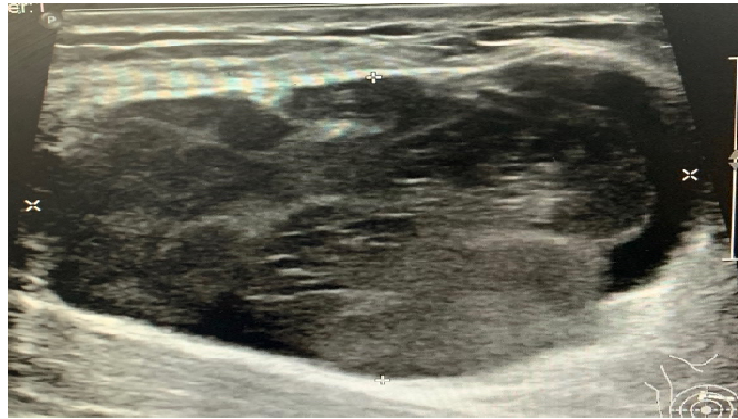
A 39 year old woman with an underlying Diabetes Mellitus Type II presented herself to the clinic with painless right breast swelling in May 2019. Clinical examination showed mass measuring 10 x 12 cm at the right breast. The breast's ultrasonography showed large heterogeneous solid nodules with cystic component measuring 3.9 x 5.9 x 10 cm at 1 o'clock in the right breast.

Fine Needle Aspiration (FNA) cytology showed benign epithelial lesions, no malignant cell. She underwent a right mastectomy. The tumor measured 10 x 15 cm at three-quarter of the right breast. The pectoralis major muscle was not involved. On gross examination, the cut section showed a large tumor occupying all quadrants measuring 120 x 15 x 70 mm, relatively circumscribed, solid and firm in consistency, the colour was whitish to grayish, irregular border area of cystic and myxoid appearance within the tumor. Microscopic examination showed a

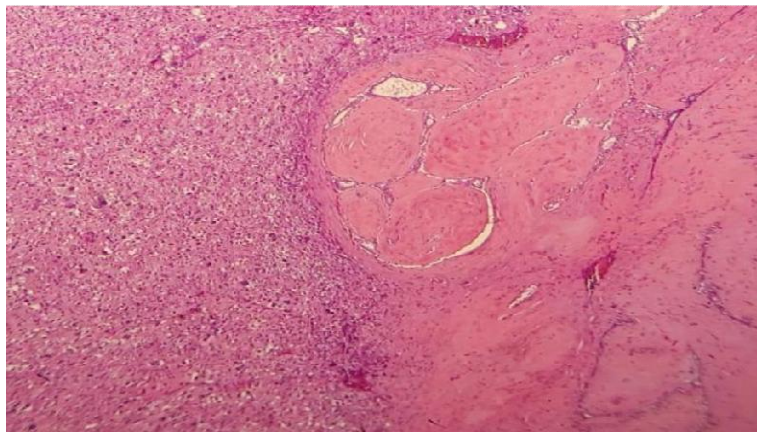
circumscribed cellular tumor with infiltrative and permeative border exhibiting increased stromal cellularity with residual benign phyllodes component at the periphery (Fig. 3). The tumor comprises marked nuclear pleomorphism of the stromal cells exhibiting enlarged cells with vesicular nuclei having prominent nucleoli and a moderate amount of eosinophilic cytoplasm and some atypical bizarre nuclei are seen (Fig. 3). Mitotic figures are 20 per 10 high power fields (HPF) (Fig. 3.1). A few cleft-like epithelial components were noted at the periphery, and areas with chondromyxoid and liposarcomatoid features were also seen (Fig. 4). Elsewhere, the breast tissue had fibroadenomatoid changes with background dense hyalinization and fibrosis. Focal lymphocytic infiltrates were noted around the duct. Areas of hemorrhage with focal necrosis and collection of haemosiderin-laden macrophages were also present. No lymphovascular invasion was identified. The nipple showed no evidence of Paget's disease. The overlying skin was unremarkable. All the resected surgical margins were free from malignancy. It was concluded as a Malignant Phyllodes tumor with free resection margins with no lymphovascular invasion. A Computed Tomography (CT) Thorax, abdomen, and pelvic was done and showed no distant metastasis. She completed 30 fractions of radiotherapy. She was well following radiotherapy and was on regular follow-up at our surgical outpatient clinic. Her surveillance mammogram showed a stable benign left breast lesions.

Patient was well until 15 months later when she had a fever associated with chills and rigors for a duration of 4 days. She also had upper abdominal pain localized at epigastric region, and was radiated to the right hypochondriac area. There was no obstructive jaundice symptoms. She had no yellowish discoloration of eyes, pale stool, and tea-colored urine. She also had normal bowel habits. On clinical assessment, she was normotensive, not tachycardia, but she had a documented fever of 37.9 °C. Abdominal examination showed no significant findings. Laboratory data were within normal range apart from the liver function test, which showed raised total bilirubin with transaminitis. Contrast-enhanced computed tomography (CECT) of the abdomen showed multiple lobulated hypodense lesion at the head, uncinate process, neck, body, and tail of the pancreas (Fig. 5). The most extensive lesion was at the head of the pancreas, measuring 2.4 x 2.2 cm. The Hounsfield Unit (HU) of the lesions

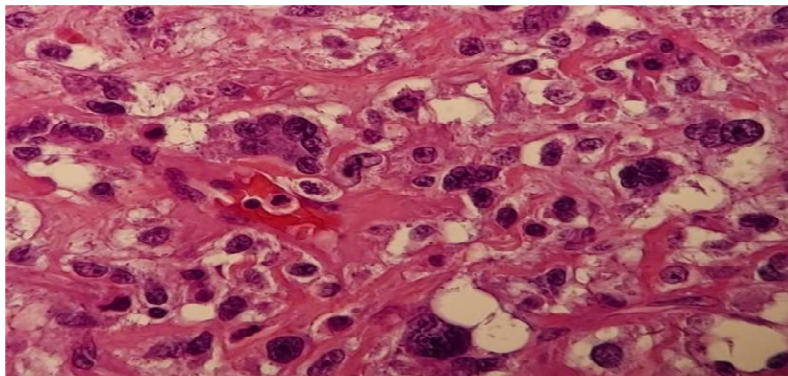
ranges between 55 to 64 in the post-contrast phase. The pancreatic had lesion that appeared to be compressing onto the distal common bile duct (CBD).



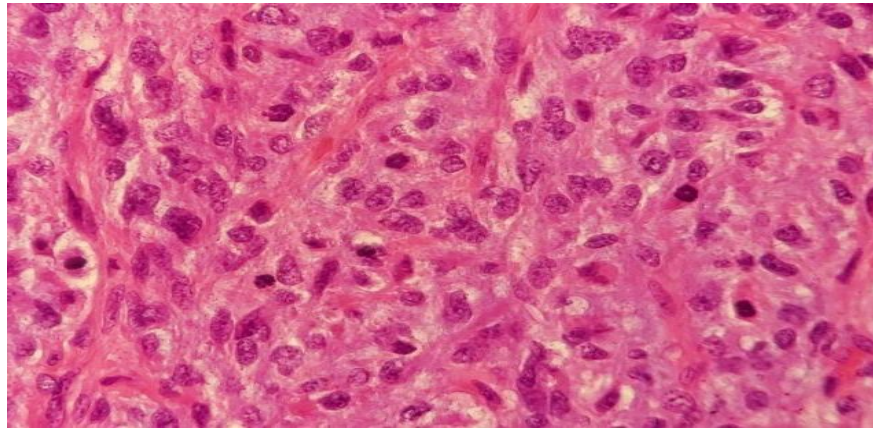
**Fig. 1. Ultrasound of the right breast demonstrating a large heterogenous solid nodule with cystic component**



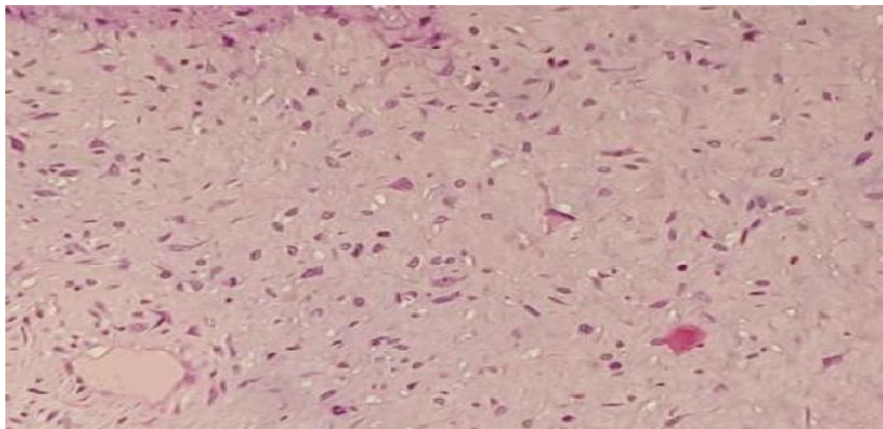
**Fig. 2. Malignant phyllodes tumor with increased stromal cellularity and marked stromal atypia (left) and residual benign phyllodes (right); Haematoxylin and eosin stain. Magnification 40x**



**Fig. 3. Marked nuclear pleomorphism of the stromal cells; enlarged cells with vesicular nuclei, prominent nucleoli and moderate amount of eosinophilic cytoplasm. A few enlarged bizarre nuclei are seen. Haematoxylin and eosin stain. Magnification 400x**



**Fig. 3.1. Increased mitotic figures (> 20 per 10 high power field, HPF). Haematoxylin and eosin stain. Magnification 400x**



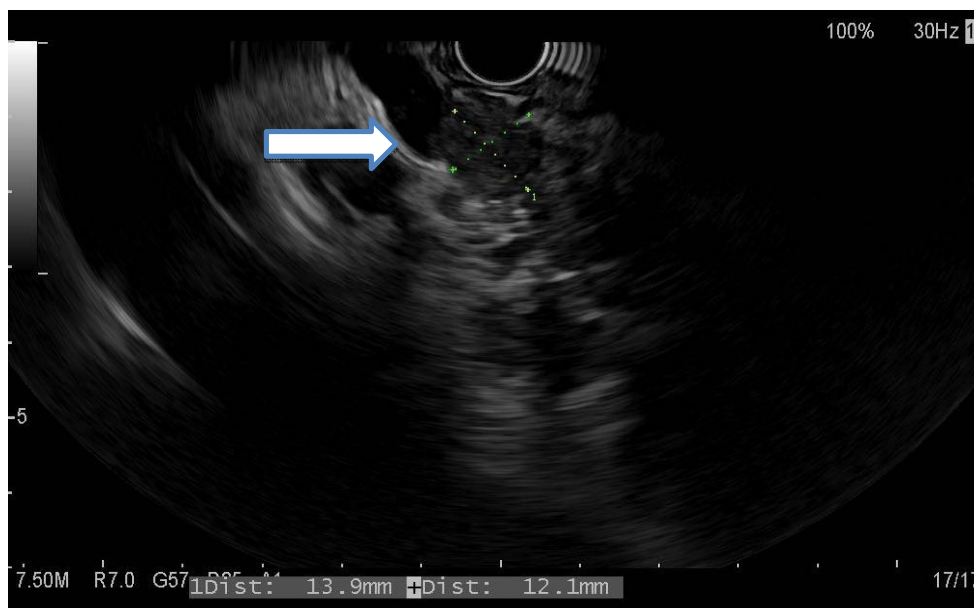
**Fig. 4. Malignant heterologous element; chondroid component; Haematoxylin and eosin stain. Magnification 100x**



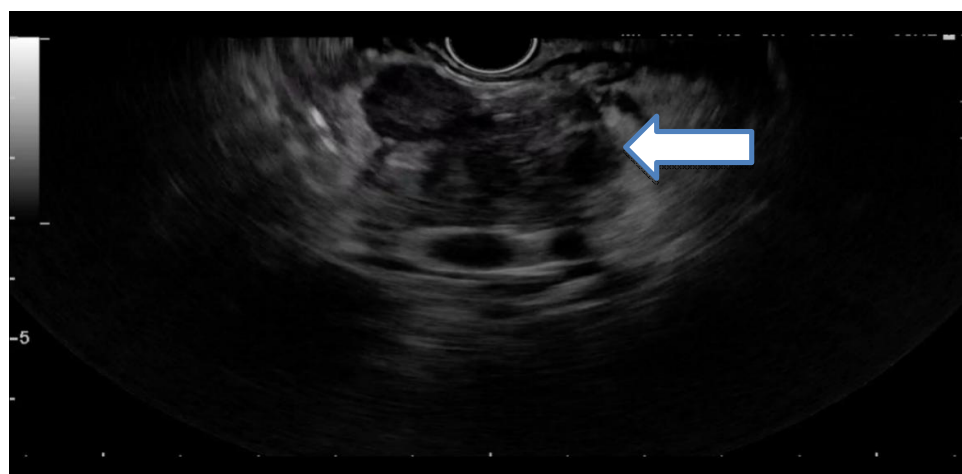
**Fig. 5. CT abdomen/pelvis with contrast show multiple lobulated hypodense lesion at the head, uncinate process, neck, body, and tail of the pancreas. The CBD was compressed**

Endoscopic ultrasonography (EUS) of the biliary system was performed and showed multiple ill-defined hypoechoic lesions with cystic degeneration seen within the pancreas. The lesions at the neck/body junction measured about 20 x 21mm, and at the body of the pancreas measured 12.5 x 13mm and 20 x 25mm. The common bile duct measured 9mm and was seen tapered abruptly into a mass measuring 12 x 13mm at the distal CBD (Fig. 6 and Fig. 7). EUS-fine needle biopsy was performed on the lesions. Histopathological results confirmed a malignant lesion in keeping

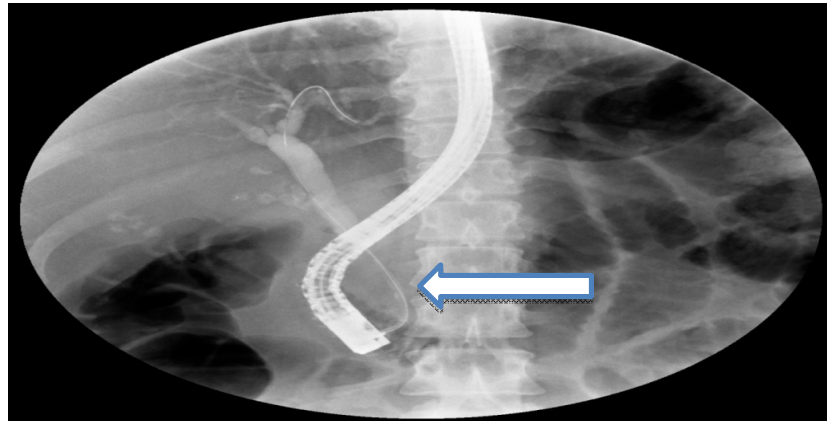
with malignant phyllodes tumor metastasis (Fig. 10). Immunohistochemistry (IHC) studies were performed to exclude other differential diagnosis. Further staging by CT Thorax showed a right lung nodule suspicious of metastases. However, both bone and liver were unremarkable. She subsequently underwent endoscopic retrograde cholangiopancreatography (ERCP), and an uncovered biliary metallic stent was inserted (Fig. 8 and Fig. 9). She was then referred to the oncology team for further assessment and treatment. However, she was not keen for any chemotherapy at this moment.



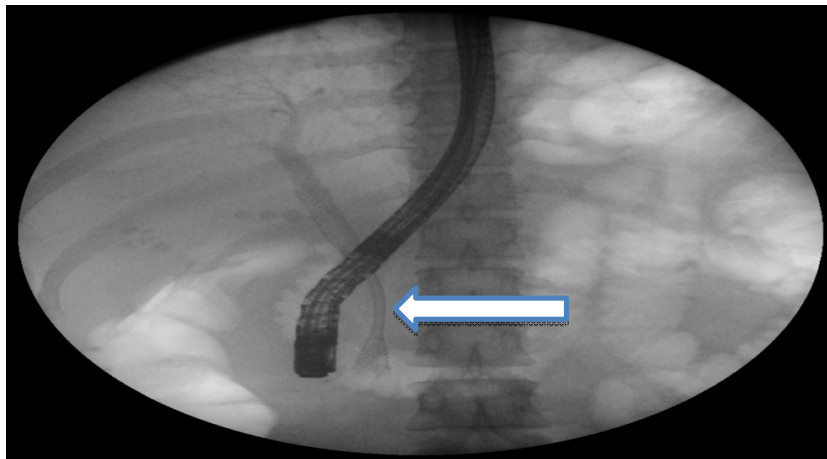
**Fig. 6. EUS image showing the distal CBD with abrupt tapering into the mass**



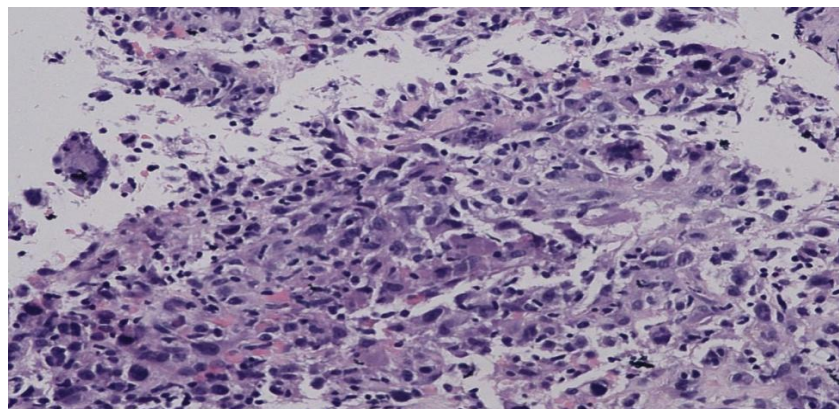
**Fig. 7. EUS image showing the hypoechoic lesion with cystic degeneration at the body of pancreas**



**Fig. 8. Fluoroscopic image showing distal CBD stricture**



**Fig. 9. Fluoroscopic image showing an uncovered metallic stent placement with narrowing at the strictured region**



**Fig. 10. Endoscopic ultrasound fine needle biopsy from pancreatic mass demonstrates malignant cells in cohesive cellular sheet exhibiting marked nuclear pleomorphism, nuclear hyperchromasia and ample amount of pale eosinophilic cytoplasm and indistinct cellular borders. Mitotic figures with aberrant forms are present. Haematoxylin & Eosin staining, original magnification 200x**

### 3. DISCUSSION

Phyllodes tumors are rare fibroepithelial neoplasm of the breast. Historically, Phyllodes tumors are identified as 'cystosarcoma phyllodes' based on the leaf-like projections extending into cystic space and sarcoma-like stroma of tumors [1]. Johannes Mullers created this term in 1838. However, the term 'cystosarcoma' was removed based on the observation that up to 70% of phyllodes tumor are benign [2]. Clinically, Phyllodes tumors are presented with a well-defined margin and painless mobile lump in the breast. The surface is bosselated. It has been postulated that the tumors have a biphasic growth pattern: slow-growing mass followed by rapid growth over weeks to months [2]. Phyllodes Tumors' average size is around 4cm, but up to 20% of Phyllodes Tumors can develop larger than 10 cm. They are more commonly found in the upper outer quadrant area of the breast [1].

Imaging modalities for Phyllodes tumors include both ultrasonography and mammography. On breast ultrasonography, they appear as a lobulated shape with a well-circumscribed margin, a low level of homogenous internal echoes, and no posterior acoustic shadow [1,3]. On mammography, it shows a well-defined lobulated oval mass with a rounded border. Some calcification may present [1,3]. However, all these findings are not specific, thus making them lack distinguishing features [4].

Histologically, a Phyllodes tumor consists of epithelial elements arranged in cleft-like ducts [5]. It is then surrounded by a predominant connective tissue stroma typically organized in a leaf-like structure [5]. The World Health Organization (WHO) classifies Phyllodes Tumors into benign, borderline, and malignant based on their histologic features. These histopathologic classifications included; margin appearance, degree of stromal cellular atypia, mitotic activity per 10 high power fields, and stromal overgrowth [6].

Benign Phyllodes Tumors are characterized by a well-circumscribed margin with minimal stromal atypia. There is no stromal overgrowth and mitoses per 10 high power field (HPF) less than five while Malignant Phyllodes tumors show infiltrating margin with severe stromal atypia. There is a significant presence of stromal overgrowth and mitoses for HPF more than 10 [7]. Malignant Phyllodes Tumors tend to have rapid growth and metastatic spread [8].

Distant metastases of malignant Phyllodes tumors can occur in approximately 10% to 20% of patients. From the literature, most distant metastases occurred without evidence of local recurrence [1,9], and they can appear from as short as one month or take up to a decade post treatment [10]. The common sites of distant metastases are at the lungs (66 - 84.5%) and bones (28 - 39%) [2]. Apart from that, several other rare metastases, including the duodenum, nasal cavity, brain, skeletal muscle, mandible, and maxilla, have been reported. A metastasis to the pancreas is extremely rare, and only a few cases have been reported. From our literature review, only 5 cases of pancreatic metastasis of malignant Phyllodes tumor were reported [4, 2,11,12,13].

From those cases, the mean age of patients who were diagnosed with malignant Phyllodes tumors metastasis to the pancreas was 45 years (range, 34 - 55 years). The youngest patient reported was 34 years old [2], and the oldest was 55 years old [11]. In comparison, the timing for pancreatic metastases emerging ranged as short as eight months [12] up to 6 years [2]. Bachet et al. reported a case of pancreatic metastases eight months after completing her radiation therapy [12]. Comparatively, our case is within these two timeframes. She was diagnosed with a distant metastasis to the pancreas after 15 months from her last surgery. Hence, the duration between the distant metastasis from the primary tumor was comparable with the other reported cases. Furthermore, we noted that in all of the cases that have been reported, a pancreatic metastasis occurred after remission of primary breast malignancy.

The clinical symptoms of pancreatic metastases are similar to primary pancreatic carcinoma [2]. Most reported cases presented were with abdominal pain, back pain, obstructive jaundice, haematemesis, and pancreatitis. Yukawa et al. reported a case of pancreatic metastasis presenting as acute retroperitoneal hemorrhage, 15 months after being diagnosed with a malignant Phyllodes tumor of the left breast. The patient had undergone a modified radical mastectomy with a transverse rectus abdominus myocutaneous (TRAM) flap presented with sudden onset of abdominal pain. CT abdomen revealed a retroperitoneal hemorrhage and tumor at the pancreatic tail, which was stabilized with angioembolization [13]. Ang TL et al. described a malignant Phyllodes Tumor patient presenting painless obstructive jaundice secondary to pancreatic head mass [11].

**Table 1. Histopathologic classification of Phyllodes Tumor by World Health Organization (WHO)**

	<b>Benign</b>	<b>Borderline</b>	<b>Malignant</b>
Margin	Pushing		Infiltrating
Stromal atypia	Minimal	Moderate	Severe
Mitoses per 10 HPF	<5	5 to 9	>10
Stromal overgrowth	Absent	Present	Present

**Table 2. Summaries of reported cases of pancreatic metastases for Malignant Phyllodes Tumors**

<b>Article</b>	<b>Age of patient (years)</b>	<b>Treatment of Primary Malignant Phyllodes tumor</b>	<b>Timing of pancreatic metastasis occurred</b>	<b>Presentation of pancreatic metastases</b>	<b>Investigation</b>	<b>Treatment</b>
Lee SE et al.	48	Right Nipple Areolar Skin Sparring Mastectomy	18months	Epigastric pain	CT Abd : Mass at body of pancreas EUS- FNAC	Open distal pancreatectomy with splenectomy Adjuvant therapy with immune-modulatory substances
Yukuwa M et al.	51	Modified Radical Mastectomy with TRAM flap	15months	Back pain	CT Abd : retroperitoneal hemorrhage with pancreatic mass	Embolisation of splenic artery Systemic chemotherapy (ifosfamide-doxorubicin)
Amir RA et al.	34	Mastectomy	6 years	Pancreatitis	CT Abd: pancreatic mass eroding caeliac artery	Unresectable
Bachert SE et al.	39	Lumpectomy	8months	Abd pain	CT Abd: : head of pancreatic mass CT biopsy	Radiation Systemic therapy with MAID chemotherapy
Ang TL et al.	55	Mastectomy	3 years	Obstructive jaundice	CT Abd :- biliary dilatation due to pancreatic head mass EUS- FNA	Palliative stenting



In the context of patient investigated for pancreatic mass with underlying carcinoma, the diagnostic dilemma would be whether the mass was benign or malignant and whether it was primary pancreatic carcinoma or distant metastasis. It is unfeasible to differentiate between primary and metastases based on clinical and radiological features alone. Endoscopic Ultrasonography (EUS) and EUS-FNA (Fine Needle Aspiration) have been considered the leading modality for diagnosing pancreatic masses [11]. Fritscher-Ravens et al evaluated the utility of EUS-FNA in patients with pancreatic masses in a single center study in Germany. The author evaluated one hundred and fourteen patients who had pancreatic masses in the CT of abdomen. Carcinoma was found in 59% of the patients (68 out of 114), in which 56 were of pancreatic origin and 12 from distant primary tumors. They concluded the importance of EUS-FNA in diagnosing carcinoma [14]. Ang TL et al. reported the first case of a pancreatic metastasis from a malignant Phyllodes tumor diagnosed by EUS-FNA. They concluded that clinical and EUS alone were not adequate to reach the diagnosis. EUS-FNA is required to confirm the presence of metastasis in the pancreas [7]. Out of 5 reported cases; EUS-FNA was used to diagnose the pancreatic metastases of malignant Phyllodes tumor in two of them [4,11]. In our case, the diagnosis of a metastasis malignant Phyllodes tumor was also established by the use of EUS-FNA cytology.

Current National Comprehensive Cancer Network (NCCN) guidelines for the management of Phyllodes tumors is surgery (Wide Local Excision or Mastectomy) with at least 1cm margin [15]. Narrow surgical margin of less than 1cm is associated with high local recurrence. However, the role of adjuvant chemotherapy and radiotherapy for Malignant Phyllodes Tumors remains uncertain. Hawkin et al. reported two complete remission cases using a combination regimen consisting of ifosfamide and doxorubicin. The patient was disease-free for 61 months [16]. In our case, the patient was treated with adjuvant radiotherapy and was well for 15 months without local recurrence.

Currently, there is no standard for treating metastasis Malignant Phyllodes tumor due to low incidence and lack of extensive prospective studies. Bachet SE et al. reported a case treated with radiation to the metastasis site followed by MAID chemotherapy (mesna, doxorubicin, ifosfamide, and dacarbazine). However, the

patient succumbed to death due to the progress of the tumor [12]. Lee SE et al. [4] performed an open distal pancreatectomy with splenectomy for isolated pancreatic metastases of malignant Phyllodes tumor of the breast. The patient subsequently proceeded with adjuvant therapy with immunomodulatory substances, and there was no evidence of recurrence during the first four months after the surgery. Yukuwa et al. [13] reported a case of pancreatic metastases presented with acute retroperitoneal hemorrhage successfully treated with catheter intervention. The patient was then treated with ifosamide-doxorubicin combination chemotherapy; however, the patient died a month later due to the disease's progression. Ang TL et al. [11] treated the patient with palliative stenting, but the author did not mention any adjuvant chemotherapy or radiotherapy. In our case, the patient developed jaundice due to the biliary system's obstruction by the pancreatic mass. A metallic stent was inserted to relieve the obstruction, and she was subsequently referred to the oncology team but she refused any further treatment.

#### 4. CONCLUSION

Even though uncommon, metastases malignant Phyllodes tumors to the pancreas do occur. It should be considered one of the differential diagnoses in evaluating pancreatic mass in a patient with a history of malignant phyllodes tumors. All clinicians must also be aware of the importance of EUS tissue acquisition in characterizing the nature of pancreatic masses. With the advent of new EUS biopsy needles, good core specimens could be obtained for better histopathological and immunohistochemical evaluations. However, there are no specific guidelines on the management of the tumor. The role of radiation and systemic chemotherapy are also unclear due to the limited number of cases.

#### CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author.

#### ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

## ACKNOWLEDGEMENTS

We would like to thank the Ministry of Health, Malaysia for kindly giving us permission to publish this article.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Mishra SP, Tiwary SK, Mishra M, Khanna AK. Phyllodes tumor of breast: A review article. International Scholarly Research Notices (ISRN Surg). 2013;361469.
2. Amir RA, Rabah RS, Sheikh SS. Malignant phyllodes tumor of the breast with metastasis to the pancreas: A case report and review of literature. Case Report Oncology Medicines. 2018;6491675.
3. Abdelkrim S, Trabelsi A, Bouzrara M, Boudagga M, Bakir D, Mokni M. Phyllodes tumors of the breast: a review of 26 cases. World Journal of Oncology. 2010;1(3):129–134.
4. Lee SE, Bae YK, Choi JH. Pancreatic metastasis from malignant phyllodes tumor of the breast. Yeungnam University Journal of Medicine (YUJM). 2020;00759.
5. Tan BY, Acs G, Apple SK, Badve S, Bleiweiss IJ, Brogi E, et al. Phyllodes tumours of the breast: A consensus review of histopathology. 2016;1:68.
6. World Health Organization; Histologic Typing of Breast Tumors, WHO, Geneva, Switzerland, 2<sup>nd</sup> Edition. 1981;2.
7. Bellocq JP, Magro G. Fibroepithelial tumours. In: Tavasoli FA, Devilee P (eds) World Health Organization classification of tumours: pathology and genetics tumours of the breast and female genital organs. IARC, Lyon. 2013;99–103.
8. Parker SJ, Harries SA. Phyllodes tumours. Postgrad Med J. 2001;77:428-35.
9. Palmer ML, De Risi DC, Pelikan A, Patel J, Nemoto T, Rosner D, Dao TL. Treatment options and recurrence potential for cystosarcoma phyllodes. Surg Gynecol Obstet. 1990;170:193-6.
10. Brooks HL, Priolo S, Waxman J, Pizzi WF. Cystosarcoma phyllodes: A case report of an 11-year survival and review of surgical experience. Contemporary Surgery. 1998; 53:169.
11. Ang TL, Ng VW, Fock KM, Teo EK, Chong CK. Diagnosis of a metastatic phyllodes tumor of the pancreas using EUS-FNA. JOP. 2007;8:35–8.
12. Bachert SE, Stewart RL, Samayoa L, Massarweh SA. Malignant phyllodes tumor metastatic to pancreas. Breast J. 2020;26: 1627–8.
13. Yukawa M, Watatani M, Isono S, Shiono H, Hasegawa H, Okajima K, et al. Pancreatic metastasis from phyllodes tumor presenting initially as acute retroperitoneal hemorrhage. Int Canc Conf J. 2013;2:238–42.
14. Fritscher-Ravens A, Sriram PV, Krause C, Atay Z, Jaeckle S, Thonke F, et al. Detection of pancreatic metastases by EUS-guided fine-needle aspiration. Gastrointest Endosc. 2001;53:65-70.
15. Taiwo A, Heather BN, Lee GW, Jessica RS, Jennifer S, Caprice CG. Current Trends in the Management of Phyllodes Tumors of the Breast. Ann Surg Onco. 2016;23(10):3199-3205.
16. Hawkins RE, Schofield JB, Wiltshaw E, et al. Ifosfamide is an active drug for chemotherapy of metastatic cystosarcoma phyllodes Cancer. 1992;69:2271–227.

© 2021 Shahimin et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:  
The peer review history for this paper can be accessed here:  
<http://www.sdiarticle4.com/review-history/66113>