

FIBROEPITHELIAL LESIONS OF THE BREAST AT THE PATHOLOGY DEPARTMENT OF THE UNIVERSITY HOSPITAL CENTER OF JOSEPH RAVOAHANGY ANDRIANAVALONA MADAGASCAR

Ranaivoson Haingo Voahangy Rabetafika¹ Andrianjafitrimo Holy Tiana² Ranaivomanana Volahasina³ Francine Andriamampionona Tsitihery Francine⁴ Randrianjafisamindrakotroka Nantenaina Soa⁵:

¹Pathology Department, Joseph Ravoahangy Andrianavalona University Hospital, Antananarivo, Madagascar

²Pathology Department, Joseph Ravoahangy Andrianavalona University Hospital, Antananarivo, Madagascar

³Pathology Department, Joseph Ravoahangy Andrianavalona University Hospital, Antananarivo, Madagascar

⁴ Pathology Department, Medical School of Fianarantsoa, Madagascar

⁵Chairman of the Pathology Department, Medical School of Antananarivo, Madagascar

Abstract

Fibroepithelial tumours are a heterogeneous group of biphasic tumours comprising dual stromal and epithelial components. The two main types are fibroadenoma and phyllodes tumour. Fibroadenoma is the most common benign breast tumour. The aim of our study is to determine their epidemiological and anatomopathological characteristics.

This is a retrospective, descriptive and analytic study of fibroepithelial breast tumors diagnosed at the Pathology Department of the University Hospital Center of Joseph Ravoahangy Andrianavalona Madagascar, from January 1, 2017, to December 31, 2021.

We have collected, 157 cases, fibroepithelial tumors of the breast accounted for 18.76% of breast pathologies. The average age was 24.79 years, with extremes of 11 and 55 years. The sex ratio was 0.033. The main clinical sign was the presence of a nodule in 87.90% of cases. The majority of samples (61.79%) were excisional biopsies. Their average size was 3.98 cm, ranging from 1 to 26 cm. On macroscopic examination, a lobulated, fasciculated, nodular appearance was observed in 49.68% of cases. Fibroadenoma Not Otherwise Specified was the predominant histological type, accounting for 95.54% of cases.

Fibroadenoma is the most common benign fibroepithelial tumor found in young women. Phyllodes tumors, on the other hand, are found exclusively in older women.

Keywords: Breast neoplasms; Epidemiology; Fibroadenoma; Phyllode Tumor

INTRODUCTION

Benign fibroepithelial breast tumors are the most common benign breast tumors in young women worldwide [3] and in Africa [4]. These are biphasic tumors with dual stromal and epithelial components that share the same histological characteristics but have highly variable clinical presentations. Due to their specific morphological and evolutionary characteristics, we conducted this study on fibroepithelial breast tumors examined at the Pathology Department at the Joseph Ravoahangy Andrianavalona University Hospital Center in Antananarivo (CHUA/JRA) Madagascar. The objectives of this study were to describe the epidemiological, clinical, and anatomo-pathological characteristics of fibroepithelial breast tumors.

MATERIALS AND METHOD

This is a retrospective, descriptive and analytic study of fibroepithelial breast tumors diagnosed at the at Pathology Department of the University Hospital Center of Joseph Ravoahangy Andrianavalona, from January 1, 2017, to December 31, 2021.

RESULTS

During the study period, the laboratory examined 837 cases of breast pathology. Fibroepithelial tumours (n = 157) accounted for 18.76% of these pathologies. Patients were on average 24.79 ± 8.05 years old at diagnosis, with the peak frequency observed in the 20–25 age group. In our series, we observed a clear female predominance, with a sex ratio of 0.033. The majority of patients 87.90% (n = 138) presented with a breast mass or nodule. The specimen type was excisional biopsy in 61.79% of cases (n = 97), followed by biopsies in 36.94% of cases and mastectomies in 1.27% of cases. The average size of the observed lesions was 3.98 ± 2.62 cm, ranging from 1.0 to 26.0 cm. The peak measurement of nodules was observed at [2.1–5.0 cm] with 67.52% (n = 106), and 37 (21.02% + 2.55%) were tumours measuring >5 cm. Fibroepithelial tumours of the breast were lobulated, fasciculated or nodular in 49.68% (n = 78) of cases, with one case exhibiting a « fern-like » appearance. Fibroadenoma (FAD) Not Otherwise Specified (NOS) was the most common type of fibroepithelial tumour of the breast, accounting for 95.54% (n = 150) of cases. We also observed the following : 0.64% (n = 1) of juvenile FAD ; 1.91% (n = 3) of complex FAD ; 0.64% (n = 1) of benign Phyllodes Tumor (PT) ; and 0.64% (n = 1) of Malignant Phyllodes Tumor (MPT). There was one case (0.64%) of FAD associated with a invasive breast carcinoma of no special type (IBC-NST). Regarding the correlation between histological type and age group, 58 cases of FAD NOS belonged to the [20-25] age group, and one case of MPT was in the >45 age group (Table V).

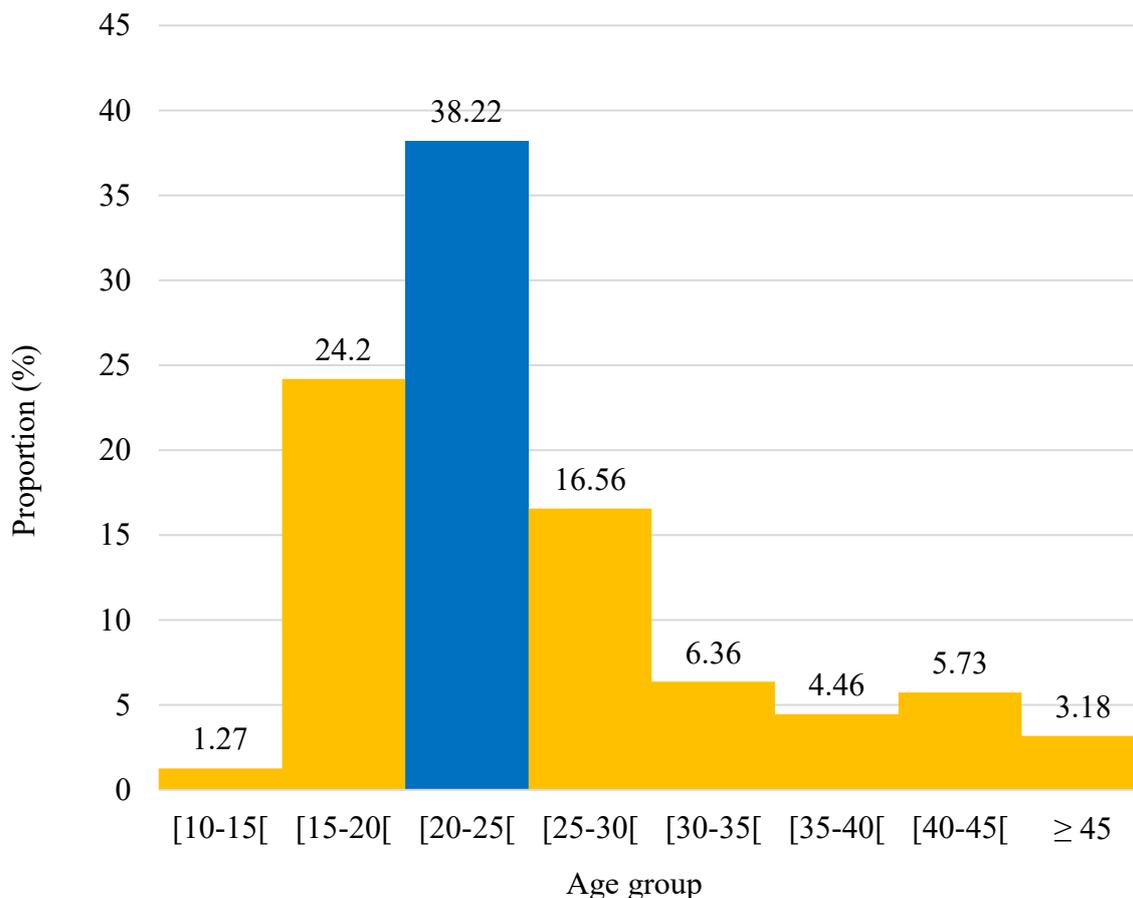


Figure 1 : Cases distribution by age group

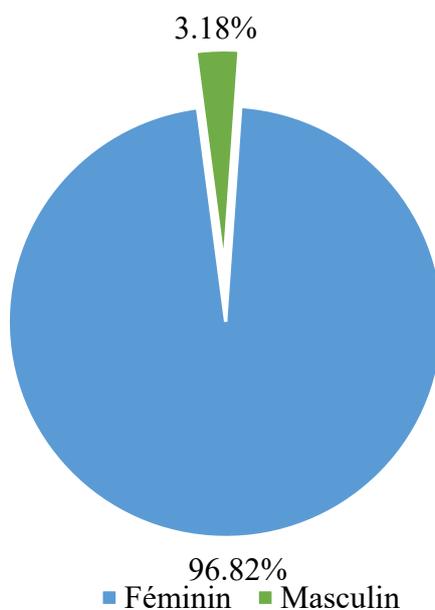


Figure 2 : Cases distribution by gender

Table I : Cases distribution by clinical information

Clinical information	Effectif n=157	Frequency 100%
Nodule /Mass	138	87.98
Cystic lésion	11	7
Others (painless, discimfort)	8	5.09

Table II : Cases distribution by sample type

Clinical information	Effectif n=157	Frequency 100%
Microbiosy	58	36.94
Excisionnal biopsy	97	61.79
Mastectomy	2	1.27

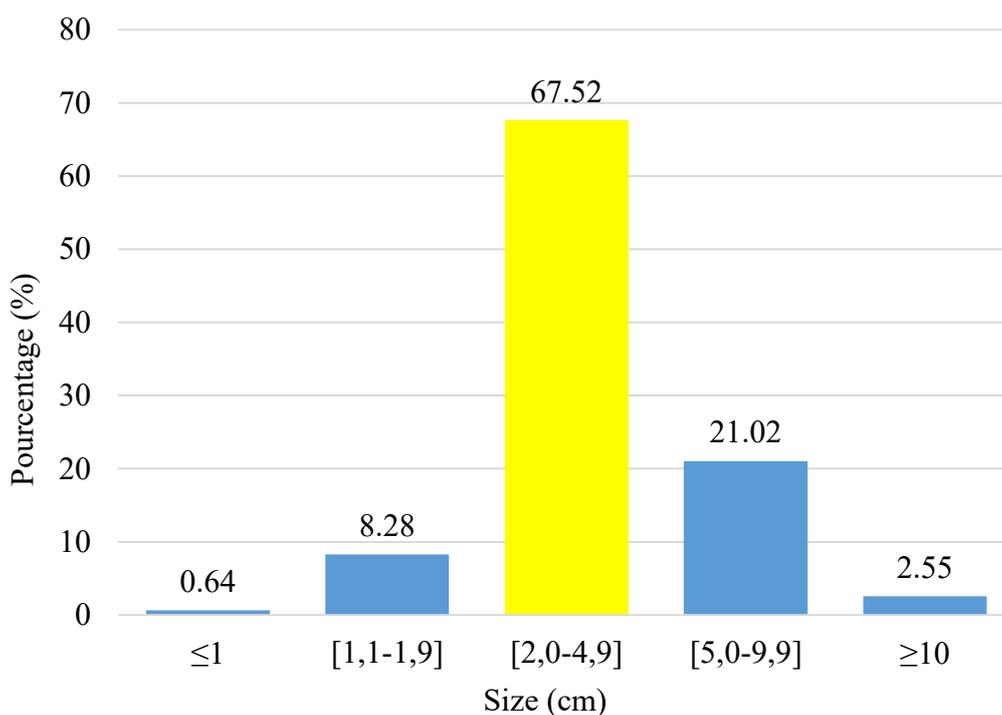


Figure 3 : Cases distribution by lesion size

Table III : Cases distribution by macroscopy appearance

Macroscopy appearance	Effectif n=157	Frequency 100%
Lobular/fasciculate/nodular	78	49.68
Fern leaf	1	0.64
Cystic	1	0.64
Hemorrhagic/necrotic remodeling	1	0.64
Encapsulated/well-defined	67	42.68
Unspecified	9	5.73

Table IV: Distribution of cases by histological type

Type histologique	Effectif n=157	Frequency 100%
FAD NOS	150	95.54
FAD complex	3	1.91
FAD juvenile	1	0.64
PT benign	1	0.64
MPT	1	0.64
FAD with IBC-NST	1	0.64

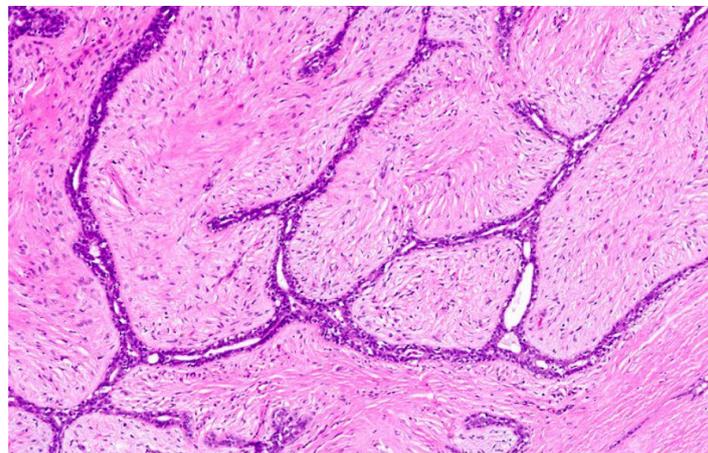


Figure 4 : Fibroadenoma NOS. (HE x 200)

Glands are compressed into linear branching structures by proliferating stroma with stromal cell without atypia.
 Pathology Department of the University Hospital Center of Joseph Ravoahangy Andrianavalona

Table V : Correlation between age group and histology type

Histology type	FAD NOS	FAD complex	FAD juvenile	TP benign	TPM	FAD with IBC-NST	Total
Age group							
[10-15[1	0	1	0	0	0	2
[15-20[38	0	0	0	0	0	38
[20-25[58	1	0	0	0	1	60
[25-30[26	0	0	0	0	0	26
[30-35[9	1	0	0	0	0	10
[35-40[7	0	0	0	0	0	7
[40-45[9	0	0	0	0	0	9
≥ 45	2	1	0	1	1	0	5
Total	150	3	1	2	1	1	157

DISCUSSION

The data from our study were similar to those in the literature, where the mean age at diagnosis was 24.79 ± 8.05 years, with extremes of 11 and 55 years. This is similar to the study by Egejuru R et al [1] in Nigeria in 2017, where they found a mean age of 22.6 ± 6.7 years with ages ranging from 9 to 60 years. Regarding the link between histological type and

age, two different studies conducted by Ugiagbe E et al in Niger in 2011 [2] and Hiremath B V et al. [3] showed that FAD commonly occurred in the third decade of life. These results are consistent with the results of our study. These figures are consistent with the theory of a probable hormonal correlation explaining the rarity of FAD before puberty and their occurrence in adolescents and women of childbearing age [4]. The incidence of FAD decreases with age, and one estimate suggests that 10% of the female population worldwide will experience an FAD once in their lifetime [5]. Juvenile FAD are relatively more common in young African Americans [6]. FAD are rare before menarche and are more common in adolescents and women under the age of 35, except in cases of complex FAD, which tend to occur about two decades later [7]. In our cases, there were three cases of complex FAD, with the patients aged 26, 33, and 47. In addition, PT mainly occurs in older women (average age: 40-50), approximately 15-20 years later than FAD [4]. We had two cases of PT, aged 45 and 55 years old.

According to a study conducted by Karki OB et al. in Nepal in 2015 [8], among patients with benign breast diseases, women (96%) predominated, with only 4% of patients being male. This clear female predominance observed both in the literature and in our study suggests a probable correlation with hormones that influence cell growth in the mammary glands [9].

In the literature, FADs generally present as painless, solitary, firm, slow-growing, mobile, well-defined nodules measuring less than 3 cm [9]. Most authors agree that they are painless in most cases [9,10]. An FAD usually presents as a painless, firm, mobile mass, often in young women aged 20 to 35. However, smaller, non-palpable FAD are increasingly being detected by screening mammography [11]. In our study, the majority of patients, 87.90% (n=138), presented with a breast mass or nodule, and 7% presented with pain or discomfort. TP generally presents as a large, firm to hard breast mass that can stretch the overlying skin considerably, which in rare cases can ulcerate [12]. In our study, the only case of malignant PT presented with skin ulceration and was large (26 cm). Paraneoplastic syndromes, including hypoglycemia secondary to the secretion of Insulin-like Growth Factor 2 (IGF-2), have been reported in association with malignant PT [13]. These signs were not reported in the request form for our case. However, there are no clinical features that can reliably distinguish between PT and FAD, or between different categories of PT [14].

In the 2016 study by Cowan et al. [11], for all patients (98.9%), diagnoses were initially made by excisional biopsy or lumpectomy, except for one, with a PT (1.1%) by mastectomy. This is similar to the results of our study, in which the majority of samples were excisional biopsies (61.7%) and two were mastectomies (1.27%), one for an FAD and one for a TP. Microbiopsy forms the basis of preoperative diagnosis of TP, but it is not accurate enough to provide perfect guidance for surgical decisions [15,16]. The diagnostic sensitivity of microbiopsy is approximately 66% [17]. Furthermore, according to some authors [18], the difficulty in evaluating a fibroepithelial tumor on micro-biopsy stems from the overlapping spectrum of histological appearance and sampling limitations.

According to the literature, FAD are generally small, <3 cm, but can be large and increase rapidly in size, especially during pregnancy, and regress during menopause. Giant DADs (>5 cm) are rare but can occur in adolescents [9]. In a study conducted by Bewtra C in Ghana in 2009 [19], the average size of FAD was 3.8 cm (range 1 to 9 cm), with 7 cases (22.5%) measuring more than 5 cm (giant FAD). This finding of a high proportion of giant FAD (23% of FAD cases) was also found in our study. Most FAD grow to 2 to 3 cm, then gradually regress or stop growing. However, about 2% of them can grow larger and become "giant FAD" [20].

According to Tan BY [12], sections of FAD are generally whitish in color, solid and lobulated in appearance, sometimes with small slits. Areas of calcification may also be present. According to Slodkowska E et al. [21], fibroepithelial tumors, particularly FADs, usually have a well-defined and pushing border (85%), sometimes with a partial or circumferential "pseudocapsule" (30% in this study). This was also found in our study, where FAD were lobulated/fasciculated/nodular in 49.68% (n=78) of cases, encapsulated or well-defined in 42.68% (n=67). PT generally presented as circumscribed solid masses [12]. Characteristically, PTs are heterogeneous in color, ranging from beige to gray or pink. The cross-sections are characteristic, resembling fern leaves. It is because of this leaf-like appearance that the tumor is called phyllodes, from the Latin word "phyllodium" meaning leaf. Large tumors may have areas of necrosis and/or hemorrhage. We had two cases of PT, one benign PT with this fern-like appearance, and the other a malignant PT that did not have this characteristic appearance but rather necrotic-hemorrhagic changes.

A retrospective cohort study conducted in Canada by Slodkowska et al. [21] reported that of 213 fibroepithelial lesions of the breast in 178 patients, 37.55% were unconventional or non-NOS FAD, which they classified as "atypical FAD" (n=80), and 62.45% were PT (n=133), of which 29.57% were benign PT, 19.14% were borderline PT, and 19.14% were malignant PT. " (n=80), and 62.45% were PT (n=133), of which 29.57% were benign PT, 19.14% were borderline PTs, and 13.61% were malignant PT. These authors used the term "atypical FAD" in their study, but in all cases the morphological criteria are the same as those observed in complex FAD according to the 2019 WHO classification [9]. In our study, complex FAD accounted for only 1.93% of all FAD. These results are similar to those obtained by Egejuru R et al [43] in Nigeria, where 5.3% (n=27) were giant FAD cases and 0.6% (n=3) were complex FAD. Several studies have demonstrated the presence of invasive breast carcinomas within or in tissues adjacent to FAD [22,23]. In our study, we had one case (0.64%) of adenofibroma associated with a IBC-NST. A retrospective cohort study conducted in Canada by Slodkowska et al. [21] reported that of 213 fibroepithelial lesions of the breast in 178 patients, 37.55% were unconventional or non-NOS FAD, which they classified as "atypical FADs" (n=80), and 62.45% were PT (n=133), of which 29.57% were benign PT, 19.14% were borderline PT, and 19.14% were malignant PT. " (n=80), and 62.45% were PT (n=133), of which 29.57% were benign PT, 19.14% were borderline PT, and 13.61% were MPT. These authors used the term "atypical FAD" in their study, but in all cases the morphological criteria are the same as those observed in complex FAD according to the 2019 WHO classification [9]. In our study, complex FAD accounted for only 1.93% of all FAD. These results are similar to those obtained by Egejuru R et al [1] in Nigeria, where 5.3% (n=27) were giant FAD cases and 0.6% (n=3) were complex

FAD. Several studies have demonstrated the presence of invasive breast carcinomas within or in tissues adjacent to FAD [22,23]. In our study, we had one case (0.64%) of adenofibroma associated with a IBC-NST.

CONCLUSION

Fibroepithelial tumors are common pathologies in women aged 20 to 25. The variability in their size and the existence of rare malignant forms justify systematic histopathological analysis.

Acknowledgments : We would like to thank all of those who have contributed for the realization of this article.

Conflict of interest : The authors declare that they have no conflict of interest.

REFERENCES

1. Egejuru RO, Nnadi IG, Duru ON. (2017) Fibroadenoma in Blacks. *Health*, 2017 ; 9(11) :1475-81. Doi : 10.4236/health.2017.911108.
2. Ugiagbe E, Olu-Eddo A. Benign breast lesions in an African population : A 25-year histopathological review of 1864 cases. *Niger Med J*. 2011 ; 52(4) : 211.
3. Hiremath BV, Hegde N. Spectrum of breast disease in an urban general surgical centre in India. *Breast Dis*. 2015 ; 35(3):179-86. doi: 10.3233/BD-150404. PMID : 25881642
4. Rungruang B, Kelley JL 3rd. Benign breast diseases: epidemiology, evaluation, and management. *Clin Obstet Gynecol*. 2011 Mar ;54(1):110-24. doi: 10.1097/GRF.0b013e318208010e. PMID: 21278510.
5. Ajmal M, Khan M, Van Fossen K. Breast Fibroadenoma. [Updated 2022 Oct 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK535345/>
6. Inaji H, Koyama H, Higashiyama M, Noguchi S, Yamamoto H, Ishikawa O, et al. Immunohistochemical, ultrastructural and biochemical studies of an amylase-producing breast carcinoma. *Virchows Arch A Pathol Anat Histopathol*. 1991;419(1):29-33.
7. Tse GMK, Lui PCW, Scolyer RA, Putti TC, Kung FYL, Law BKB, et al. Tumour angiogenesis and p53 protein expression in mammary phyllodes tumors. *Mod Pathol Off J U S Can Acad Pathol Inc*. oct 2003;16(10):1007-13.
8. Karki O, Kunwar D, De A. Benign Breast Diseases: Profile at a Teaching Hospital. *Am J Public Health Res*. 2015;4.
9. Tse GMK, Koo JS, Thike A. WHO Classification of Tumours Editorial Board : Breast tumours. 5è édition. Lyon, France : International Agency for Research on Cancer [En ligne] 2019. [consulté le 12 févr 2022]. Consultable à l'URL: <https://publications.iarc.fr/581>.
10. Tan PH. Fibroepithelial lesions revisited: implications for diagnosis and management. *Mod Pathol Off J U S Can Acad Pathol Inc*. janv 2021;34(Suppl 1):15-37.
11. Cowan ML, Argani P, Cimino-Mathews A. Benign and low-grade fibroepithelial neoplasms of the breast have low recurrence rate after positive surgical margins. *Mod Pathol*. mars 2016 ; 29(3):259-65.
12. Tan BY, Tan PH. A Diagnostic Approach to Fibroepithelial Breast Lesions. *Surg Pathol Clin*. mars 2018;11(1):17-42.
13. Reisenbichler ES, Krontiras H, Hameed O. Beta-human chorionic gonadotropin production associated with phyllodes tumor of the breast: an unusual paraneoplastic phenomenon. *Breast J*. 2009;15(5):527-30.
14. Visvader JE, Stingl J. Mammary stem cells and the differentiation hierarchy: current status and perspectives. *Genes Dev*. 1 juin 2014 ; 28(11):1143-58.
15. Zhou ZR, Wang CC, Sun XJ, Yang ZZ, Yu XL, Guo XM. Diagnostic performance of core needle biopsy in identifying breast phyllodes tumors. *J Thorac Dis*. nov 2016;8(11):3139-51.
16. Yazdankhah A, Ahmadi H. Management of Benign Phyllodes Tumor With Close Margins: A Case Presented in Multidisciplinary Session With Clinical Discussion and Decision Making. 2018;5(3):5.
17. Dessauvagie BF, Lee AHS, Meehan K, Nijhawan A, Tan PH, Thomas J, et al. Interobserver variation in the diagnosis of fibroepithelial lesions of the breast: a multicentre audit by digital pathology. *J Clin Pathol*. août 2018 ; 71(8):672-9.
18. Li JJX, Tse GM. Core needle biopsy diagnosis of fibroepithelial lesions of the breast: a diagnostic challenge. *Pathology (Phila)*. oct 2020;52(6):627-34.
19. Bewtra C. Fibroadenoma in women in Ghana. *Pan Afr Med J*. 21 juill 2009;2:11.
20. Davies JD, Page OL, Anderson TJ. Diagnostic histopathology of the breast. *J Pathol*. 1988 Novembre; 156(3):271-2.
21. Slodkowska E, Nofech-Mozes S, Xu B, Parra-Herran C, Lu FI, Raphael S, et al. Fibroepithelial lesions of the breast: a comprehensive morphological and outcome analysis of a large series. *Mod Pathol*. juill 2018;31(7):1073-84.
22. Wu YT, Chen ST, Chen CJ, Kuo YL, Tseng LM, Chen DR, et al. Breast cancer arising within fibroadenoma: collective analysis of case reports in the literature and hints on treatment policy. *World J Surg Oncol*. 10 nov 2014;12:335.
23. Hashimoto T, Toyono M, Fuyama S. A Case of Mammary Pagetoid Carcinoma with a Coexisting Fibroadenoma. *Austin J Surg*. 2014;1(9):2381-9030.