International Journal of Surgery Case Reports 97 (2022) 107408

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.elsevier.com/locate/ijscr

Case report

A Very rare case report of male invasive micropapillary breast carcinoma in China and review of literature

Qin Ou [a,b], Ying-dong Li [a], Jun Chen [a], Lin-lin Yuan [a], Wenfang Li [a,*]

[a] Department of General Surgery, The Taihe Hospital Affiliated to Hubei University of Medicine, Shiyan City, Hubei Province 442000, China
[b] Pathology Institute of HBMU, Hubei University of Medicine, Shiyan City, Hubei Province 442000, China

ARTICLE INFO

Keywords:
Breast cancer
Male
Case report
Invasive micropapillary carcinoma

ABSTRACT

Introduction: To report a rare case of male breast micropapillary carcinoma (MBMC) with early metastasis of axillary lymph nodes, the molecular characteristics were further studied in both primary and metastatic foci. In addition, we have reviewed similar published cases in the literature and tried to outline the molecular characteristics of this disease.

Presentation of case: A 63-year-old male patient presented with a painless mass on the medial side of left breast and was pathologically diagnosed with MBMC. Postoperative examination revealed 80 % invasive ductal carcinoma (IDC) and 20 % invasive micropapillary carcinoma (IMPC) in the mass, with a histological grade WHO III. There were 25 axillary lymph nodes, 11 of which were metastatic, including 5 macrometastasis and 1 micrometastasis, with a lymph node metastasis rate of 44 % (11/25). Pathological TNM stage: pT2N2M0. Immunohistochemical results in primary foci: AR (90 %, +), HER- 2 (1 +) and ER (90 %, +), PR (60 %, +), E - cadherin (+), EGFR (−), GATA - 3 (90 %, 3 +), Ki - 67 (50 %). Lymph node metastasis: AR (40 %, strong +), HER-2 (2+), ER (90 %, strong +), PR (40 %, strong +), Ki-67 (50 %). AR and Ki-67 were obviously expressed in both primary and metastatic foci. A mixture of IDC and IMPC was found in lymph node metastases, both of which expressed varying degrees of AR and Ki-67.

Clinical discussion: MBMC is easy to early metastasized to lymph node. In this case, there was no significant difference between primary and metastatic cancer in molecular results. It is positive for ER and PR, but negative for HER-2 in this patient. There is few data on male HER-2 expression, HER-2 expression is deficient in this case. AR is found to be positive in 50 % of MBMC cases, although their clinical relevance has not been established yet. The significance of EGFR in the prognosis of MBMC remains unclear, however, EGFR positive expression is not found in this patient.

Conclusions: MBMC is a rare disease characterized by early lymph node metastasis, high histological grade, positive ER and PR, and generally negative HER-2. The molecular biological characteristics and prognostic significance of MBMC need to be further studied in order to develop the optimal treatment strategy.

1. Introduction

Male breast cancer (MBC) is a rare malignant tumor in the male population. Due to the influence of various factors such as psychological and medical environment, many male patients do not pay attention to breast nodules, resulting in later stages after diagnosis than women [1]. Invasive micropapillary carcinoma (IMPC) is found in the small intestine, bladder, lung and other organs. The tumor cells are characterized by nest-like, papillary, or small glandular tubular tumor cells, and lack of mesenchymal components such as fibrous vascular tissue in the center of tumor cluster [2]. IMPC is a special pathological classification of invasive ductal cancer (IDC), accounting for 3.8–5.9 % of all breast cancer types, with early lymph node metastasis [3]. When papillary structure reaches 100 % in IMPC, it is called simple IMPC, otherwise, it is called mixed IMPC [4].

Male breast micropapillary carcinoma (MBMC) has features of early metastasis, late staging, and poor prognosis [5]. At present, there is no clear diagnosis and treatment plan for MBMC, and the existing treatment measures are mostly based on the diagnosis and treatment experience of female breast cancer, and the treatment effect is not ideal. The clinical

* Corresponding author.
E-mail address: wenfangli79@163.com (W. Li).

https://doi.org/10.1016/j.ijscr.2022.107408
Received 23 May 2022; Received in revised form 24 June 2022; Accepted 8 July 2022
Available online 15 July 2022

data of a patient with MBMC admitted to our hospital are summarized as follows. The present work has been reported in line with the SCARE 2020 criteria [6].

2. Medical records

Patient, ×××, male, 63 years old, occupied as a farmer, healthy in the past, was admitted to Taihe Hospital in October 2021. The patient had no allergies and/or adverse reactions and no special family history. The patient complained as "left breast mass found more than 1 month ago" by self-presentation. One month ago, the patient inadvertently found a painless mass in the left breast without tenderness or nipple discharge. Physical examination on admission: the breasts were symmetrical, and there was no nipple retraction or secretions. A mass about 30.0 × 20.0 mm in size could be touched at 10–12 o'clock in the left mammary gland, indicating unclear boundary, uneven surface, crab foot change, visible calcification points. The mass was touched hard and poor mobility. Local skin was slightly depressed, and there was no redness, or "orange skin change" in local skin. There was no obvious abnormality in the contralateral breast. Color ultrasound examination suggested that there was a hypoechoic mass in the left mammary gland, about 32 * 23 mm in size, with unclear boundary, irregular shape, angular edge, crab-like change, aspect ratio larger than 1, and multiple dotted strong echoes (Fig. 1A). Left axillary lymph node appeared a diameter about 15 * 5 mm, abnormal shape, unclear boundary, disappeared lymphatic hilum structure.

On October 29, 2021, a puncture biopsy of the left breast mass was performed under local anesthesia. Postoperative pathology showed invasive cancer (puncture tissue of the left breast). The lung, abdomen and pelvis CT scan were performed and suggested no distal metastasis was observed, and bone scan also suggested no distal metastasis in the bone. On October 31 the patient undergoed left breast modified radical in general anesthesia and the breast tissue moved by the surgery (Fig. 1B), Intraoperative frozen pathological results revealed five axillary sentinel lymph node metastasized. Left axillary lymph node dissection was performed simultaneously. Postoperative examination results: (Left breast and ipsilateral axillary lymph nodes) mixed invasive carcinoma was considered, including 80 % IDC (histological score 2 + 3 + 3 = 8 points, WHO III) and 20 % IMPC (histological score 3 + 3 + 1 = 7 points, WHO III), with vascular and nerve invasion (Fig. 2). And the tumor surface skin were negative. There were 25 axillary lymph nodes, 11 of which were metastatic, including 5 macrometastasis and 1 micrometastasis, with a lymph node metastasis rate of 44 % (11/25). Pathological TNM stage: pT2N2M0.

Immunohistochemical method was adopted to examine the molecular expression characteristics of androgen receptor (AR), human epidermalgrowth factor receptor-2 (HER-2), estrogen receptor (ER) , epidermal growth factor receptor (EGFR), progesterone receptor (PR) in this case. And immunohistochemical results: AR (90 %, +), Her-2 (1 +) and ER (90 %, +), PR (60 %, +), E - cadherin (+), EGFR (−), GATA - 3 (90 %, 3 +), Ki - 67 (50 %). Among them, AR (Fig. 3A & B) and Ki-67 (Fig. 3C & D) were significantly expressed in both primary and metastatic lesions, and both IDC and IMPC were positive. Lymph node metastasis: AR (40 %, strong +), HER-2 (2+), ER (90 %, strong +), PR (40 %, strong +), Ki-67 (50 %). In addition, A mixture of IDC and IMPC was found in lymph node metastases (Fig. 4A), both of which expressed varying degrees of AR (Fig. 4B) and Ki-67 (Fig. 4C).

The patient has completed 8 cycles of EC-T chemotherapy and 1 month of adjuvant radiotherapy on the left chest wall and axilla after surgery, and no signs of recurrence have been found up to now. The patient was instructed to continue to plan endocrine therapy after discharge, taking letrozole tablet orally, 1 tablet per time, once a day, and closely observing the subsequent changes of the disease. The follow-up was done by periodic clinical examination and lung, abdomen and pelvis CT scan were performed to rule out distal metastasis every six months. The patient still survived now without any recurrence.

3. Discuss

3.1. Diagnosis and treatment of IMPC

IMPC is a special type of invasive ductal carcinoma with an incidence of 3.8 % to 5.9 % [7]. In 1993, Siriaunkgul and Tavassoli distinguished IMPC as a separate type of invasive ductal carcinoma, where morphological and molecular differences in tumor cells make IMPC more prone to metastasis alone and more prone to metastasis when mixed with conventional invasive ductal carcinoma [8]. At present, the diagnostic criteria for IMPC are not uniform. IMPC components accounting for more than 75 % of breast cancer could be diagnosed as IMPC, while some people believed that IMPC components accounting for more than 50 % of breast cancer could be diagnosed as IMPC. Fu Li concluded that IMPC could be diagnosed as long as there was IMPC component in cancer nests, even if IMPC component was less than 10 % [9].

IMPC is an extremely rare disease in male patients and has rarely been reported in the literature. Burga et al. published a case series of 788 male breast cancer patients whose primary histological type was pure invasive ductal carcinoma (84.7 %) [10]. Male IMPC patients had a mean age of 69.8 years [11]. This figure is slightly higher than for

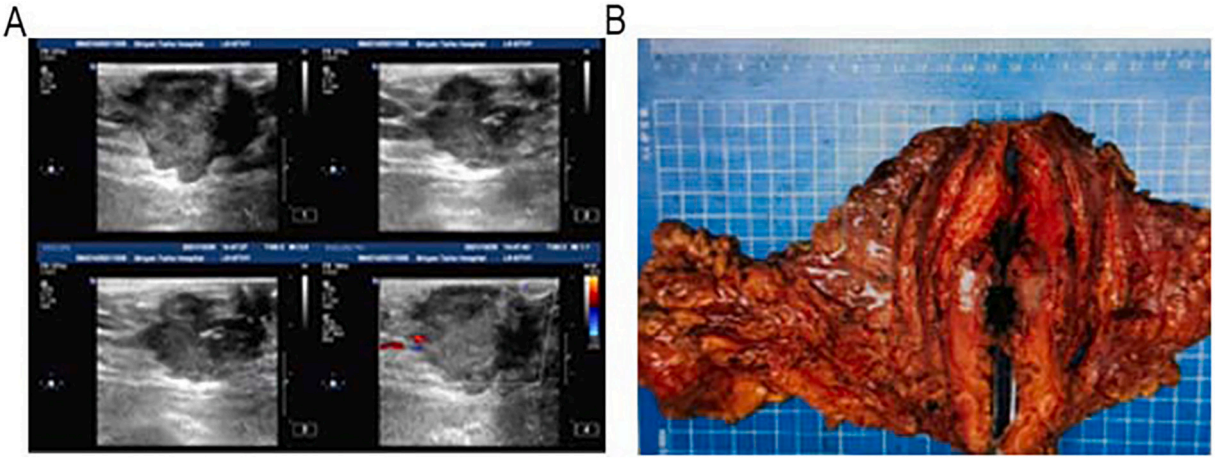

Fig. 1. The images of the breast mass by ultrasound and the breast tissue moved by the surgery.
A. Ultrasound image of the breast mass, indicating unclear boundary, uneven surface, crab foot change, visible calcification points; B. The whole breast tissue moved by the surgery.

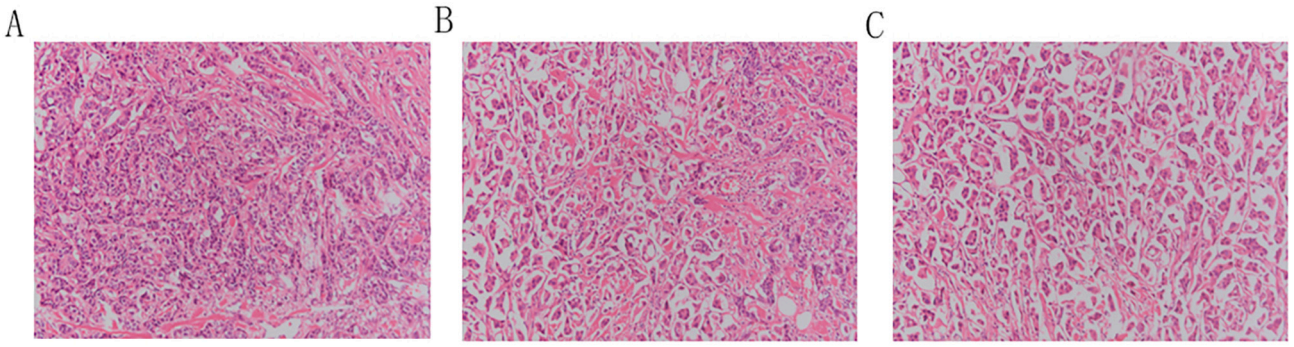

Fig. 2. HE staining suggested primary invasive ductal carcinoma, invasive micropapillary carcinoma, and a mixture of the two.
A. Primary invasive ductal carcinoma; B. Primary invasive ductal carcinoma mixed with micropapillary carcinoma; C. Primary invasive micropapillary carcinoma.

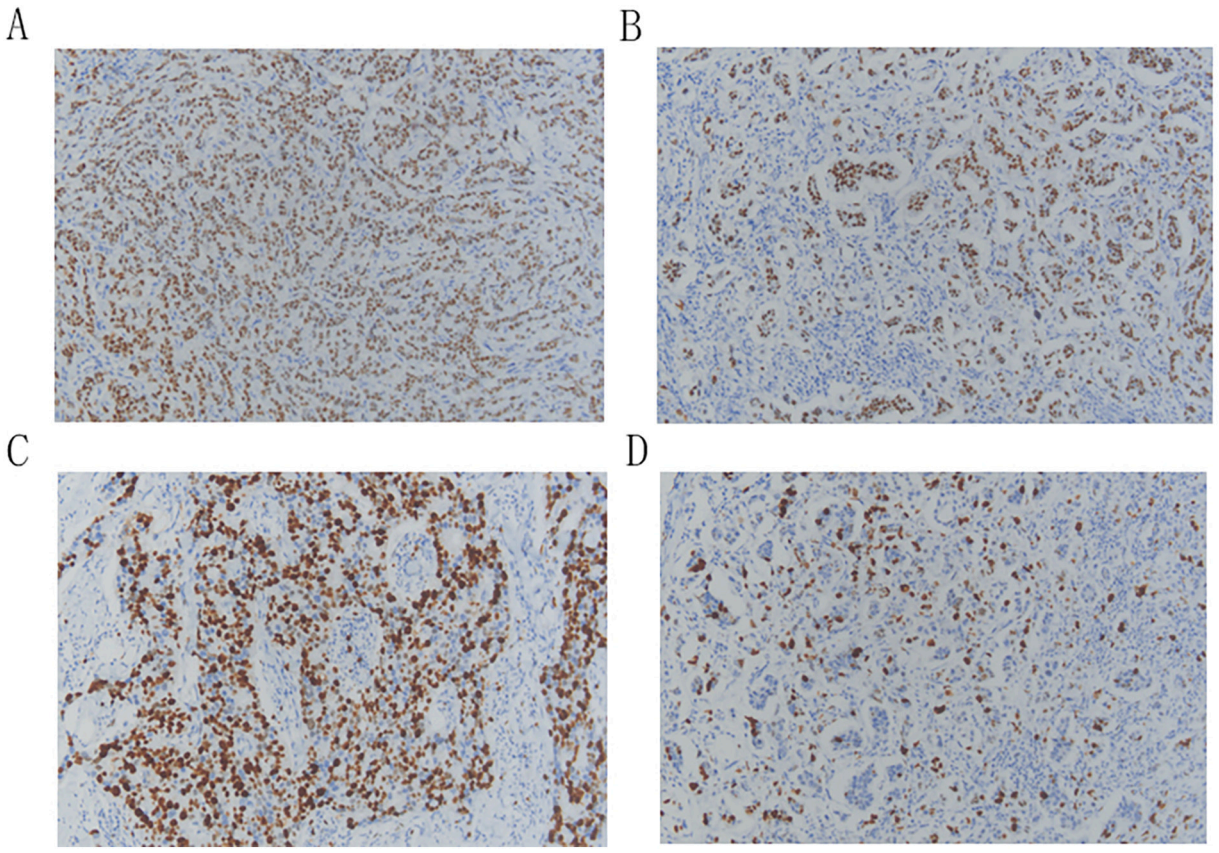

Fig. 3. SP immunohistochemical detection of AR and Ki-67 in primary invasive ductal carcinoma and invasive micropapillary carcinoma.
Positive AR expression in part of primary primary invasive ductal carcinoma; B. Partial AR positive expression in primary invasive micropapillary carcinoma; C. Ki-67 was positively expressed in part of primary invasive ductal carcinoma; D. Ki-67 was positively expressed in part of primary invasive micropapillary carcinoma.

women, possibly due to the overall rarity of breast cancer among male patients and a decline in breast cancer awareness among patient populations.

3.2. Clinical features of MBMC

IMPC is easy to early metastasized to lymph node is the most prominent characteristics, some patients before early diagnosis, cancer cells already metastasized throughout the body through the blood vessels, lymphatic system, the risks of recurrence of primary focal distance and metastasis of cancer cells were reduced [12]. As early as 2004, Pettinato et al. reported that IMPC lymph node metastasis rate was as high as 80 % [13]. Chemokine receptors play an important role in tumor metastasis, and IMPC had higher CXCR4 expression, which was related to IMPC lymph node metastasis [14]. Fu Li et al. [15] showed that IMPC loss genes PRDM16 and IGSF9 were related to IMPC lymph node metastasis and poor prognosis. In this case, the lymph node metastasis rate was as high as 44 % and the number of metastases was high. At the same time, there were several macrometastatic lymph nodes, indicating that IMPC structure might increase the malignant degree of MBMC.

In this case, 80 % IDC (histological score 2 + 3 + 3 = 8 points, WHO III) and 20 % IMPC (histological score 3 + 3 + 1 = 7 points, WHO III) were characterized by high histological grade. Primary immunohistochemical results: AR (90 %, strong +), HER-2 (1+), ER (90 %, strong +), PR (60 %, strong +), lymph node metastasis: AR (40 %, strong +), HER-2 (2+), ER (90 %, strong +), PR (40 %, strong +), Ki-67 (50 %) were both

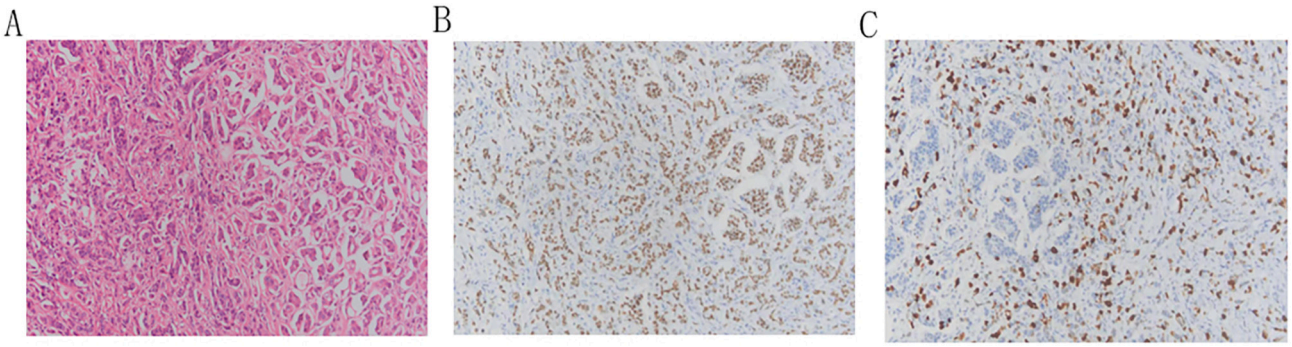

Fig. 4. HE and SP immunohistochemical results of infiltrating ductal carcinoma and micropapillary carcinoma with axillary metastatic lymph node.
A. HE staining suggested a mixture of infiltrating ductal carcinoma and micropapillary carcinoma with metastatic axillary lymph nodes. B. Partial AR expression in invasive ductal carcinoma and invasive micropapillary carcinoma with metastatic axillary lymph nodes; C. The expression of Ki-67 in infiltrating ductal carcinoma and infiltrating micropapillary carcinoma in axillary metastatic lymph nodes.

positive for ER/PR and negative for HER-2, and there was no significant difference between primary and metastatic cancer molecular detection results. Data on molecular typing characteristics of MBMC are limited. Coyle et al. reported that a patient was positive for ER and PR, but negative for HER-2 [5]; Ishita et al. also reported a patient with MBMC who was positive for ER and PR, but negative for HER-2 [16]. It was noted in this case that both ER and PR were positive. The high positivity of these two receptors in male breast cancer might be due to the low hormone levels of these two receptors, enabling them to bind and achieve a good hormonal response through increased ER and PR.

HER-2 oncoprotein is a potentially useful prognostic marker for breast cancer in women, but there are few data on male HER-2 expression [17]. This case report also shows that HER-2 expression is deficient. AR is positively correlated with ER in MBC, suggesting the importance of hormone crossover, but in ER+/PgR low subgroup, AR status is negatively correlated with histological grade and lymph node status, which might be involved in the progression of MBC [18]. AR was found to be positive in 50 % of MBMC cases, although their clinical relevance had not been established [19]. The positive rate of AR in this patient was 40 %, which might play a role in the malignant progression of MBMC. The significance of EGFR in the prognosis of MBMC in males is still unclear, while it indicates poor prognosis in females [20]. EGFR positive expression was not found in this patient. Similarly, little is known about changes in the p53 gene in male breast cancer, and no association between survival and p53 expression has been observed to date.

4. Conclusions

MBMC patients have a poor prognosis, more prone to lymph node metastasis, resulting in late staging, and easy to delay diagnosis under the pressure of psychological, economic, medical and other aspects. The molecular characteristics usually appear HER-2 negative and ER/PR positive. There is still no unified international standard for the treatment of MBMC patients at present, and the diagnosis and treatment guidelines for female patients are often used for reference, inevitably ignoring the physiological differences. Therefore, early diagnosis and individualized treatment are the keys to improve the overall survival rate of patients.

Funding

No funding.

Ethical approval

Ethical approval has been permitted by our institution Ethical committee. A written consent of publication of this case report was achieved by the author from the patient.

Consent

An informed written consent was taken from the patient for reporting this case and the accompanying images.

We have omitted the identifying details if they are not essential.

Contribution

This paper was written and performed by Qin Ou, some clinical information was provided by Jun Chen and Ying-dong Li, revised and guided by Geng Wang, supported and study designed by Wenfang Li.

Registration of research studies

This is not a 'First in Man' study. It only explained a rare case of male invasive micropapillary breast carcinoma in China.

Guarantor

Wen-fang Li.

Provenance and peer review

Not commissioned, externally peer reviewed.

Declaration of competing interest

The Authors declare that there is no conflict of interest in this paper.

References

[1] S. Fox, V. Speirs, A.M. Shaaban, Male breast cancer: an update, Virchows Arch. 480 (1) (2022) 85–93.
[2] N. Kanomata, J. Kurebayashi, Y. Koike, R. Yamaguchi, T. Moriya, CD1d- and PJA2-related immune microenvironment differs between invasive breast carcinomas with and without a micropapillary feature, BMC Cancer 19 (1) (2019) 76.
[3] Y. Sun, W. Gu, G. Wang, X. Zhou, The clinicopathological and prognostic characteristics of mucinous micropapillary carcinoma of the breast, Histol. Histopathol. 18436 (2022).
[4] G.I. Verras, L. Tchabashvili, F. Mulita, I.M. Grypari, S. Sourouni, et al., Micropapillary breast carcinoma: from molecular pathogenesis to prognosis, Breast Cancer (Dove Med Press) 14 (2022) 41–61.
[5] E.A. Coyle, H. Taj, I. Comba, J. Vasquez, V. Zayat, Invasive micropapillary carcinoma: a rare case of male breast cancer, Cureus 12 (9) (2020), e10571.
[6] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, for the SCARE Group, The SCARE 2020 guideline: updating consensus Surgical CAse REport (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230.
[7] G.D. Lewis, Y. Xing, W. Haque, T. Patel, M.R. Schwartz, et al., The impact of molecular status on survival outcomes for invasive micro papillary c arcinoma of the breast, Breast J. 25 (6) (2019) 1171–1176.
[8] J.T. Stranix, M.J. Kwa, R.L. Shapiro, J.L. Speyer, Invasive micropapillary carcinoma of the male breast: case report and review of the literature, Cancer Treat. Commun. 3 (2015) 44–49.

[9] J. Lv, Q. Shi, Y. Han, W. Li, H. Liu, et al., Spatial transcriptomics reveals gene expression characteristics in invasive micropapillary carcinoma of the breast, Cell Death Dis. 12 (12) (2021) 1095.
[10] M. Yalaza, A. İnan, M. Bozer, Male breast cancer, Eur. J. Breast Health 12 (2016) 1–8.
[11] T. Tsushimi, H. Mori, T. Harada, Y. Ikeda, H. Ohnishi, Invasive micropapillary carcinoma of the breast in a male patient: report of a case, Int. J. Surg. Case Rep. 4 (11) (2013) 988–991.
[12] J. Kulka, L. Madaras, G. Floris, S.F. Lax, Papillary lesions of the breast, Virchows Arch. 480 (1) (2022) 65–84.
[13] G. Pettinato, C.J. Manivel, L. Panico, L. Sparano, G. Petrella, Invasive micropapillary carcinoma of the breast: clinicopathologic study of 62 cases of a poorly recognized variant with highly aggressive behavior, Am. J. Clin. Pathol. 121 (2004) 857–866.
[14] F. Liu, R. Lang, J. Wei, Y. Fan, L. Cui, et al., Increased expression of SDF-1/CXCR4 is associated with lymph node metastasis of invasive micropapillary carcinoma of the breast, Histopathology 54 (6) (2009) 741–750.
[15] Q. Shi, K. Shao, H. Jia, B. Cao, W. Li, et al., Genomic alterations and evolution of cell clusters in metastatic invasive micropapillary carcinoma of the breast, Nat. Commun. 13 (1) (2022) 111.
[16] Ishita Pant, S.C. Joshi, Invasive papillary carcinoma of the male breast: report of a rare case and review of the literature, J. Cancer Res. Ther. 5 (3) (2009) 216–218.
[17] J. Shuja, I. Ahmad, S. Arshad, H. Manzoor, S. Kakar, et al., A case report of triple-positive micropapillary carcinoma of the male breast, Breast Care (Basel) 13 (3) (2018) 192–194.
[18] Cristian Scatena, Rosa Scarpitta, Lorenzo Innocenti, Mario Miccoli, Rachele Biancotti, Androgen receptor expression inversely correlates with histological grade and N stage in ER +/PgR low male breast cancer, Breast Cancer Res. Treat. 182 (1) (2020) 55–65.
[19] R.B. Everson, M.E. Lippman, E.B. Thompson, W.L. McGuire, J.L. Wittliff, et al., Clinical correlations of steroid receptors and male breast cancer, Cancer Res. 40 (1980) 991–997.
[20] R. Kornegoor, A.H. Verschuur-Maes, H. Buerger, M.C. Hogenes, P.C. de Bruin, et al., Molecular subtyping of male breast cancer by immunohistochemistry, Mod. Pathol. 25 (3) (2012) 398–404.