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Successful treatment of accessory breast cancer with endocrine therapy[#]

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Accessory breast cancers in males are extremely rare, and only a few cases have been reported in the literature. In this paper, an 87-year-old male patient was diagnosed with an accessory breast cancer by means of computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography-computed tomography (PET-CT), and immunohistochemistry based on needle biopsy, and has undergone successful resection and postoperative adjuvant endocrine therapy. He was the oldest male patient with an accessory breast cancer reported in the Chinese Hospital Knowledge Database and PubMed literature from 1975 to 2015.

Accessory breasts develop from normal undegraded breasts at an occurrence rate of 2%–6% (Gutermuth *et al.*, 2006). Cancer of accessory breasts is a rare form of breast cancer that usually occurs at an incidence rate of 0.2%–0.6%, usually in the axilla or inguinal region (Bi *et al.*, 2015). Because accessory breast cancer in men, especially the elderly, is extremely rare, missed and erroneous diagnoses often occur, which result in higher instances of metastasis


at an early stage and poor prognosis. Even though the principles of diagnosis and postoperative treatments are the same as those for normal breast cancer, it was discovered that the prognosis was different in female and male patients over 70 years of age.

An 87-year-old man was hospitalized, complaining of a right axillary mass that had developed 4 years earlier. The mass has the approximate size of a bean, and was initially granular and then had gradually grown and adhered to the skin. The mass was first diagnosed as a sebaceous cyst, and surgical excision of the tumor was recommended. The mass was examined by CT every six months for nearly two years, and it was found to continuously increase in size. Ultrasound examination showed that the size of the mass ranged from 1.5 cm×1.0 cm×0.8 cm to 2.3 cm×1.7 cm×1.1 cm with a clear boundary and less intact structure. Upon admission, the patient's general physical state was good; the right axillary mass was about 2 cm in diameter with a hard texture, less clear boundary, and mild skin adhesion, and without activity or tenderness (Fig. S1). MRI examination of the breast showed a subcutaneous, nearly round signal on the right side of the axillary, measuring about 1.2 cm×2.0 cm×1.7 cm with a clear boundary (Fig. S2). Ultrasound and MRI examinations revealed no obvious abnormalities in the bilateral mammary gland. PET-CT showed a right axillary high metabolic nodule with abnormal radioactive concentration (the maximum standardized uptake value (SUV_{max})=5.2), which confirmed the malignant signs. The largest cross-sectional area of the nodule was about 2.1 cm×1.2 cm, and there was no obvious abnormally high metabolic lesion in the contralateral breast region (Fig. 1). Ultrasound-guided needle biopsy showed fibrous stroma fixed with heteromorphic glands and mucus in the stroma. The possibility of invasive breast cancer was high, as indicated by the following immunohistochemistry results: estrogen receptor (ER, +, >75%),

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progesterone receptor (PR, +, >75%), human epidermal growth factor receptor-2 (HER-2, ++), p120 (film, +), keratin 7 (CK7, +), CK20 (-), villin (-), carcino-embryonic antigen (CEA, -), thyroid transcription factor (TTF, -), and Napsin A (-) (Fig. 2). The diagnosis of right-side accessory breast cancer was ultimately confirmed. The patient had a history of hypertension

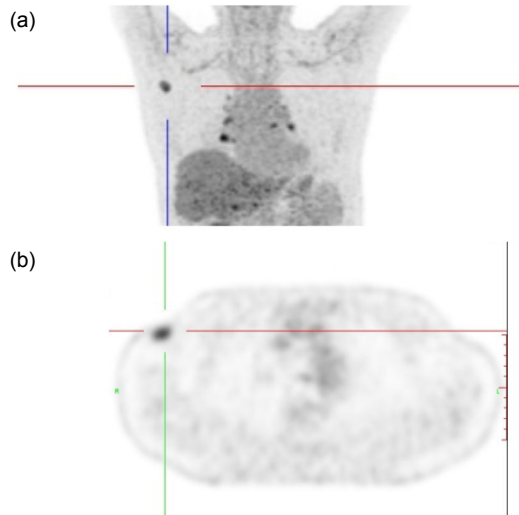


Fig. 1 Positron emission tomography-computed tomography (PET-CT) findings

A right axillary high metabolic nodule with abnormal radioactive concentration and the largest cross-sectional area of the nodule was about 2.1 cm×1.2 cm in coronal section (a) and cross section (b)

and diabetes for more than 10 years, of senile tremor and obsolete cerebral infarction for 4 years, and of kidney stones and benign prostatic hyperplasia for several years. Bilateral neck and breast regions revealed no other masses. Considering the patient's good general condition, surgery was recommended. Right accessory breast cancer radical surgery, i.e., dissection of accessory breast and surrounding tissues and axillary lymph node, was performed with the consent of the patient and his relatives (Fig. S3). During the operation, a fusiform incision measuring 6 cm in length and 3.4 cm in width was made along the edge of the tumor under the right axillary (Fig. S1). The tumor, axillary fat, and lymph nodes were resected together, and a negative pressure drainage tube was placed. The postoperative pathological diagnosis was right axillary mucinous adenocarcinoma and partial papillary, with a tumor measuring 2.0 cm×1.5 cm×1.2 cm. Cancer tissues did not involve the skin and tissues along cutting edges of the long and short axes, and metastasis carcinoma was not found in the right axillary lymph nodes (0/3). A small amount of accessory breast tissue was seen around the tumor tissue. Immunohistochemistry showed the following: ER (+, >75%), PR (+, >75%), p120 (film, +), HER-2 (+), CK20 (weak, +), CK7 (+), synaptophysin (SYN, focal, +), epithelial membrane antigen (EMA, outer

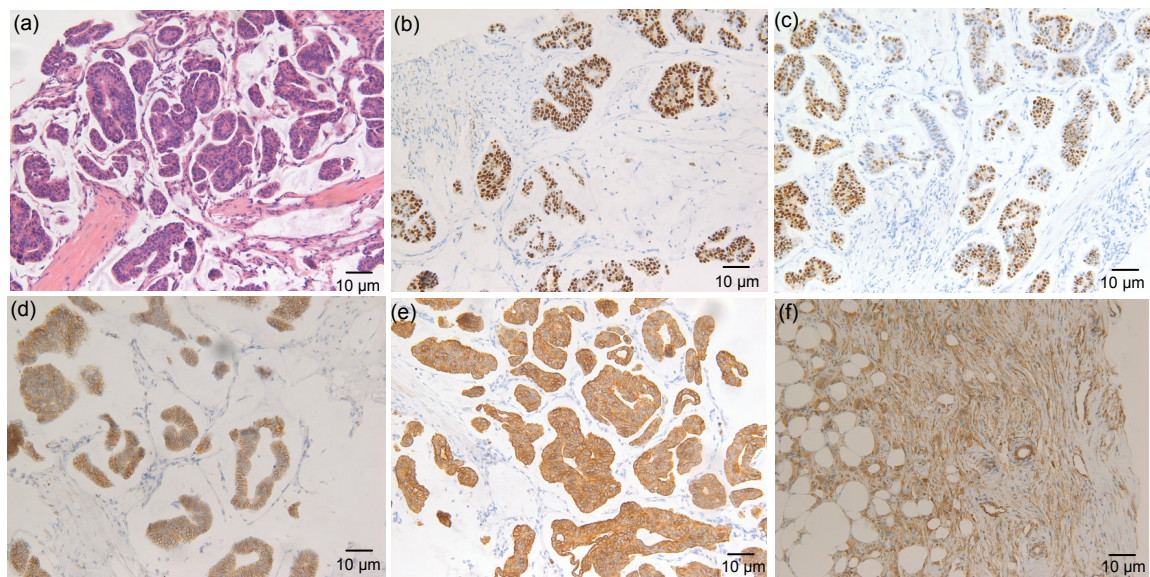


Fig. 2 Pathological images before operation

(a) H&E staining, ×20. (b-f) Immunohistochemical staining results, ×20: (b) ER (+, >75%); (c) PR (+, >75%); (d) HER-2 (++); (e) CK7 (+); (f) p120 (film, +). H&E: hematoxylin and eosin; ER: estrogen receptor; PR: progesterone receptor; HER-2: human epidermal growth factor receptor-2; CK7: keratin 7

rim, +), proliferating cell nuclear antigen Ki-67 (+, <25%), Napsin A (-), E-cadherin (E-cad, -), transcription intermediary factor-1 (TIF-1, -), chromogranin A (cgA, -), and HER-1 (-) (Fig. 3). No distant metastasis was seen in this patient; this was considered to be due to the fact that only three lymph nodes were removed from this thin, elderly male patient, which were fewer than those from a healthy young woman with accessory breast cancer or breast cancer radical surgery. The pathological stage was T1cN0M0, which belongs to Stage I accessory breast cancer. Postoperative endocrine therapy was administered at the standard dose of oral tamoxifen citrate tablets at

20 mg/d without adjuvant therapies such as chemotherapy or radiotherapy. The patient was followed up for two years without recurrence, or lung or liver metastasis.

In the present case, a rare case of accessory breast cancer in an 87-year-old male patient was studied. The patient had a high risk for recurrence and metastasis, as was indicated by the tumor diameter of 2.0 cm and HER-2 (+), which suggested chemotherapy as adjuvant therapy (Hao *et al.*, 2012); however, the patient was elderly, and considering chemotherapy-related toxicity, adjuvant chemotherapy was not considered suitable for him. Postoperative adjuvant

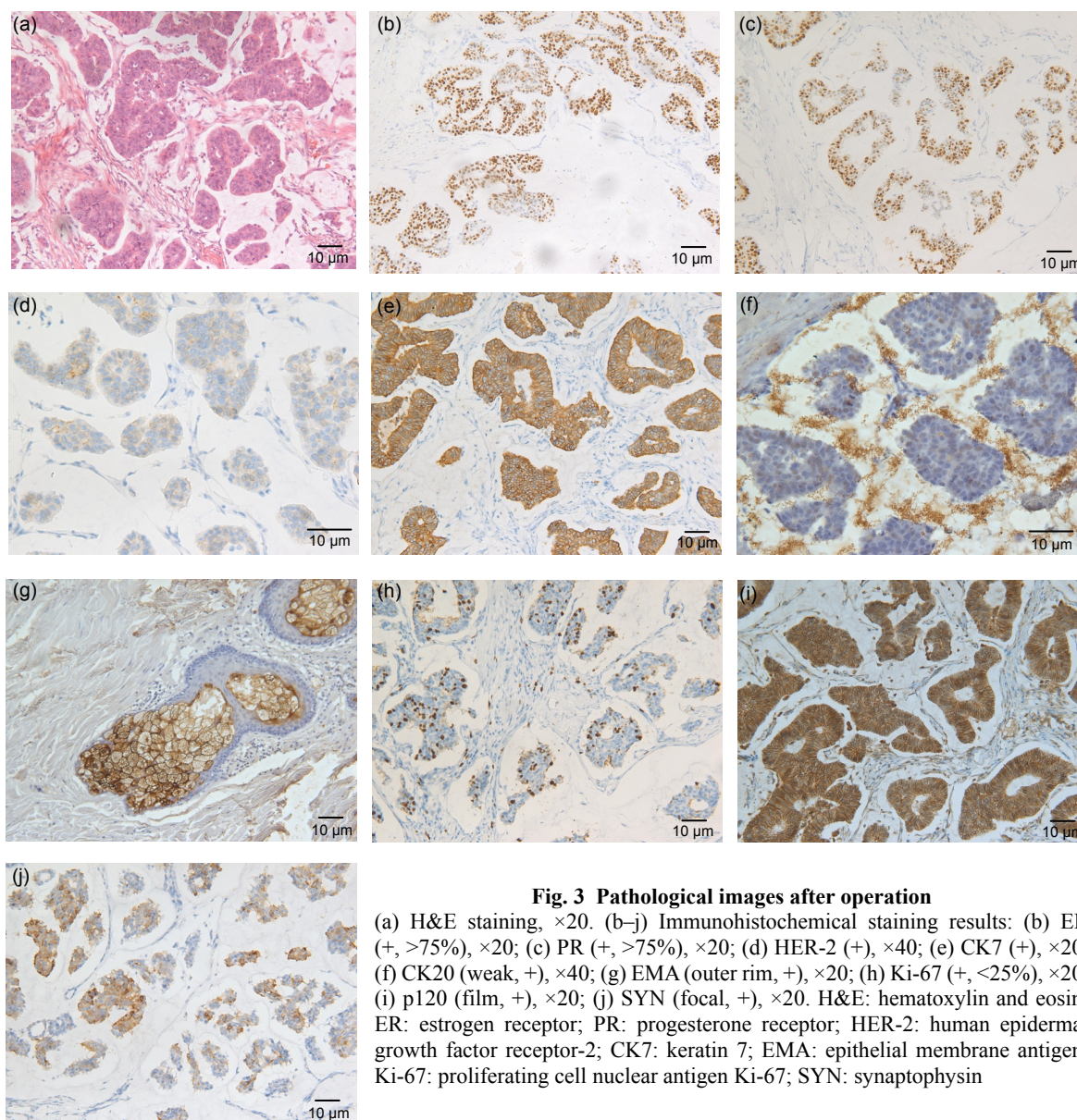


Fig. 3 Pathological images after operation

(a) H&E staining, ×20. (b-j) Immunohistochemical staining results: (b) ER (+, >75%), ×20; (c) PR (+, >75%), ×20; (d) HER-2 (+), ×40; (e) CK7 (+), ×20; (f) CK20 (weak, +), ×40; (g) EMA (outer rim, +), ×20; (h) Ki-67 (+, <25%), ×20; (i) p120 (film, +), ×20; (j) SYN (focal, +), ×20. H&E: hematoxylin and eosin; ER: estrogen receptor; PR: progesterone receptor; HER-2: human epidermal growth factor receptor-2; CK7: keratin 7; EMA: epithelial membrane antigen; Ki-67: proliferating cell nuclear antigen Ki-67; SYN: synaptophysin

endocrine therapy was necessary because of the increased estrogen level in vivo as the main indicator of the proliferation of breast cancer cells. Therefore, tamoxifen was chosen for adjuvant endocrine therapy for two years and the patient was followed up termly.

Care should be taken because sweat gland ductal carcinoma in the axillary is easily misdiagnosed as metastatic breast cancer. Still, the transitional area from a normal sweat gland duct can be seen in the pathological changes of sweat gland ductal carcinoma, whereas ductal carcinoma of the breast gland derives from the breast duct or the inside of the mammary gland. The differential diagnosis between ductal carcinomas of sweat and breast glands can normally be made by pathological examination. A mass that is easily misdiagnosed as tumor lymph nodes by MRI can be confirmed as accessory breast cancer by PET-CT and immunohistochemistry results, which indicates that PET-CT is a helpful supplementary diagnostic method for accessory breast cancer diagnosis in male patients along with the traditional immunohistochemistry examination. In conclusion, this study can serve as a useful reference for clinical manifestations, diagnosis, treatment, and prognosis of accessory breast cancer in very elderly males.

A brief literature review of male accessory breast cancer

In the Chinese Hospital Knowledge Database from 1975 to 2015, there were two separate case reports of male accessory breast cancer (Gou, 1987; Liu and Wang, 2014), and 20 cases altogether with female patients in the retrospective analyses. Seven case reports in the PubMed literature were in English, of which one case was American (Camisa, 1980), three cases were Chinese (Lin and Wang, 2012; Gao *et al.*, 2014; Bi *et al.*, 2015), and three cases were Japanese (Takeyama *et al.*, 2010; Yamamura *et al.*, 2012; Yoshida *et al.*, 2012).

Camisa (1980) reported on an elderly man with accessory breast tissue occurring on the posterior portion of his left thigh. Takeyama *et al.* (2010) confirmed the diagnosis of accessory breast cancer of a 58-year-old Japanese male patient with the following procedures. First, cancer was confirmed to derive from accessory breast tissue irrespective of breast

cancer by contrast-enhanced CT scan. Second, histological examination by incisional biopsy revealed the possibility of malignancy, and there existed a glandular lobule structure or intraductal component. Third, detailed examination of the head and neck regions, lungs, and upper and lower gastrointestinal systems revealed no evidence of a primary tumor focus. Fourth, postoperative hematoxylin and eosin (H&E) staining and immunohistochemical staining demonstrated the positivity of ER, PR, and metastasis in the lymph node, but excluded sweat gland or sebaceous gland carcinoma. In another case, Liu and Wang (2014) used PET-CT to confirm that a 66-year-old male patient had no malignant tumors in any other areas of the body except an accessory breast.

The treatment of male accessory breast cancer is primarily based on surgery, and radical resection is recommended (Jiang, 2015). Lin and Wang (2012) reported a 65-year-old male with accessory breast cancer who underwent radical mastectomy, which included right breast, right pectoralis major muscle, right pectoralis minor muscle, and right axillary I, II, and III lymph node dissection. Liu and Wang (2014) reported a male patient who underwent right side breast cancer radical mastectomy under general anesthesia, much the same as reported by Lin and Wang (2012).

Compared to normal breast cancer, the indication of neoadjuvant chemotherapy is more applicable in accessory breast cancer. Before 1990, the CMU program (colchicine, methotrexate, and uramustine) was widely used; since 1990, CEF (cyclophosphamide, doxorubicin/epirubicin, and fluorouracil), CMF (cyclophosphamide, methotrexate, and fluorouracil), or TE (taxane and anthracyclines) has been used. Anthracyclines, such as doxorubicin or epirubicin, decrease the annual cancer recurrence risk by 2% and death risk by 11%, and further decrease the absolute benefit by 3.2% and 2.7%, respectively (Litière *et al.*, 2012; Burger *et al.*, 2013). Taxanes, such as paclitaxel and docetaxel, are suitable for patients with positive lymph nodes. Yamamura *et al.* (2012) reported that a 61-year-old male with mammary carcinoma originating in an accessory mammary gland in the axilla was subjected to four courses of CEF chemotherapy (cyclophosphamide at 500 mg/m², epirubicin at 100 mg/m², and 5-fluorouracil at 500 mg/m²) every three weeks. The tumor shrunk from 85 to 55 mm in

diameter, which was confirmed by CT. Wide radical excision was then performed with the preservation of the axillary vein and brachial plexus.

Male breast cancer is a hormone-dependent tumor with the expressions of ER, PR, and HER-2; the positive rates of ER and PR are about 80%–90%, which are higher than that in females (75%) (Giordano *et al.*, 2004; Zhang and Liu, 2008). Ribeiro and Swindell (1992) reported that out of a total of 39 cases of male breast cancer patients receiving tamoxifen treatment, the 5-year disease-free survival rate increased from the previously seen 28% to 56%, and the 5-year overall survival rate improved from 44% to 61%. Giordano *et al.* (2004) reiterated that endocrine therapy was the gold standard for the treatment of male breast cancer. Because 80% of estrogen in a male is converted from androgen catalyzed by aromatase and the remaining 20% is secreted directly in the testes, aromatase inhibitors mostly inhibit the conversion of androgen to estrogen. A patient who is ER- and PR-positive is more sensitive to endocrine therapy. In this paper, the 87-year-old male received tamoxifen citrate tablet treatment, and there was no cancer occurrence or metastasis for 2 years.

Accessory breast carcinoma in males generally presents a poorer prognosis than that in females because the diagnosis tends to be delayed. Bi *et al.* (2015) reported a 56-year-old Chinese male diagnosed with right accessory breast carcinoma (PT1N1M0) who underwent four surgical excisions of a primary ectopic breast carcinoma and developed local lymph node and opposite supraclavicular lymph node metastasis. Ultimately, the patient developed pulmonary and bone metastasis. Yoshida *et al.* (2012) reported on a 73-year-old Japanese man who had multiple bone metastases already present when the diagnosis of accessory breast cancer was established. The patient was then treated with trastuzumab; however, lymph nodes and brain metastases developed, and the patient died 6 months after surgery.

In conclusion, clinical manifestation, imaging examination, biopsy, and postoperative pathological examination are necessary for the diagnosis of accessory breast cancer, even for elderly male patients. Early treatment is important because of high malignancy and easy metastasis in the axilla or groin where many lymph nodes may be present. The treatment of such cancer adheres to the comprehensive treatment

principle of surgery, radiotherapy, chemotherapy, endocrine therapy, and biological target treatment. It is seen that accessory breast cancer in elderly male patients is slow-growing, late-metastasis, and hormone-dependent; therefore, it is suggested that the main comprehensive treatment methods should be local cancer resection, lymphadenectomy, endocrine therapy, and the treatment of comorbid diseases to prolong life and improve the quality of life. Radiotherapy and chemotherapy are dependent on the patient's physical condition.

Compliance with ethics guidelines

Chun-xi WANG, Shu-li GUO, and Li-na HAN declare that they have no conflict of interest.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from the patient for being included in the study.

References

- Bi, L., Li, J., Shi, Z., *et al.*, 2015. Male accessory breast cancer successfully treated with endocrine therapy: a case report. *Oncol. Lett.*, **10**(4):2495-2498. <http://dx.doi.org/10.3892/ol.2015.3602>
- Burger, A.E., Pain, S.J., Peley, G., 2013. Treatment of recurrent breast cancer following breast conserving surgery. *Breast J.*, **19**(3):310-318. <http://dx.doi.org/10.1111/tbj.12105>
- Camisa, C., 1980. Accessory breast on the posterior thigh of a man. *J. Am. Acad. Dermatol.*, **3**(5):467-469. [http://dx.doi.org/10.1016/S0190-9622\(80\)80110-1](http://dx.doi.org/10.1016/S0190-9622(80)80110-1)
- Gao, Y.G., Zhang, S.H., Wang, Y., 2014. A case of accessory mammary cancer in a male patient and a literature review. *Eur. J. Gynaecol. Oncol.*, **35**(4):452-455.
- Giordano, S.H., Cohen, D.S., Buzdar, A.U., *et al.*, 2004. Breast carcinoma in men: a population-based study. *Cancer*, **101**(1):51-57. <http://dx.doi.org/10.1002/cncr.20312>
- Gou, Z.Y., 1987. Male accessory breast cancer: a case report. *Chongqing Med.*, **16**(2):63 (in Chinese).
- Gutermuth, J., Audring, H., Voit, C., *et al.*, 2006. Primary carcinoma of ectopic axillary breast tissue. *J. Eur. Acad. Dermatol. Venereol.*, **20**(2):217-221. <http://dx.doi.org/10.1111/j.1468-3083.2005.01362.x>
- Hao, J.Y., Yang, C.C., Liu, F.F., *et al.*, 2012. Accessory breast cancer occurring concurrently with bilateral primary invasive breast carcinomas: a report of two cases and literature review. *Cancer Biol. Med.*, **9**(3):197-201. <http://dx.doi.org/10.7497/j.issn.2095-3941.2012.03.008>
- Jiang, X., 2015. Macrophage-produced IL-10 limits the

- chemotherapy efficacy in breast cancer. *J. Zhejiang Univ.-Sci. B (Biomed. & Biotechnol.)*, **16**(1):44-45.
<http://dx.doi.org/10.1631/jzus.B1400352>
- Lin, Y., Wang, Y., 2012. Case report of a male primary breast carcinoma of axillary accessory mammary gland. *Clin. Breast Cancer*, **12**(2):142-144.
<http://dx.doi.org/10.1016/j.clbc.2011.09.004>
- Litière, S., Werutsky, G., Fentiman, I.S., et al., 2012. Breast conserving therapy versus mastectomy for stage I-II breast cancer: 20 year follow-up of the EORTC 10801 phase 3 randomised trial. *Lancet Oncol.*, **13**(4):412-419.
[http://dx.doi.org/10.1016/S1470-2045\(12\)70042-6](http://dx.doi.org/10.1016/S1470-2045(12)70042-6)
- Liu, H.Y., Wang, Y., 2014. Clinical pathological characteristics of male accessory breast cancer: analysis of 1 cases and literature review. *Chin. J. Clin. Res.*, **27**(1):83-84 (in Chinese).
- Ribeiro, G., Swindell, R., 1992. Adjuvant Tamoxifen for male breast cancer (MBC). *Br. J. Cancer*, **65**(2):252-254.
<http://dx.doi.org/10.1038/bjc.1992.50>
- Takeyama, H., Takahashi, H., Tabei, I., et al., 2010. Malignant neoplasm in the axilla of a male: suspected primary carcinoma of an accessory mammary gland. *Breast Cancer*, **17**(2):151-154.
<http://dx.doi.org/10.1007/s12282-009-0098-8>
- Yamamura, J., Masuda, N., Kodama, Y., et al., 2012. Male breast cancer originating in an accessory mammary gland in the axilla: a case report. *Case Rep. Med.*, **2012**:286210.
<http://dx.doi.org/10.1155/2012/286210>
- Yoshida, Y., Sakakibara, A., Watanabe, T., et al., 2012. Extraordinarily large protruding accessory breast cancer in a man. *J. Am. Acad. Dermatol.*, **67**(5):e230-e231.
<http://dx.doi.org/10.1016/j.jaad.2012.04.034>
- Zhang, J., Liu, Y., 2008. HER2 over-expression and response to different chemotherapy regimens in breast cancer. *J. Zhejiang Univ.-Sci. B*, **9**(1):5-9.
<http://dx.doi.org/10.1631/jzus.B073003>

List of electronic supplementary materials

- Fig. S1 Delineation of surgical resection before operation
Fig. S2 Magnetic resonance imaging (MRI) findings of the breast
Fig. S3 Cut-down accessory breast cancer

中文概要

题目：副乳腺癌内分泌成功治疗的研究

概要：本文介绍一例 87 岁男性患者，右腋下肿物 4 年，通过电子计算机断层扫描（CT）、磁共振成像（MRI）、正电子发射计算机断层显像（PET-CT）和肿物穿刺活检免疫组化确诊为副乳腺癌。进行肿物手术切除，术后内分泌辅助治疗。男性副乳腺癌的案例少见，只有零星的文献报道。在 1975~2015 年中国医院知识库和 PubMed 文献数据库记录中，本文的患者是年龄最大的男性副乳腺癌患者。

关键词：副乳腺癌；高龄男性；内分泌治疗