A Rare Case of Isolated Adrenal Metastasis of Invasive Ductal Breast Carcinoma

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SUMMARY
Introduction Isolated adrenal metastases of invasive ductal breast carcinoma are extremely rare. We report a case with isolated left adrenal metastases, verified three years after diagnosed breast carcinoma.

Case Outline A 58-year-old female patient with a right breast tumor, clinically staged as IIIA (T2N2M0) started neoadjuvant anthracycline chemotherapy after biopsy which revealed invasive ductal breast carcinoma. Immunohistochemical findings of tumor biopsy showed hormonal steroid receptors for estrogen and progesterone negative, and human epidermal growth factor receptor 2 (HER2) positive. After 4 cycles of chemotherapy and partial tumor regression the patient underwent radical mastectomy. Definite histopathological analysis confirmed the diagnosis of invasive ductal carcinoma. The patient continued treatment with adjuvant chemotherapy to cumulative dose of anthracyclines, postoperative radiotherapy and adjuvant trastuzumab for one year. Three years later abdominal computerized tomography showed tumor in the left adrenal gland as the only metastatic site. Left adrenalectomy was performed and histopathological finding confirmed breast cancer metastases. Postoperatively, the patient received 6 cycles of docetaxel with trastuzumab and continued trastuzumab until disease progression. One year after left adrenalectomy control abdominal computerized tomography showed a right adrenal tumor with retroperitoneal lymphadenopathy. Treatment with capecitabine was continued for one year, but eventually she developed brain metastasis causing lethal outcome.

Conclusion In order to better understand metastatic pathways of invasive ductal breast carcinoma, publications of individual patient cases diagnosed with rare metastatic sites should be encouraged. This might improve our understanding of metastatic behavior of breast cancer and stimulate further clinical research.

Keywords: adrenalectomy; breast cancer; invasive ductal carcinoma; metastasis

INTRODUCTION

Isolated adrenal metastases originating from invasive ductal carcinoma (IDC) of the breast are extremely rare. On the other side, metastases in adrenal glands are very frequent autopsy findings and in most cases they originate from lung, renal and gastrointestinal cancers [1, 2].

The most frequent type of invasive breast carcinoma is IDC with frequency of 70 to 85% of all breast cancer patients [3, 4]. Clinical and pathological findings confirm that IDC is mostly associated with lung, liver, bone and brain metastases and rarely affects adrenal glands, while invasive lobular carcinoma (ILC) has a high potential of spreading into the gastrointestinal system, gynecological organs, peritoneal and retroperitoneal structures [5, 6]. Generally, adrenal gland metastases coming from breast cancer are characteristic of ILC and they are frequently associated with multiple endocrine organs metastases [7]. Adrenal metastases, especially isolated metastases, coming from IDC are less often. So far, only one case of isolated adrenal metastasis from IDC with immunohistochemical (IHC) profile, estrogen receptor (ER) negative, progesterone receptor (PR) negative and human epidermal growth factor receptor 2 (HER2) positive is described and published in literature by Liu et al. [8] in 2010.

It has been shown that adrenal gland metastases are the indicator of an advanced disease and are usually accompanied multiple organ metastases involvement [6]. Adrenal metastases in the majority of cases are asymptomatic and could be detected predominately on autopsy [2]. Nowadays, due to more sophisticated imaging procedures used in a routine follow-up, they are discovered more often. Available studies with other solid tumors with isolated adrenal metastases have shown that adrenalectomy has significant influence on prolonged survival [1, 2, 7, 9]. Due to its rare occurrence, the recommendations for optimal treatment of adrenal metastases originating from breast carcinoma are still missing.

CASE REPORT

We present a clinical case of a 58-year-old female patient with a lump in her right breast. There was no family history of breast or ovarian cancer in primary relatives. Clinical examination revealed a right breast mass, clinically
staged as IIIA (T2N2M0) according to the UICC TNM classification. Mammography demonstrated a 50×40 mm mass with associated microcalcifications. Excisional biopsy confirmed infiltrative ductal carcinoma, Nottingham histological grade (HG) 2 and nuclear grade (NG) 2. IHC findings revealed a tumor with ER negative, PR negative, HER2 positive 3+ (the percentage of cells with complete intense membrane staining was 100) receptor staining. The patient was started on treatment at the Institute for Oncology and Radiology of Serbia in July 2007 with neo-adjuvant FAC chemotherapy (5-fluorouracil 500 mg/m² day 1, doxorubicin 50 mg/m² day 1, cyclophosphamide 500 mg/m² day 1, every three weeks). After four cycles of chemotherapy, a partial response, i.e. 50% of reduction in size for both breast tumor and axillary lymph nodes was detected and radical mastectomy was performed in October 2007.

Definite histopathology (HP) analysis of tumor after radical mastectomy confirmed IDC, HG2, NG2, with maximal tumor diameter of 25 mm, and one positive axillary lymph node out of 16 examined. She was post-menopausal for the period of three years. As she had no other comorbidities and her performance status was 0, we continued treatment with 4 cycles of adjuvant FAC chemotherapy, postoperative radiotherapy of the right chest wall (42.5 Gy in 16 fractions) and adjuvant trastuzumab (first dose 8 mg/kg, followed by 6 mg/kg every three weeks) for the period of one year after which she went on regular checkups.

Three years after diagnosed primary breast cancer at her regular check-ups, abdominal ultrasound showed enlarged left adrenal gland, in diameter of 49×48 mm. Tumor marker CA 15-3 was elevated up to 205.7 (normal range 0.0–25.0 U/ml). Abdominal computerized tomography (CT) confirmed the enlarged left adrenal gland with the tumor mass of 48×47.6 mm in diameter. Additional diagnostic work-up, CT scan of the chest and bone, have confirmed that metastasis in the left adrenal gland was the only pathological finding. Laboratory tests and hormonal status examination excluded the primary disease of adrenal gland. The basal cortisol was within the normal range and dexamethason (1 mg) suppression was normal. Also, the level of catecholamines was normal. Electrolyte balance was within the range of normal values. The patient was asymptomatic and fully active with performance status of 0. She was obese and no other comorbidities were detected. Since abnormality of the left adrenal gland was highly suspected to be metastatic lesion, the left adrenalectomy was performed in October 2010.

HP analysis confirmed metastasis of breast cancer in the left adrenal gland tissue (Figure 1). IHC phenotype was CK7 +/-, CK 20 -, vimentin -, estrogen +, gross cystic disease fluid protein -15 (GCDFP-15) +/-, with ER score 6 (+4+2), 40% of tumor cells had middle staining intensity of nucleus (Figure 2). PR score 3 (2+1), 5% of tumor cells had poor staining intensity and HER2 was 2+, 20% of tumor cells show complete membrane staining with middle intensity (Figure 3). Chromogenic in situ hybridization (CISH) analysis of HER2 gene amplification was positive. Marker of cell proliferation Ki-67 was high (50% of cells show immunoreactivity).

She started treatment with docetaxel plus trastuzumab and after 6 cycles of docetaxel she continued therapy with trastuzumab alone with no evidence of disease. One year after left adrenalectomy was performed, abdominal CT scan showed enlargement of the right adrenal gland.
Adrenal gland metastases in most cases originate from lung cancer (35.4%), followed by gastric cancer (14.3%) and esophageal cancer (12.1%), while only in 2.9% of cases they originate from breast cancer, none of them with IDC histology. In a recent study of 3,726 patients and with intention to present the entire receptor status in tumor samples obtained after radical mastectomy, we found that the receptor status remained consistent between primary and metastatic sites. However, HER2 status stayed positive both in primary cancer (HER2 3+) and in the adrenal metastases (CISH positive). Several studies have reported discordance in up to 40% for hormone receptors and up to 20% for HER2 status between primary tumor and metastases [13, 14, 15]. It is unclear if these changes in receptor expression are a true biological phenomenon or may result from technical variables. Recent analysis using next generation sequencing technologies by Gerlinger et al. [16] performed on multiple samples obtained from primary renal cell carcinomas and associated metastatic sites showed that no two samples were genetically identical. They reported that about two-thirds of the mutations present in a single biopsy were not present in biopsies taken from across the same tumor. This and other data raise the possibility that presentation of a tumor molecular profile obtained from a single biopsy sample may not be adequate for appropriate tumor treatment.

We would like to emphasize that our patient was treated according to the standard clinical protocol for the treatment of locally advanced breast cancer in 2007. The reason why IHC analysis of steroid receptors and HER2 status in tumor samples obtained after radical mastectomy was not done at that time was due to the limited resources and Institute's recommendation that receptor status should be obtained either from the initial biopsy or after definitive surgery. However, for the purpose of this manuscript and with intention to present the entire receptor status profile over time we performed IHC analysis of steroid receptors and HER2 of the primary tumor after radical mastectomy and found the following receptor status: ER positive score 7 (4+3), 40% of the cells showed strong membrane staining; PR positive score 6 (3+3), 25% of the cells showed strong membrane staining; HER2 2+, 20% of the cells showed moderate membrane staining, CISH positive; Ki-67 was 5%. Current treatment options and the availability of IHC analysis from the primary tumor after mastectomy would likely have an impact on the course and outcome of our patient's disease. However, the aim of this manuscript was to present this extremely rare metastatic site of IDC.
ectomy increases survival in patients having disease-free interval (DFI – from the moment of diagnosed primary cancer until the appearance of isolated adrenal metastasis) longer than 6 months [1, 17-20]. The abovementioned patient described by Liu et al. [8] lived three years after adrenalectomy without signs of the breast cancer disease. Understanding the pattern of relapse at a very early stage can help direct clinicians to appropriate and targeted therapies and may contribute to better overall survival by blocking or delaying the onset of metastases.

The isolated adrenal gland metastases from IDC of the breast are extremely rare, almost asymptomatic and so far only one clinical case was described and published. Hereby, we present our clinical case of isolated adrenal metastasis from IDC treated with adrenalectomy and post-operative chemotherapy. Since such cases are very rare, treatment recommendations are not expected in the near future, however publications of individual clinical cases might be valuable in further clinical diagnosis, treatment and research of breast cancer patients.

REFERENCES


Редак случај изоловане метастазе инвазивног дукталног карцинома дојке у надбубрежној жлезди

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КРАТАК САДРЈА

Увод Изоловане метастазе инвазивног дукталног карцинома дојке у надбубрежној жлезди су изузетно ретке. Представљамо случај изоловане метастазе у левој надбубрежној жлезди откривене три године од дијагнозе примарног тумора дојке.

Приказ болесника Жена стара 58 година започела је лечење локално одмаклог карцинома десне дојке, клиничког стадијума IIa (T2N2M0), неодјуантном антрациклинском хемиотерапијом након што је биопсијом потврђено да је реч о инвазивном дукталном карциному дојке. Имунохистохемијска анализа показала је да је реч о тумору с негативним стероидним рецепторима за естроген и прогестерон, док је рецептор хуманог епителног фактора раста 2 (HER2) био позитиван. Након четири циклуса хемиотерапије и парцијалне регресије тумора учинена је радикална мастектомија десне дојке. Конечна патохистолошка анализа потврдила је да је у питању инвазивни дуктални карцином дојке. Лечење је настављено адјуантном хемиотерапијом до кумулативне дозе антрацилина, постоперационом зрачном терапијом и адјуvantним трастузумабом. Након три године од примарне дијагнозе компјутеризоване томографије адоломена откривена је метастаза тумора у левој надбубрежној жлезди као једино место метастазе. Учинена је лево адреналектомија и патохистолошка потврђена метастаза карцинома дојке. Болесница је после операције примила шест циклуса доцетаксела уз трастузумаб, који је настављен до прогресије болне. Годину дана након леве адреналектомије контроверзен скенер адоломена откривао је тумор у десном надбубрежу с ретроперитонеалном лимфаденопатијом. Лечење је настављено капецитанобином у првом годину дана, након чега су откривене метастазе мозга које су узроковале смртни исход.

Закључак Ради случаја болесника једна метастаза у левој надбубрежној жлезди, која је узроцила смртни исход.

Кључне речи: адреналектомија; карцином дојке; инвазивни дуктални карцином; метастаза

Примљен • Received: 28/10/2013
Прихваћен • Accepted: 19/12/2013