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CLINICAL CASE

Metastatic jejunal neuroendocrine tumor to the breast: Case report and literature review

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Abstract

Neuroendocrine tumors (NETs) are the most prevalent neoplasm of the small bowel; these present a diagnostic challenge because of their low prevalence and non-specific clinical manifestations. Breast metastasis is rare. We present the case of a 55-year-old female with a painful nodule in the right breast. Mammography reported a solid mass, BBIRADS 4C, with no axillary lymph nodes. Biopsy reported infiltrating ductal carcinoma. Conservative surgery was performed. Histopathology findings are compatible with a well-differentiated (G2) metastatic NET with a gastrointestinal primary. Ga. DOTANOC positron emission tomography/computed tomography scan showed proximal jejunum diffuse mucosal thickening with two foci of increased radiotracer uptake with adjacent adenopathies.

Keywords: *Neuroendocrine tumors. Metastasis. Breast.*

Tumor metastásico neuroendocrino de yeyuno a mama: reporte de caso y revisión de la literatura

Resumen

Los tumores neuroendocrinos son la neoplasia de intestino delgado más frecuente. Presentan un difícil diagnóstico debido a su baja prevalencia y manifestaciones clínicas no específicas. Las metástasis a mama son raras. Presentamos el caso de una paciente de sexo femenino de 55 años, con presencia de masa dolorosa en mama derecha. La mastografía demostró una lesión sólida, BI-RADS (Breast Imaging-Reporting and Data System) 4C, sin adenopatías axilares. La biopsia reportó carcinoma ductal infiltrante. Se realizó cirugía conservadora de mama. Los hallazgos histopatológicos fueron compatibles con tumor neuroendocrino de origen gastrointestinal. La tomografía por emisión de positrones/tomografía computarizada (PET/CT) con galio DOTANOC reportó aumento de la captación de radio trazador en yeyuno proximal, con adenopatías adyacentes.

Palabras clave: *Tumor neuroendocrino. Metástasis. Mama.*

Introduction

Neuroendocrine tumors (NETs) are epithelial tumors with neuroendocrine differentiation. They are one of the most prevalent types of small-bowel neoplasms[1]. They usually present as a slow-growing tumor, with some features common to all NETs and others specific to the organ of origin. NETs present a diagnostic challenge because of their low prevalence and non-specific clinical manifestations. NETs of ileum and jejunum are usually diagnosed in patients in their fifties or sixties, with an equal incidence among males and females[2]. Most of

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these tumors are non-functioning, but approximately 20% of patients can present with liver metastases and carcinoid syndrome. Lesions are usually < 2 cm, with muscularis propria invasion and metastasis to regional lymph nodes[3]. Clinical manifestations are non-specific; abdominal pain, diarrhea, weight loss, bleeding, or bowel obstruction. Prognosis is poor, with a 5-year survival of 65% for patients with localized disease and 36% for those with distant metastases[4].

Breast metastases presenting clinical manifestation of jejunal NETs are rare, with only a few cases reported in the literature.

Case report

A 55-year-old female with a family history of breast cancer and colon cancer and a medical history of hypertension and gastroesophageal reflux disease presented to our office with a chief complaint of the right breast pain. On physical examination, a 6 mm firm nodule in the right upper quadrant of the right breast was palpable. Axillary adenopathy was not found. A mammography showed asymmetric density and a 0.52 × 0.63 cm solid mass with irregular borders was found in the ten radii, line C of the right breast (BIRADS 4C). Doppler complement did not show vascularity. Axillary lymph nodes were normal. A needle biopsy reported infiltrating ductal carcinoma with no specific pattern with SBR 7 (3+2+1) and light desmoplasia. Lymphovascular involvement was observed, with no perineural involvement. Seric chromogranin was normal (88, normal value 0.92).

Conservative surgery with sentinel node biopsy was performed. Pathology reported an 8 mm tumor in subcutaneous tissue, with no perineural or lymphovascular involvement and negative margins. Immunohistochemistry showed diffuse Chromogranin A, synaptophysin, and CDX2 positivity, with Ki67 reported in 5%. GATA3 GCDFP-15, mamoglobin, and TTF-1 were negative. Morphologic and immunohistological findings are compatible with a well-differentiated (G2) metastatic NET with a gastrointestinal primary. The sentinel node was negative.

Ga.DOTANOC positron emission tomography/computed tomography (PET/CT) scan showed proximal jejunum diffuse mucosal thickening with two foci of increased radiotracer uptake (standardized uptake value [SUV]max 11.9), adjacent 15 mm mesenteric adenopathy with increased uptake (SUVmax 21.2), 7 mm mesorectal lymph node with increased uptake (SUVmax 8.7), 10 mm left inguinal lymph node with increased uptake (SUVmax 15.5), and middle sacral crest focal activity with no visible lesion (SUVmax 11.4).

Discussion

Carcinoid tumors are comprised of slow-growing tissue originating in enterochromaffin cells, which makes them neuroendocrine. They are most frequently found in the respiratory or gastrointestinal tracts. Their most frequent clinical presentation is called carcinoid syndrome: diarrhea, abdominal pain, and flushing. When dealing with gastrointestinal tract tumors, carcinoid syndrome presents when the liver cannot process the polypeptides produced by the tumoral cells (serotonin, substance P)[4].

Breast metastases are uncommon, representing < 1% of malignant breast tumors. Carcinoid metastases in breast tissue are rare, comprising between 0.5% and 1% of metastatic breast neoplasms[5]. The first case was reported in 1957 as an autopsy finding from a patient who had died 30 years before. The patient was found to have a primary small bowel carcinoid tumor with breast and liver metastases[6]. Metastatic breast carcinoids present as single or multiple, firm, well-circumscribed lesions, not unlike breast fibroadenoma, or ductal adenocarcinoma[7]. A 1998 review of 13 case reports found that the most common primary site for carcinoid breast metastases is the small bowel, more specifically the ileum. Other primary sites, including the appendix, duodenum, pancreas, lungs, and ovary, were also reported. Eight of these 13 patients were initially thought to have a primary breast tumor and were treated with mastectomy. The diagnosis of metastatic carcinoid tumor was made after reviewing the slides from the surgical specimen[8]. Misdiagnosis of metastatic breast carcinoid tumors is not uncommon as organoid nests of cells with rosette-like structures that are similar to solid or cribriform ductal carcinoma *in-situ* {Gupta: dw}. Metastatic carcinoid cells in breast tissue can also express estrogen receptor (ER), progesterone receptor (PR) (+) stains, and complicating their diagnosis[9].

Diagnosis using imaging studies is not simple, as primary tumors share many characteristics observed in NET metastases. In mammography, NETs of the breast present as well-circumscribed masses, usually without calcifications. Ultrasonography can present as solid and irregular hypoechoic masses with increased vascularity, although they usually have better defined borders than primary breast tumors. Their size can vary, with one case series reporting masses of 3-18 mm[10]. Magnetic resonance imaging shows primary tumors and NET metastases as small, well-circumscribed, and oval enhancing masses with dynamic kinetics in the

initial phase and rapid washout in the delayed phase[11]. Specialized imaging techniques such as OctreoScan[11] or 18F-DOPA-PET[12] can be used to locate the primary tumor when a NET metastasis is suspected.

Correct pathological diagnosis can also be challenging to achieve. Suspicious clinical history is also paramount to help pathologists correctly identify the tumor as a NET metastasis. In a 2006 review of the literature that included 15 breast metastases from gastrointestinal NETs, nine patients presented with a breast metastasis as the first manifestation of an occult NET. Six had a preliminary diagnosis of breast carcinoma and ended up undergoing surgical procedures treatment[13]. Another study showed that out of 18 patients with breast tumors, 44% were misdiagnosed as primary breast cancers[14].

Treatment of small intestine NETs is surgical as R0 resections can be curative[15]. However, this is frequently not possible due to disease progression. Surgical treatment involves resection of the primary tumor, locoregional mesenteric lymph node dissection, and metastasectomy. For tumors located in the terminal ileum, an oncologic right hemicolectomy should be performed. In patients with advanced disease, tumor resection improved survival even when R0 resection was not feasible[16]. Metatstasic NET treatment is controversial, Boudreaux et al.[17] reported a low mortality and complications rates, with prolonged survival with cytoreductive surgery.

Conclusion

Breast metastases are a diagnostic challenge for physicians. They can mimic breast cancer, and a mistaken diagnosis can subject a patient to unnecessary surgical treatment. They should always be suspected, especially in patients with atypical presentations. Treatment should be surgical and be tailored specifically to each patient's needs.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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