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Case Report

Unusual Presentation of Metastatic Breast Cancer; Dyspeptic Complaints (A Case Report)

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Introduction

It is uncommon for breast cancer to metastasize to the gastrointestinal tract, and the colon and rectum are the most typical locations, followed by the stomach. Gastric metastasis most common primary source is breast cancer. Gastric metastases are usually disregarded in individuals with dyspeptic symptoms because they frequently undergo symptomatic medications or are treated for it as a side effect of cancer treatment. Endoscopic evaluations are important at this stage. The development of linitis plastica, a frequent gastroscopy finding, makes the diagnosis susceptible to error if deep and numerous biopsies are not performed. In this case, a patient without a history of cancer is presented. During test for dyspeptic complaints, the patient's breast cancer metastasis to the stomach was diagnosed

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70 years old patient with no personal or family history, in November 2021, when she visited to the Internal Medicine Department with complaints of nausea and loss of appetite, a suspicious lesion in the corpus was observed in the esophago-gastro-duodenoscopy and biopsy was taken.

Upon detection of acinar and trabecular tumoral infiltration in the biopsy specimen, advanced immunohistochemically staining was performed and the result was reported as invasive lobular carcinoma metastasis of the breast. Then in the breast Ultrasonography (USG) a possible malignant lesion with lobulated contours in the upper middle part of the left breast and multiple, conglomerated pathological lymph nodes in the left axilla and left subclavian region were detected. In addition to these findings, breast MR imaging revealed band-like satellite tumoral lesions in the upper and lower outer quadrants of the left breast.

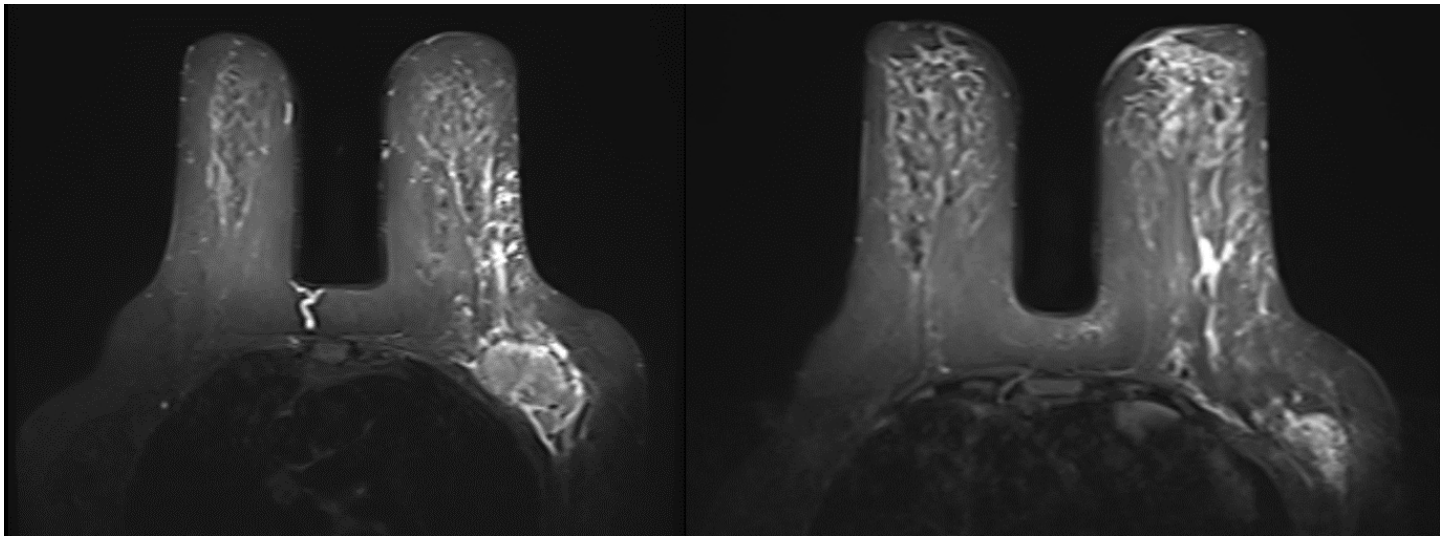

Figure 1: Breast MRI.

Invasive lobular carcinoma was found after the true-cut biopsy of the patient's left upper middle breast. (ER: +, PR:-, HER-2:-, Ki-67:13%).

PET/CT scan was performed for systemic staging and pathological uptakes in the area corresponding to the lesion identified in breast MRI; metastatic conglomerated lymph nodes filling the left axilla and extending into subpectoral space; a metastatic increase in gastric corpus wall thickness; metastatic lymph nodes in the left internal iliac, bilateral common iliac and paraaortocaval areas; 2 cm metastatic involvement on the right of the cerebellum; multiple lytic metastasis in the skeletal system has been reported.

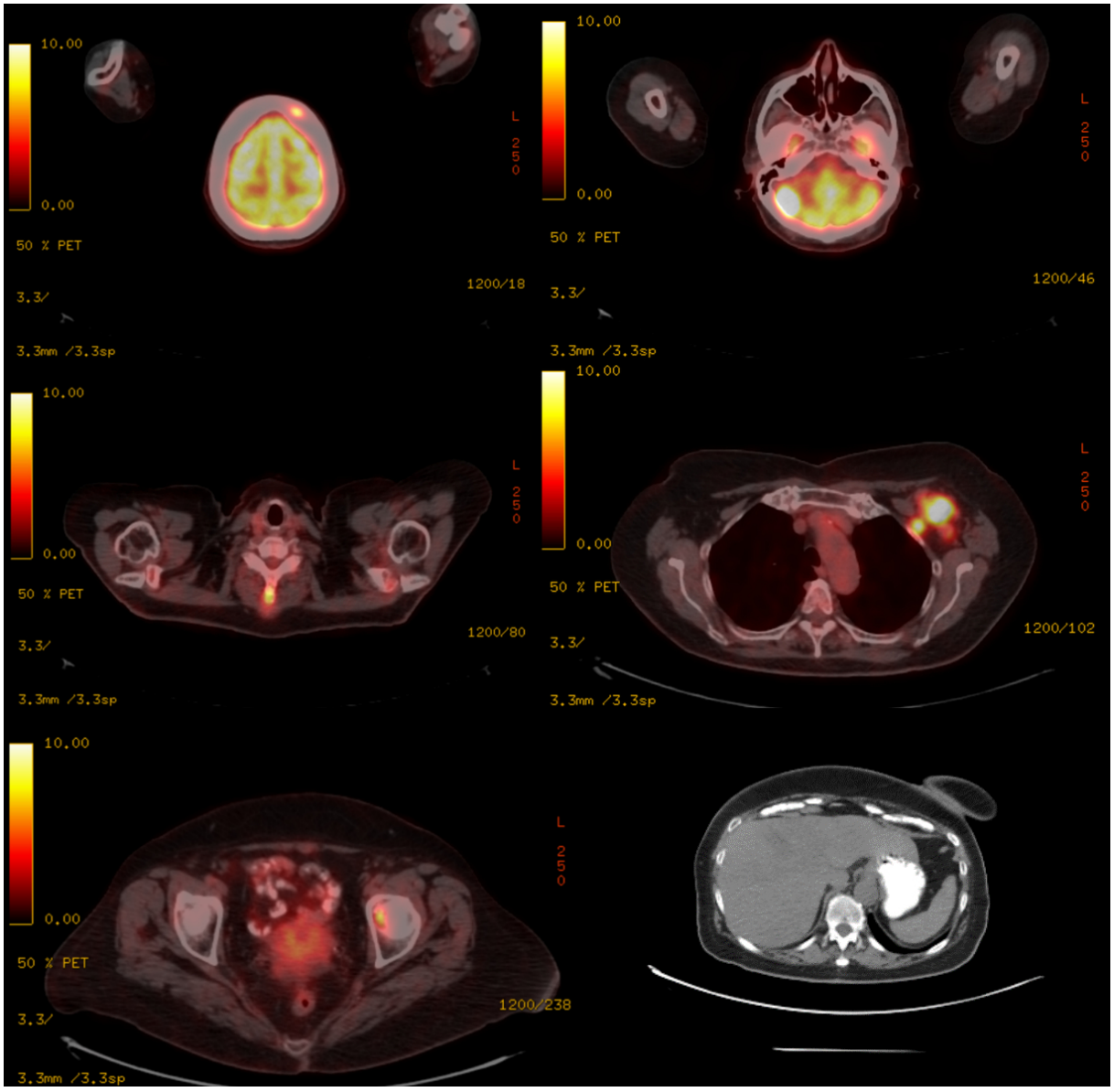

Figure 2: PET/CT.

Cranial MRI was requested after PET/CT interpretation and osseous lesions with contrast enhancement of 18 mm lesion in the left frontal bone at the level of convexity and 9 mm lesion in the parafalcin area at the level of the left parietooccipital bone; milimetric punctate enhancement area next to the lesion at the level of the left parietooccipital bone and in the right suboccipital bone; 6 mm enhancing nodular lesion in the right putamen; enhanced nodular lesion with 2 cm peripheral vasogenic edema area in the lateral part of right cerebellar hemisphere; in the supraventricular area, a linear 4.5 mm enhancement in the sulcal space in the right frontal area and juxtacortical millimetric contrast enhancement in the inferior of this area; an increase in the pituitary gland height and infundibulum thickness and heterogeneous contrast enhancement was observed, significant enhancements were observed in the posterior wall of the sphenoid sinus in the dorsum sella and clivus in terms of metastasis.

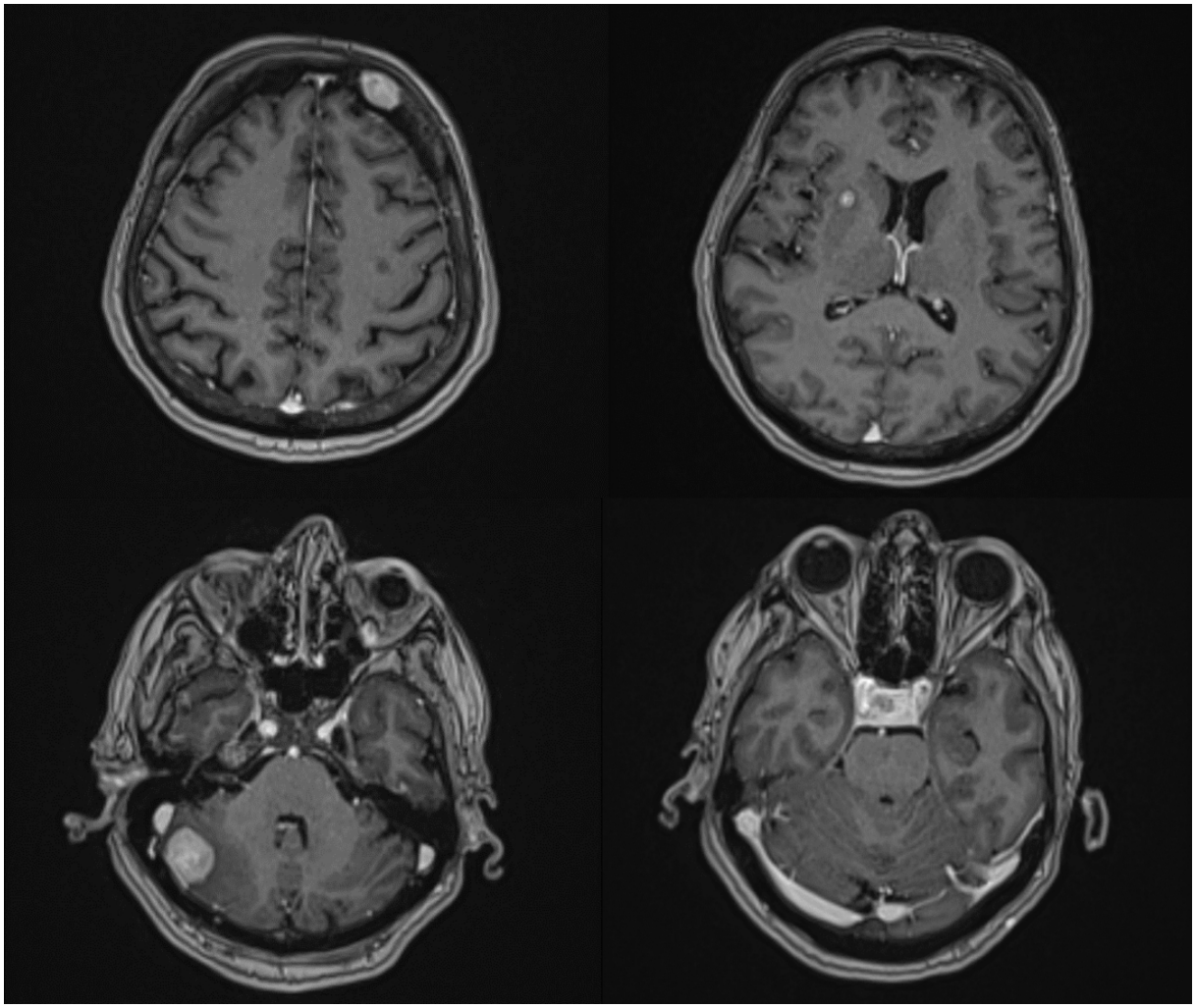

Figure 3: Cranial MRI.

The patient was referred to us for palliative radiotherapy after beginning Palbociclib and Letrozole, and we provided 24 Gy/3fr stereotactic radiation treatment to the right cerebellum and frontal region. Following that, the patient was referred for chemotherapy and hormone treatment and called back after two months for response assessment.

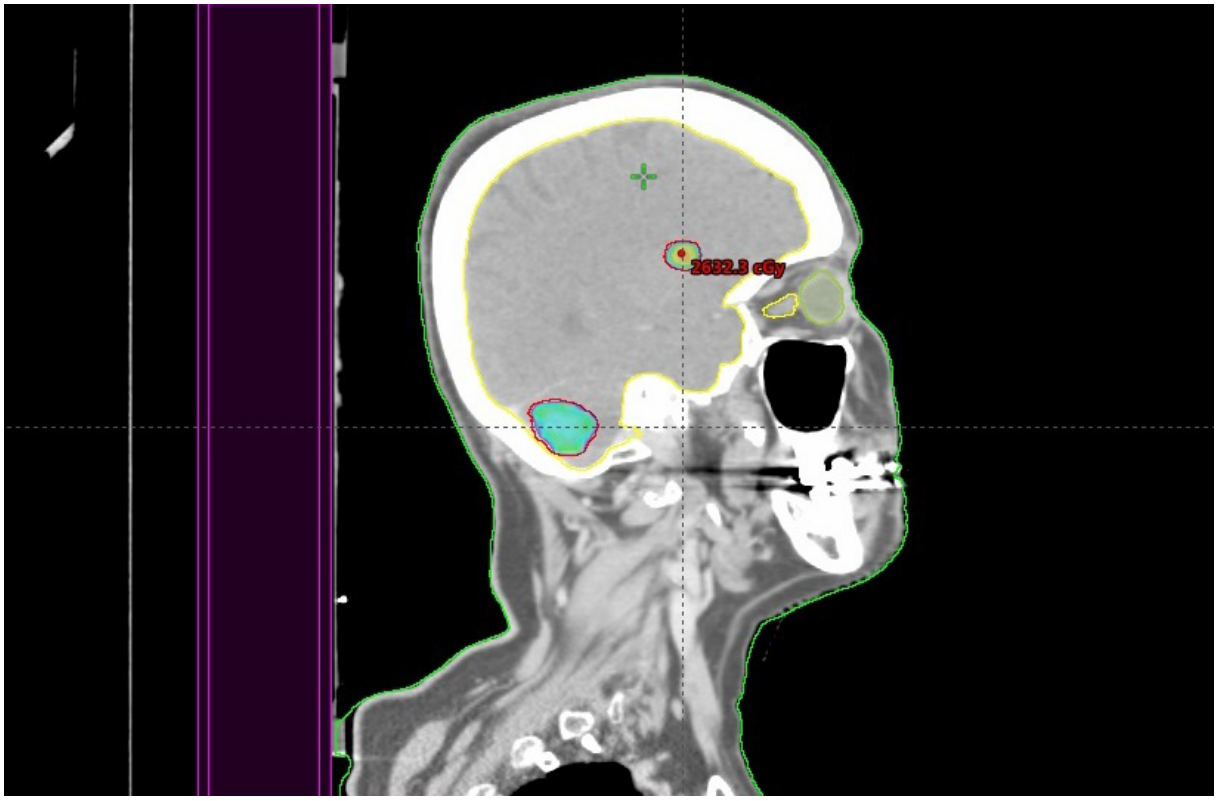

Figure 4: Radiotherapy Plan.

Discussion

The colon and rectum (45%) are the most frequent sites of gastrointestinal metastases of breast cancer, followed by the stomach (28%) [25]. In autopsy series, the rate of gastric metastasis is 8–18% whereas it is only 0.1-0.3% in retrospective studies [1,12]. The fundus and antrum are where involvement most frequently occurs [12]. Breast cancer (27.9%) is the most common source of gastric metastases, followed by lung (23.8%), esophagus (19.1%), renal cell carcinoma (7.6%) and malignant melanoma (7%). Compared to other types of breast cancer, Invasive Lobular Carcinoma (ILC) more often metastasizes to the stomach. In Taal's study, lobular carcinoma was found to be the main pathology of breast-derived stomach metastases (83%) [31]. Although the exact cause of lobular histology metastasizing more frequently is unknown, some authors theorize that this may be due to particular lobular cell tropism. Studies have revealed that E-cadherin expression loss is more common in ILKs than in Invasive Ductal Carcinoma (IDC). Loss of E-cadherin expression in lobular cells reduces adhesion, which may be related to the pattern of metastasis. Typically, it occurs years after the diagnosis and therapy (median time from diagnosis is 5 to 7 years). Some authors advise regular upper endoscopy because of the dormancy status, especially in cases of breast cancer with invasive lobular carcinoma [3]. Additionally, when any gastric symptoms are noticed in breast cancer cases, therapeutic side effects may be taken into account. Delaying therapy and reducing survival rates may result from this. Therefore, every gastric symptom should be subjected to endoscopic assessment first. The most common endoscopic finding, as in our case, is diffuse infiltration in the stomach wall that mimics linitis plastica, although other findings include ulcers, polyps, and external compression. Evaluations and biopsies may yield non-pathological results since most patients' involvement is superficial because infiltration in the hematogenous and lymphatic spread of breast cancer metastases is often restricted to the submucosal and seromucosal layers. Large and in-depth biopsies are therefore necessary for diagnosis. This is thought to be an important factor in the rate being so high in the autopsy series but lower during the period of life [2,4-6,9,10,13,15,17,18].

Gastric metastases manifest with nonspecific symptoms. While our case presented with nausea, patients may also experience abdominal pain, bleeding, weight loss, anorexia, dyspepsia, and early satiety. Gastric perforation has also been reported in one case [4].

The differential diagnosis of primary gastric cancer and metastasis is based on clinical, endoscopic and histological findings. Signet ring cells can be seen on histological examinations, making

it difficult to differentiate primary gastric adenocarcinoma from metastatic breast cancer. There is a case report of breast cancer metastasis treated for 13 years as stage 4 gastric carcinoma in the literature [8]. Consequently, immunohistochemical markers are crucial in the differential diagnosis. In the immunohistochemical staining of breast cancer metastases; ER, PR, CK7, GCDFP-15(Gross Cystic Disease Fluid Protein-15) are stained positive while CK20, CA19-9, CDX2-3 are stained negative [7,8]. Due to the fact that weak-moderate ER and PR positivity has been observed in 12–32% of primary gastric cancers, alone ER/PR and HER status may not be adequate to discriminate [19]. However, it should be noted that these results were found using first-generation ERβ-targeting antibodies, which are no longer commonly utilized. Taal et al. investigated whether antibodies against ERα could be used in differential diagnosis and did not observe ERα expression in any primary gastric carcinoma [19]. The same study also shown a substantial correlation between breast metastases and the lack of E-cadherin expression. In another study by Chu PG et al., CK20 was not found positive in any breast cancer [20]. In a study by O'Connell et al., while CK-7 is expressed in 90% of breast cancers, it was observed to be 50-64% positive in primary gastric adenocarcinomas [21]. GCDFP-15 is a protein detected in the plasma and macroscopic breast cyst fluid of patients with breast cancer [16,29]. Positive monoclonal GCDFP-15 staining was found to be low sensitive (55-76%) and highly specific (95-100%) in diagnosing breast cancer metastasis [23,34]. Cytoplasmic positivity of GCDFP-15, absence of E-cadherin and ER-a positivity are indicative of primary breast cancer [19,22]. Since it has high sensitivity in breast cancer, cytoplasmic mammaglobin positivity is also useful in demonstrating that the tumor originates from the breast [26,27].

Guidelines for treatment don't yet exist. In small solitary tumors and oligometastatic disease, the tumor should be excised within safe limits if possible and immunohistochemical examination should be performed. Chemotherapy and hormone therapy are the main treatment options for large tumors depending on the hormone and HER2 receptor status, while surgical treatments should be considered palliative in cases such as obstruction [3,11]. According to a study reported by McLemore et al., median survival with palliative surgical resection was found to be prolonged in selected patients which had only gastrointestinal metastases, although it was not statistically significant (44 vs 9 months) [13]. In 12 cases of gastric metastatic breast cancers reported by Rodrigues et al., 4 patients underwent surgery, and these 4 patients had better survival than other patients (38 vs 14 months) [24]. After diagnosis, patients have a median survival time of 24 to 58 months [1,12,15].

According to Taal's study, 94% of patients have other concurrent distant metastases, most commonly in the skeletal system (60%) [30]. A single-center research carried out in France found that 57% of patients have current or previous metastases and metastases most commonly seen in the peritoneum and skeletal system [12]. These results demonstrate the importance of future investigations for detecting other distant metastases in patients with gastric metastases.

In conclusion anamnesis, examination, strict follow-up, and endoscopic evaluations when necessary, should be performed in patients who are not diagnosed with cancer and present with dyspeptic complaints. Especially women over 40 years of age if biopsy is going to be taken it should be deep and multiple. Advanced immunohistochemical examination should be done on patients with signet ring cells histology so that metastasis is not overlooked during evaluation. GCDFP-15 and ER-a positivity and loss of E-cadherin should be a guide for breast cancer metastasis. It should be kept in mind that concomitant distant metastases are also common in patients with gastric metastases of the breast, and further investigation should be performed. In the treatment of small solitary tumors and oligometastatic disease, removal with safe surgical margins is a priority; but in large tumors, with the hormone and HER2 receptor status, hormone therapy and chemotherapy should play the main role, surgery should be used in palliative conditions such as obstruction.

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