Case Report

An unusual case of colonic adenocarcinoma development in the region of disseminating lobular breast carcinoma infiltration: diagnostic approach and review of the literature

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Abstract: We present an unusual case of colon cancer development in bowel segment involved with lobular breast carcinoma infiltration. 80 year old Caucasian woman was diagnosed with right colon carcinoma due to rectal bleeding and obstructive symptoms. She had nine years clinical history of lobular, well differentiated breast cancer with five years of postoperative tamoxifen therapy, disseminating to bones and pleural cavities two years prior to hemicolectomy. On microscopic examination under the colonic adenocarcinoma and in the whole length of the resected bowel segment, massive infiltration of lobular carcinoma was discovered. She remains alive under the palliative hormone and chemotherapy. In our paper we discuss clinical and pathological issues concerning metastases of breast cancer into the gastrointestinal tract as well as rare colocalization of colonic and breast cancers within the same intestinal segment. Review of the literature is also presented accordingly.

Keywords: Lobular breast carcinoma, colonic adenocarcinoma, coexistence, diagnosis

Introduction

Invasive breast carcinoma is established to widely disseminate even in the latent period after the initial surgery. Ductal adenocarcinoma of the breast usually metastasizes to lymph nodes, bones and lungs, while invasive lobular carcinoma is likely to give metastases to other, quite extraordinary, sites, including gastrointestinal tract (GI), peritoneum, pleura and brain. The reason of this dichotomy can be partly attributed to discohesive nature of the neoplastic cells due to different genetic alterations within the adhesion molecules [1]. According to several reports, the frequency of GI involvement in breast cancer patients is around 1% [2]. Given the fact that most of the metastases occur years after the initial treatment, the possibility of the breast cancer dissemination remains within the scope of differential diagnosis of GI lesions.

There have been few reports about the synchronous occurrence of the adenocarcinoma of the colon and disseminating breast carcinoma, with undistinguishable clinical symptoms, e.g. bleeding, ileus and/or colon perforation [3].

We report a case of unexpected coexistence of colonic adenocarcinoma within the region of breast cancer infiltration of intestinal wall.

Case report

A 71-year-old Caucasian woman with irrelevant family history was diagnosed with invasive carcinoma of the right breast in core biopsy, in January 2002. She underwent the right breast lumpectomy in March 2002. Histopathological diagnosis of lobular breast carcinoma was established-well differentiated (G1) lobular carcinoma of classical, alveolar, solid subtype was recognized with lobular carcinoma in situ (CLIS)
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Gross examination revealed the existence of exophytic ulcerated tumor of 4 cm in diameter, located in the proximal segment of the large bowel, with macroscopic features of pericolic fat tissue invasion. The remaining parts of the small and large bowel walls seemed unchanged. The microscopic diagnosis of moderately differentiated colonic adenocarcinoma was established. The cancer penetrated the full thickness of the colonic wall, invading the pericolic fat tissue with several foci of tumor budding at the front of invasion (Figure 1). The cancer emboli were present in vessels, and four out of 14 lymph nodes were involved with adenocarcinoma metastases.

Surprisingly, beneath the colon adenocarcinoma the additional neoplastic component was discovered with massive infiltration of non-cohesive malignant cells with signet-ring morphology, individually dispersed or arranged in a single-file linear pattern (Figure 2). These cells were present both under the adenocarcinoma and in the entire length of the small and large bowel segments, involving surgical margins, with no penetration towards the intestinal epithelium (Figure 3). Due to patient’s medical history and morphology, breast lobular carcinoma invasion was suspected. The immunohistochemical profile of the colon carcinoma was CK20 (+), CDX2 (+), E-cadherin (+), CK7 (-), ER (-), PGR (-), chromogranin (-), synaptophysin (-), while the breast carcinoma was CK20 (-), CDX2 (-), E-cadherin (+), CK7 (+), progesterone receptor (+++), estrogen receptor (+++), chromo-

Figure 1. Invasion front of the colon cancer with tumor budding. H&E staining, magnification ×100.

Figure 2. Intestinal wall infiltration with the lobular breast cancer. Discohesive cells are arranged in nests and dispersed in a single-file linear pattern (see inlet). H&E staining, magnification ×40 [inlet-magnification ×200].

Figure 3. Lobular breast cancer infiltration in the submucosa of the large bowel-no bridging toward mucosa and intestinal epithelium is seen. H&E staining, magnification ×200.
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Figure 4. Immunohistochemical staining for CK7 (A), CK20 (B), and estrogen receptor (C) at the interface between colon and lobular breast cancers. Magnification ×200.

Figure 5. Concurrent colon and lobular breast cancer metastases within the same lymph node – immunostaining for estrogen receptor; colon cancer in the upper part of the figure. Magnification ×40.

granin (+/-), synaptophysin (-) (Figure 4). Moreover, six out of 14 lymph nodes displayed lobular breast carcinoma metastases. In one of the lymph nodes both colonic and breast carcinoma metastases were present (Figure 5). The omental involvement with lobular breast carcinoma was confirmed solely on microscopic grounds, while macroscopically the omentum seemed intact. Of note, no areas of intermingling of both components could be observed.

After the surgery, the patient started palliative hormone and chemotherapy due to dissemination of breast carcinoma. The disease is disseminated and stable and she is alive at the age of 84 now.

Discussion

Gastrointestinal tract is infrequent location of the breast cancer dissemination. The metastases may occur late after operation-usually 4-5 years after the surgery to 20 or even 30 years, as reported by Benfiguig et al. and Jafferbhoy et al. [4-6]. In the big series presented by Borst et al. invasive lobular carcinoma was more likely to give metastases to GI tract than invasive ductal carcinoma, with the incidence of 4.5% and 0.2%, respectively [7]. As to the location of metastases, stomach is the most, and rectum the least frequent site of metastatic involvement [8].

It is speculated whether the history of breast carcinoma is a risk factor for developing the subsequent GI malignancy. Older reports established such risk to be 20% higher [9], and showed the breast carcinoma to be a risk factor of development of the second primary malignant disease in the later period, including gastrointestinal tract [10]. More recent studies based on Surveillance Epidemiology and End Results (SEER) database estimate such risk not to be increased at all, unless the patient is a carrier of BRCA1 gene mutation, with contradictory impact of the latter factor [11-13]. Therefore, as a relation between breast and subsequent GI cancers is speculative, no special strategy for breast cancer patients has been officially introduced in clinical management [14].

According to some studies similar environmental factors may be responsible for co-development of breast and GI cancers, namely high socio-economic status acting pro-, and low fat and high fiber diet acting against [15, 16]. The impact of previous tamoxifen therapy for developing GI cancer is equivocal. According to study by Curtis et al. tamoxifen therapy does not increase the risk of GI cancer, while in the additional analysis by Newcomb the modest increase was demonstrated, only in women during the 5 years after initiation of breast cancer therapy [17, 18].
Most studies point to the advanced age as a risk factor of developing malignancies - both in breast and GI tract. In the SEER database more than two thirds to develop both cancers were 65 years of age or older, as our patient was [19]. In the big series analyzed by Pappo et al. the mean time period between breast cancer and GI cancer occurrence amounted to 9.2 years (range 3 months - 21 years) [20]. In our patient it is exactly 9 years.

There were very few reports about coexistence of breast cancer metastases and adenocarcinoma in GI tract. In fact, only Jafferbhoy et al. described the case of synchronous GIST, colon and breast adenocarcinoma with double colonic polyp metastases [6]. In their paper breast cancer metastases and colonic adenocarcinoma were located in different segments of the large bowel, and breast metastases developed in polypoid, macroscopically visible lesions. To our knowledge we present the first case of colon carcinoma developing in the region involved with infiltrating lobular carcinoma. Some issues should be underlined at this point. Gross sectioning of the surgical specimen displayed ulcerating typical colon cancer, while the breast cancer infiltration, even though dispersed and massive, was only visible microscopically and occupied the entire resected segment. Would it have been recognized if it hadn’t been a clinical bleeding from the colonic lesion remains uncertain. Nevertheless it proves that the tissue involvement, particularly in lobular carcinoma of the breast, can be much dispersed and yet clinically silent.

Our patient has been proved to have disseminated disease already in 2009. Knowing that she had pleural and bone metastases one can assume that subclinical GI involvement could have been presented already at this point. Having in mind several cases of intratumoral metastases or cases of metastases into different tumor one could speculate whether neoplastic environment can be a driving force for developing a second malignancy. If that would be the point, one could expect the intermingling between the two components, which is not the case here. On the other hand, developing colonic adenocarcinoma with many extracellular mediators can overgrow and push aside the other neoplastic component, especially discohesive in nature as lobular carcinoma cells.

There are also many cases of gastrointestinal mucosa involvement with breast carcinoma invasion, where the necessity of endoscopic investigation occurs. Identification of neoplastic cells within the gastrointestinal mucosa can be very challenging in the endoscopic biopsy specimen, even for the experienced pathologist, since the infiltrating cells of the lobular carcinoma are very small and are located between unchanged mucosal glands.

Nazareno et al. underlines that any new GI symptoms in patients with previous breast cancer history should be considered as metastases until ruled out [21]. Detailed and complete histological diagnosis is mandatory for the appropriate treatment approach, and possibly longer survival [22, 23].

Disclosure of conflict of interest
None.

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References
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