Long-Standing Scirrhus Breast Carcinoma en Cuirasse

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Key Words

Breast Cancer: scirrhus, Lobular

Summary

Background: The stromal reaction may be one of the key factors in the development of breast carcinomas. **Case Report:** We report the case of an 80-year-old female patient who ignored a very slow growing, extensive scirrhus breast carcinoma for almost 20 years duration. **Results:** Histopathology analysis revealed a Scarff Bloom Richardson (SBR)3-grade, estrogen receptor (ER)-positive (80%), progesterone receptor (PR)-positive (10%), HER2/neu-negative, lobular-invasive, scirrhus breast carcinoma with large cells. **Conclusion:** A strong peritumoral fibrous stromal reaction may explain the long-standing evolution of the tumor without any distant metastases.

Schlüsselwörter

Mammakarzinom: szirrhös, lobulär

Zusammenfassung

Hintergrund: Die Stromareaktion könnte als einer der Schlüsselfaktoren bei der Entwicklung von Brustkarzinomen angesehen werden. **Fallbericht:** Wir berichten vom Fall einer 80-jährigen Patientin, die ein sehr langsam wachsendes, ausgedehntes szirrhöses Brustkarzinom über einen Zeitraum von fast 20 Jahren ignorierte. **Ergebnisse:** Die histopathologische Analyse zeigte ein Scarff-Bloom-Richardson (SRB) Grad 3, Östrogenrezeptor (ER)-positives (80%), Progesteronrezeptor (PR)-positives (10%), HER2/neu-negatives, lobulärinvasives, szirrhöses Brustkarzinom mit großen Zellen. **Schlussfolgerung:** Eine starke peritumorale, fibrotische Stromareaktion könnte die lang andauernde Entwicklung des Tumors ohne Bildung entfernter Metastasen erklären.

Introduction

An 80-year-old female patient presented with a right breast retraction consistent with a large, hard and fibrous carcinoma, the so-called 'cancer en cuirasse' (fig. 1) [1]. At actual presentation, long-standing permeative nodules surrounded the primary breast tumor and enlarged ipsilateral axillary lymph nodes were found. The onset of symptoms had started 20 years before, but the patient had ignored the progression of the slow-growing local tumor. Histopathology analysis revealed a Scarff Bloom Richardson (SBR)3-grade, estrogen receptor (ER)-positive (80%), progesterone receptor (PR)-positive (10%), HER2/neu-negative lobular-invasive scirrhus breast carcinoma with large cells (fig. 2).

A whole-body multidetector computed tomography (CT) examination confirmed the presence of right axillary adeno-

pathies with no distant metastasis. Skin retraction was shown overlying a 200 × 150 mm tumor, at clinical inspection and on 3-dimensional breast CT reformation scans (fig. 3).

Discussion

Scirrhus (etymology: Greek, skirrhos, hard) carcinomas are histologically characterized by the presence of hard, fibrous, particularly invasive tumors in which the malignant cells occur singly or in small clusters or strands in dense connective tissue [1]. Such types of breast carcinomas are mostly reported in elderly women and may indicate slow-growing tumors leading to limited local invasion and few distant metastases [2, 3]. Scirrhus carcinomas are usually ductal carcinomas whereas scirrhus lobular types have been reported very rarely [4].

Fig. 1. Scirrhus breast cancer called ‘cancer en cuirasse’. An 80-year-old woman presenting with global breast retraction and biopsy-proven malignant permeative nodules on the overlying skin (arrows).

Fig. 3. 3-Dimensional multidetector CT reformation of the right breast. Volume-rendering, CT scan reformation clearly shows the strong fibrous skin/nipple retraction and enlarged veins at the periphery. Despite the invasion of the whole mammary gland and the areolar plaque involvement, neither internal thoracic adenopathy nor distant metastases were depicted on the total-body CT scan, 20 years after initial clinical presentation.

The so-called ‘cancer en cuirasse’ reflects the strong extensive fibrotic process that causes the chest wall encasement as a breastplate would do [2, 5]. Stromal reaction in cancer has been interpreted as either promoting tumor angiogenesis and physical fibrillar matrix components or creating a barrier to entrap the tumor.

Fig. 2. Histological section of the breast specimen (hematoxylin-eosin stain, × 200). The histological section shows clusters of tumoral cells surrounded by dense extensive fibrous stroma rich in collagen fibers (arrows) and the presence of few fibroblasts.

Breast fibromatosis is an uncommon differential diagnosis to consider in such a case, as it may simulate breast carcinoma. Fibromatosis of the breast consists in benign infiltrative proliferation of fibrous tissue [6]; similarly, Riedel thyroiditis in the neck is a differential diagnosis of thyroid cancer [7]. Some authors reported an improved clinical outcome in scirrhus carcinoma presenting with stromal reaction associated with desmoid-type fibromatosis (DTF), while others presenting with a solitary fibroblastic fibrous tumor displayed a poor prognosis [8, 9]. The DTF core gene set has thus been reported as a robust descriptor of a distinct stromal response, being associated with improved clinical outcome in breast cancer patients. Thus, not all fibrosis types appear to be equivalent.

Although such a dense fibrous stromal reaction may reflect a slow-growing tumor [8, 10–12], scirrhus breast carcinomas would be older than other kinds of tumors and thus may have a poorer prognosis [12]. However, according to the literature, the definition of scirrhus carcinoma warrants further redefinition or correction as this term is overused because any cancer may present with a stellar stromal reaction. We do state that the term of scirrhus carcinoma should be limited to cancers presenting with an intense stromal reaction and a low cellularity [1].

As a matter of fact, Baltzer et al. [13] reported on a case of large invasive breast carcinoma with absence of contrast medium enhancement on the magnetic resonance imaging (MRI) scan due to an almost missing tumor angiogenesis. This carcinoma had a low cellularity and a strong desmoplastic reaction. We believe that, in such a genuine scirrhus cancer, the strong desmoplastic reaction may preclude local

angiogenesis, thus explaining a lower contrast uptake on CT scan perfusion [14] and a subsequent very slow local tumor growth. Furthermore, Masamune et al. [15] reported a relationship between poor angiogenesis-related hypoxia and the development of fibrosis in pancreatic cancer. Moreover, as stated by Rhee [16], a stiff restrained matrix provides a high tension state, besides cytoskeletal reorganization. This phenomenon is analogous to granulation tissue and wound contraction that induce stress fiber formation and focal adhesion and thus would limit tumor growth.

Angiogenesis is a complex, multistep process driven by many local signals within the tumor. Tumor cells stimulate the formation of stroma, which excretes a variety of growth factors, cytokines, and proteases. Tumor-associated macrophages (TAMs) are major components of the tumor stromal matrix that may elicit diverse aspects of tumor growth as either positive or negative regulators [17–19]. In breast carcinoma, large numbers of infiltrating T cells and TAMs are often observed. Macrophage infiltration into tumors is regulated by several cytokines and chemokines, in particular macrophage chemoattractant protein-1 (MCP-1). MCP-1 is produced not only by tumor cells but also by stromal cells. Although high concentrations of TAMs may correlate with poor prognosis, MCP-1 may activate monocyte cytostatic function against tumor cells [20]. Finally, mammary adipose tissue-derived stem cells (ASCs) that locate adjacent to the breast tumor may incorporate into tumor vessels and differentiate into endothelial cells, thus leading to tumor growth and metastasis [21]. In our case,

we hypothesize that the fibrous stroma had inhibited the tumor cell spread by the secretion of MCP-1 or by cytostatic cytokines/chemokines and precluded vessel incorporation of ASCs for almost 20 years.

Conclusions

In conclusion, the very slow local tumor progression reported herein may be partly due to its estrogen dependency (postmenopausal status), but above all to the combined strong stromal reaction and the tumor cell hypoxia. This precluded stromal angiogenesis and may explain such a long-standing evolution despite a high SBR histological grade (3). Moreover, in situ production of cytostatic agents such as MCP-1 may have inhibited malignant breast cell growth for almost 20 years. A better understanding of stromal contributions to cancer progression will likely increase our knowledge of the combinatorial signals that support and promote tumor growth, and eventually result in the designation of new therapeutics targeting the stroma in breast cancer patients.

Conflict of Interest

The authors have no sponsorship or funding arrangements relating to the article 'Long-Standing Scirrhus Breast Carcinoma en Cuirasse' and no possible conflicts of interest to disclose.

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