Long-Standing Scirrhous Breast Carcinoma en Cuirasse

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Key Words
Breast Cancer: scirrhous, 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 scirrhous 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, scirrhous breast carcinoma with large cells. Conclusion: A strong peri-tumor fibrous stromal reaction may explain the long-standing evolution of the tumor without any distant metastases.

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) \cite{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 scirrhous breast carcinoma with large cells (fig. 2).

A whole-body multidetector computed tomography (CT) examination confirmed the presence of right axillary adenopathies 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
Scirrhous (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 \cite{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 \cite{2,3}. Scirrhous carcinomas are usually ductal carcinomas whereas scirrhous lobular types have been reported very rarely \cite{4}.
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 scirrhous 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], scirrhous 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 scirrhous 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 scirrhous 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 scirrhous cancer, the strong desmoplastic reaction may preclude local...

Fig. 1. Scirrhous 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. 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.

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.
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 secretes 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 chemotactic 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 (post-menopausal 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 Scirrhous Breast Carcinoma en Cuirasse’ and no possible conflicts of interest to disclose.

**References**