The Breast (2005) **14**, 3–10

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THE BREAST

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ORIGINAL ARTICLE

'Pure' invasive apocrine carcinoma of the breast: a new clinicopathological entity?

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Received 24 February 2004; received in revised form 5 May 2004; accepted 7 June 2004

KEYWORDS
Apocrine glands;
Neoplasm;
Invasiveness;
Breast neoplasms;
Neoplasms;
Histological type;
Treatments;
Prognosis;
Treatment outcome

Summary Invasive apocrine carcinoma (IAC) of the breast has a similar prognosis to infiltrating ductal carcinoma not otherwise specified (IDC-NOS). The existence of a pure IAC subtype (PIAC) and its possible prognostic implications have not been fully investigated. To this end, pathological inclusion criteria for the diagnosis of PIAC were defined and three pathologists reviewed their slides blind to identify it. To assess its clinical behavior, a case–control evaluation was performed, for which 122 cases were selected. There was 100% agreement among the pathologists on the diagnosis: PIAC was identified in 37 cases and IDC-NOS, in 68, while 17 cases were categorized as complex IAC. The probability of 6-year survival was 0.72 for PIAC and 0.52 for IDC-NOS ($P = 0.02$), and was still better after adjustment for tumor grade and axillary status. PIAC may be a distinct clinicopathological entity with a less aggressive behavior than high-grade IDC-NOS and might be regarded as an independent prognostic factor in early breast cancer.

Introduction

Although first described by Krompecher in 1916,[1] invasive apocrine carcinoma (IAC) of the breast is still a controversial clinicopathological entity,[2–5] with a prognosis reported to be similar to that of infiltrating ductal carcinoma not otherwise specified (IDC-NOS) of the mammary gland.[6,7] Since most authors suggest that this subtype and IDC NOS are comparable in their clinical behavior, IAC has received little attention in the literature and there is no consensus on clear-cut reproducible morphological diagnostic criteria.[5,7–10] We set up the hypothesis that identification of a 'pure' IAC

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0960-9776/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.breast.2004.06.003

subtype using reproducible pathological criteria will define a subgroup of patients who may have a different outcome.

For these reasons, we designed and conducted this investigation with the aim of delineating microscopic criteria for the diagnosis of pure IAC. To assess its clinical behavior, the outcome in this subgroup was compared by means of a matched-pairs analysis with that achieved in patients with comparable combined histological grades (CHG), such as IDC-NOS with scores of 7, 8, and 9.[11]

Materials and method

Each of the three participating pathologists reviewed all charts from his/her own institution blind to retrieve eligible patients diagnosed from 1991 to 2001. For the purposes of this study, the microscopic criteria detailed in this paper for the definition of pure IAC were agreed by all three pathologists in the group for case retrieval.

Diagnosis: techniques and methods

All samples were stained with a standard hematoxylin–eosin (HE) technique. All but 1 patient underwent determination of estrogen and progesterone receptors with monoclonal antibodies using the avidin–biotin–peroxidase system (Verctor's ABC Vectastain) with immunolabeling techniques in paraffin-embedded plugs. A guideline specifying the microscopic criteria to be used, among other things, was distributed to the three pathologists, who reviewed and reclassified the histological preparations independently.

Each case was defined according to the following inclusion and exclusion criteria.

Test group

Inclusion criteria

The major criteria were required to be met; their presence was mandatory and all had to be present in at least 75% of the microscopic fields studied (Figs. 1A and B). These were: (a) large cells with abundant eosinophilic cytoplasm, usually granular, in cells with a nucleus-to-cytoplasm ratio of 1:2 or more;[2,12] (b) round and/or pleomorphic, large and vesicular, nuclei compared with those in the apocrine metaplasia[2,13]; and (c) cells with sharply defined borders or linear and well-defined cell margins.[2,12,13]

There were also minor criteria, i.e., criteria whose presence was favorable but not mandatory: (a) prominent nucleoli in a high percentage of the fields (more than 50%); and (b) apical convexity (cytoplasmic snout) of the cytoplasm when there were luminal spaces.[14]

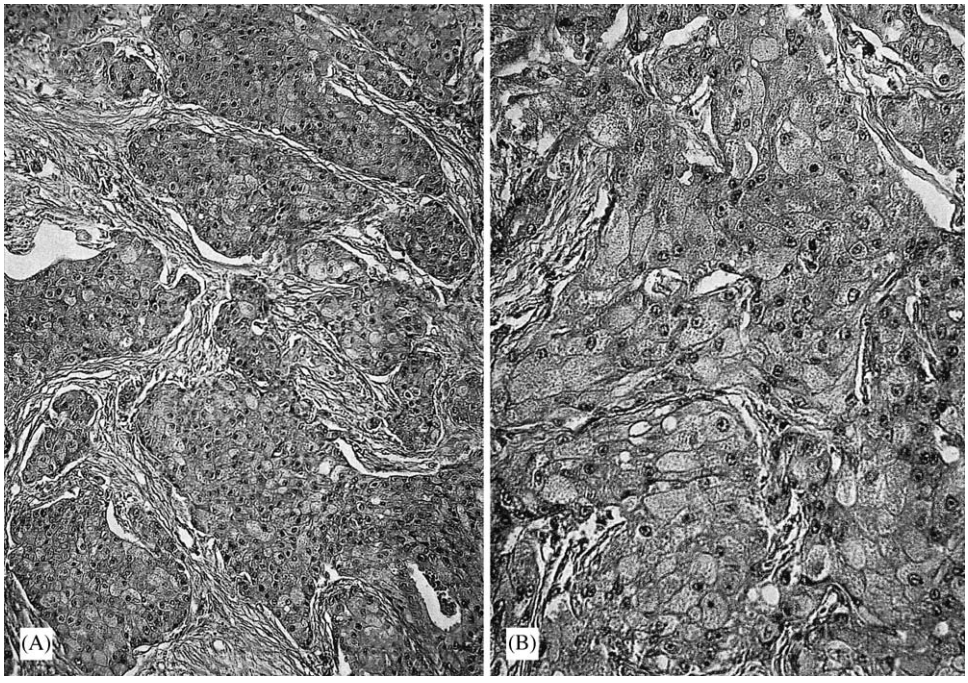

Figure 1 Inclusion criteria: (A) low-power micrograph with 100% of large cells with abundant eosinophilic cytoplasm and round nuclei; (B) granular eosinophilic cytoplasm, large nuclei with prominent nucleoli and neatly defined border of the cell.