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PATHCHAT

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Triple-negative breast cancer

Introduction

Breast cancer is the most common cancer among women worldwide, with approximately 1.7 million cases diagnosed annually. In South Africa, the incidence is 40 new cases per 100 000 persons per year. The incidence of breast cancer varies across the world between races and regions[1].

Despite the lower incidence of breast cancer in Africa, the mortality continues to be extremely high, with survival much lower than that seen in other parts of the world[2].

Currently, cancer is classified by combining histo-morphological information (histological subtype and grading) in conjunction with the TNM staging. Using microarray technology, breast cancers were found to cluster into four groups: oestrogen receptor positive (ER+)/ luminal group, normal breast-like group, human epidermal growth factor 2 receptor (HER2+) group and a basal-like group[3]. It was later found that basal-like breast cancers were associated with the shortest survival times and poor clinical outcome[4].

Recently, Kapp, Jeffrey, Langerod, Borresen-Dale, Han and Noh (2006)[5] suggested a less complex molecular classification that directly compares different gene microarray datasets from various investigators. The three molecular subtypes described by Kapp et al. (2006) are ER+/HER2-, ER+/HER2+ and ER-/HER2-. This classification was shown to significantly predict overall survival and probability of distant metastasis.

Triple negative breast cancer (TNBC) is a recently coined term used to describe a subtype of breast cancer that lacks expression of the three primary breast tumour markers: oestrogen receptor, progesterone receptor (PR) and HER2 protein as demostrated using immunohistochemistry and/or fluorescence in situ hybridisation (FISH) on formalin-fixed and paraffin-embedded tissue. Clinicians caring for breast cancer patients became aware of TNBC shortly after the introduction of HER2 testing in the late 1990s[6].

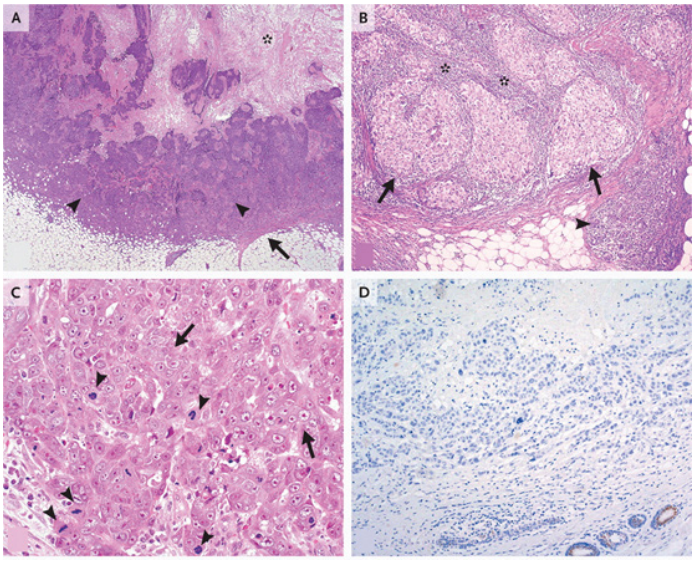

Figure 1 (left): Histologic and immunohistological features of triple negative breast cancer
A: The neoplasms typically have pushing margins, with central necrotic areas.
B: A prominent lymphocytic infiltrare can sometimes be seen at the periphery of the tumour.
C: The neoplastic cells are arranged in solid sheets or nests. Numerous mitotic figures are visualised.
D: The neoplastic cells are negative for oestrogen receptor, progesterone receptor and HER2 immunohistovhemical staining.

Source: Foulkes W, Smith I and Reis-Filho. 2010. Triple-negative breast cancer. *The New England Journal of Medicine* 363:1938–1948.

Clinicopathologic features

TNBC accounts for approximately 10 to 20% of all breast cancers[3, 9 10] and up to 25% of high-grade tumours. There is a clustering of TNBC in premenopausal women and in women of African descent[7].

At diagnosis, TNBC is larger in size, with a maximum diameter of > 5 cm, and has pushing borders with central areas of necrosis. There is often a prominent lymphocytic infiltrate at the periphery of the tumour. The neoplastic cells are arranged in solid sheets and have a high nuclear grade and an elevated mitotic count[8].

Prognosis

TNBC is a biologically aggressive tumour that shows rapid growth and confers a poor prognostic factor in terms of disease free and overall survival, as it is difficult to treat due to its lack of effective therapeutic targets.

Treatment

Women with TNBC do not benefit from targeted therapies such as anti-oestrogen and anti-Her 2 agents due to the absence of specific receptor sites. Sytemic chemotherapy is currently the mainstay of treatment. These patients have a worse outcome after chemotherapy than patients with other types of breast cancer. Chemotherapy does, however, improve outcomes[9].

Conclusion

TNBC has attracted attention because of its aggressive clinical course and lack of effective treatment methods. This has important implications for the choice of systemic therapies to be utilised in management.

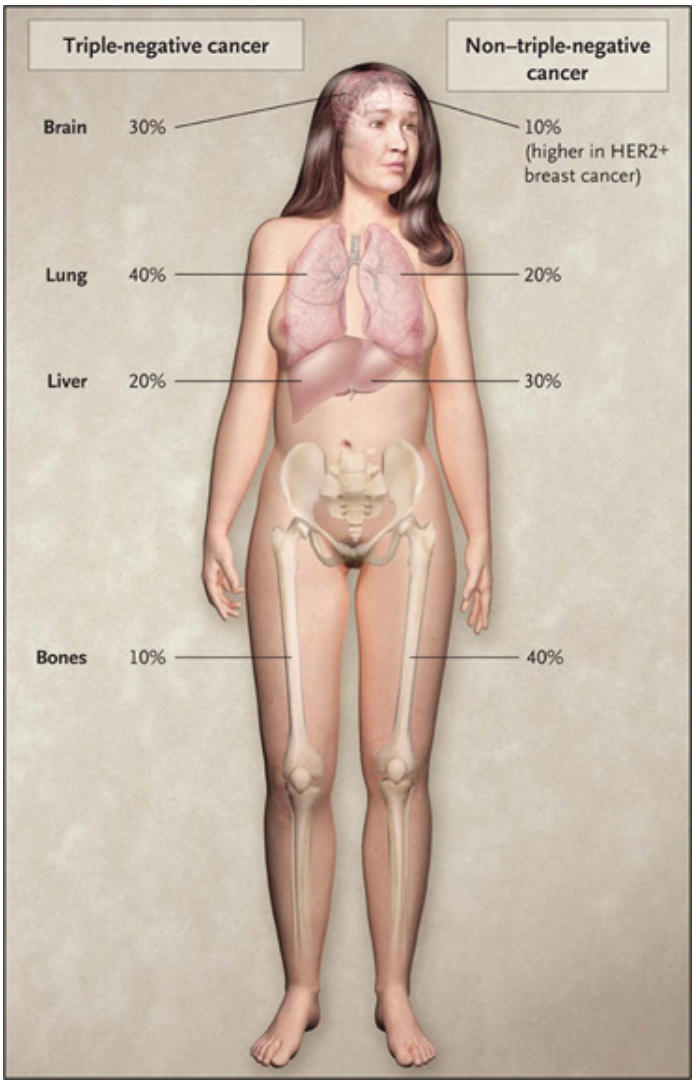

Figure 2 (above): Sites of first distant recurrence in cases of metastatic triple negative breast cancer compared with non-Triple negative breast cancer.

Source; Foulkes W, Smith I and Reis-Filho. 2010. Triple-negative breast cancer. *The New England Journal of Medicine*363:1938–1948.

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