Keynote Lecture

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A Darwinian eye view of cancer

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"Nothing in biology makes sense except in the light of evolution"

(Th. Dobzhansky, 1937)

Biologists and medical researchers in seeking to understand complex diseases such as cancer usually focus on proximate or immediate causes. For example, resistance to drug X is caused by gene Y amplification; exposure to agent A causes cancer via mutation in gene B. This is not an invalid perspective, indeed it has provided great insights and benefits. But it is myopic. What is missing are the causal pathways, distal effects and historical contingencies that effect all diseases.

Darwinian medicine is a new discipline that provides a novel perspective on why our bodies are vulnerable to common diseases. It takes on board the principles of evolutionary biology in the context of how human bodies have been historically engineered. Some of the central ideas include the following:

The importance of mismatches between prior evolutionary adaptations (e.g. to the Stone Age) and our current novel environments and lifestyles.

The lack of perfection in evolutionary engineering of our bodies resulting in design faults, trade-offs and inherent risks.

The inevitability of natural selection where there is genetic diversity and competition, e.g. between us and infectious organisms; between us and cancer cells.

In this lecture, I will discuss how these principles apply to cancer and may contribute to an understanding of cancer causation, its underlying biology and clinical intransigence.

References

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Poster Session

Breast cancer

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Anthracyclin-based neoadjuvant chemotherapy for large breast carcinoma: predictors and significance of breast preserving surgery.

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Background: Breast preservation is the main benefit yielded by neoadjuvant chemotherapy and treatment sequence could be tailored according to expected likelihood of conservative surgery. The aim of this study was to determine the predictors and the significance of breast conserving surgery in patients with large breast cancer treated with an epirubicin-based neoadjuvant chemotherapy.

Material and Methods: Between January 1987 and December 2001, 594 patients with invasive T2-3 breast carcinoma ineligible for breast conserving surgery were treated with 3 or 4 courses of an anthracyclin-based primary chemotherapy (AVCMF, FAC or FEC), surgery and radiation therapy. Mean age was 50 years (24-76). The mean initial tumour size was 49 mm: 409 T2 and 185 T3. The nodal status were as follows: 260 N0, 324 N1, 10 N2. The histology, determine on pre-chemotherapy core needle biopsy, was an infiltrating ductal carcinoma for 528(89%) patients and a lobular for 66(11%) patients. The estrogen receptor status was positive for 364 patients (61%), negative for 147 (25%) and unknown for 83 (14%). The initial Scarff-Bloom and Richardson histologic grade were as follows: 40 (7%) grade I, 307 (52%) II, 199 (33%) grade III, 48 (8%) undetermined. Predictors of breast preservation were tested in a univariate and multivariate analysis. Prognostic significance of breast preservation was tested in a Cox regression model.

Results: A complete clinical response was obtained for 51 pts (8%) and a regression>50% for 279 pts (42%). A stable disease or a progressive disease was observed for 264 patients (40%). After primary chemotherapy, the mean tumor size was 31 mm and 287 (48%) patients were eligible for breast conserving surgery while 307 patients underwent a mastectomy. Initial size>5 cm ($p<.001$), lobular histology ($p=.001$), SBR I and II grade ($p=.002$), estrogen receptor status ($p=.026$) and multicentrity ($p<.001$) were associated with breast conserving ineligibility whereas age, chemotherapy regimen, presence of microcalcification, nodal status and time period were not. In the multivariate analysis (logistic regression), initial size, histological type and grade, multicentricity were independent predictors of breast preserving surgery. In the multivariate survival analysis, failure of breast preserving surgery was associated with a 3.3 relative risk of metastatic event ($p=.07$).

Conclusions: Our results suggest that predictive factors of breast preserving surgery (initial size, histological type and grade, multicentricity) could be taken into account before deciding a neoadjuvant chemotherapy as failure of breast preserving surgery is associated with a poor outcome.