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Molecular genetic tools can save one-in-three patients chemotherapy

By Professor Justus Apffelstaedt, issued by Mango OMC

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Experienced doctors have observed that some patients with very early cancers, against all expectations, rapidly develop metastases and die, which lead to several research groups toward the end of the 1990s embarking on projects to understand why.

In many cases, although the primary tumour has been radically excised and tests conducted to ascertain whether metastases have taken place have proven negative, the patient still presents with metastases to organs separate from the primary excision site some time after the removal.

“As the primary tumour has been removed and cannot be the source of metastases any longer, these metastases must have been present at the time of treatment yet are obviously undetectable with current diagnostic methods,” says Professor Justus Apffelstaedt of the University of Stellenbosch.

In the realm of breast cancer in the 1950's, researchers noted that approximately one of three patients with breast cancer, whose lymph nodes were not infiltrated by cancer, still went on to develop metastases and died. This indicated that breast cancer can spread via the blood stream without initially infiltrating the lymph nodes.

One risk management solution was to ensure that all patients underwent chemotherapy, thereby lessening their risk of the tumour metastizing; however, the physical and emotional costs of this therapy (from which only 10 - 20% of patients benefit) lead to further questioning on what characteristics (aside from the tumour size and the presence of lymph node presentation) could “red card” aggressive tumours.

In the late 1990s, molecular genetic tools became available that allowed for the assessment of activity of individual genes, also known as transcriptional profiling.

As we know, genes and their products rule all life processes by being either switched “on or off”. With the help of complex molecular genetic techniques, research groups were able to identify groups of genes which govern the process of metastatic dissemination. These genes were summarized in gene profiles such as the MammaPrint test of the Netherlands Cancer Institute, the Oncotype Dx test in the United States, the Rotterdam Profile of the University of Rotterdam. Still others are in various stages of development.

Available in South Africa, the MammaPrint test assesses the activity of 70 genes in a tumour and establishes either a “good” or a “poor“ profile.

On average, around 60% of patients have a poor and 40% a good prognosis profile.

Patients with a poor prognosis profile have a one-in-two chance of developing metastases and dying within 10 years. These patients therefore need aggressive chemotherapy to improve their survival, even in the case of small tumours and no lymph node infiltration.

In contrast, those who have a good prognosis profile have a four-in-100 chance of developing metastases and dying within 10 years and therefore do not require aggressive therapy.

What this means is that one-in-three patients will be saved chemotherapy. “This is a major relief to patients as chemotherapy is the most dreaded part of breast cancer therapy,” comments Professor Apffelstaedt. “A startling

experience is that while a large number of patients are saved from having to undergo chemotherapy, there are a small number of patients, who with conventional prognostication are thought not to need chemotherapy, but whose tumours then have a poor prognosis profile. These patients need chemotherapy despite having very small tumours and no lymph nodes involved. It is particularly important for these patients to be identified with the help of transcriptional profiling to improve their chances of survival."

As common to these types of tests, the MammaPrint test is a logistically complex test: Tissue samples are taken from the fresh tumour within 30 minutes of resection, put in a special medium and airfreighted to the Netherlands Cancer Institute for analysis, which takes about 10 days. Therefore, the test is restricted to centres with a special interest in breast cancer.

The test can also be viewed as pricey. When you offset the cost of a test of this nature—- approximately R 18 000—wjth chemotherapy—on average being R100,000-00—it still represents a significant saving of health care resources.

Although still only available in certain private practices, there are efforts afoot to provide this test also in the state sector.

Editorial contact
Nicole Capper
Tel: +27 (21) 424 6208
Fax: 086 512 2194
Cell: +27 (73) 148 3561
www.mango-omc.com

ABOUT THE AUTHOR

Associate Professor, University of Stellenbosch and Head: Breast Clinic, Tygerberg Hospital