

NEW PERSPECTIVES IN BARRETT'S OESOPHAGUS

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Most of us have been brought up on the dogma that one important complication of reflux oesophagitis is Barrett's oesophagus which in turn is the precursor of adenocarcinoma of the oesophagus. It appears that this view gives too gloom a picture of what is actually happening.

Carcinoma of the oesophagus is not a common cancer in Malta. According to data from the Cancer Registry, between 1998 -2000 there were 27 new cases (21 males, 6 females) with a mortality of 29 (22 males, 7 females).

It has always been a worry that chronic reflux leads to irritation and inflammation of the lower part of the oesophagus, which eventually leads to intestinal metaplastic changes, dysplasia and eventually adenocarcinoma.

These concepts relating to carcinogenesis seem now to be in need of a considerable degree of revision, if not complete overhaul, following data published recently by Brian J. Reid, MD, from the Division of Human Biology and the Division of Public Health Sciences at the Fred Hutchinson Cancer Research Center in Seattle, Washington¹.

He and his colleagues studied 248 patients involving over 20,000 person-months of follow-up. They investigated the changes in chromosomes in these patients using sophisticated computerised technology to assess single nucleotide polymorphisms.

As expected, they found several changes in the DNA of these patients, including small localised deletions involving particularly chromosome 9 (9p), which occurred in either one or both of the chromosomes. These changes were found in 69%

of the patients studied, but remained more or less stable over time - involving a follow-up period of up to two decades - and therefore were of no prognostic significance from the cancer progression point of view.

On the other hand, in about a third of the patients, there were more significant changes, sometimes involved gains or losses of large chromosomal regions, or even whole chromosomes. These involved chromosomes 17, 15 and 13 but not other chromosomes.

Dr Reid believes that these changes tend to occur suddenly, a couple of years before cancer becomes manifest. He states "... we found that the cells had undergone a genome doubling, such that single surviving chromosome 17s were now being replicated. And that was occurring right before the development of cancer."

He concluded that Barrett's patients could be classified into 'progressors' and 'non-progressors.' The majority of patients were non-progressors, meaning that they were at no obvious risk of developing cancer.

These findings have considerable implications both in the understanding of the process of carcinogenesis, as well in applied clinical practice.

It has always been assumed that cancer progression is a linear process, often taking decades before clinical manifestations become obvious. These findings, on the other hand imply that the evolution of cancer is not linear but 'punctuate', namely, completely different mutations/deletions can take place relatively suddenly, producing a specific alteration in the DNA.

From the clinical point of view, Dr Reid believes that this behaviour explains why "current strategies grossly fail to detect cancer in patients diagnosed with Barrett's oesophagus." Dr Reid emphasized that less than 1% of patients diagnosed with Barrett's oesophagus develop cancer each year and concludes that doctors are scaring patients unnecessarily. His advice to doctors is this: "After you tell a patient that they have Barrett's and that only a very small minority develop cancer, just stop."

In his opinion, patients should be assessed by techniques (such as the ones described in the paper) which can select those at high risk, to avoid unnecessary panic and over-investigation of those who are at a much lesser risk.

Chromosome changes, including aneuploidy and polyploidy are a common occurrence in cancer cells. What is unique to these findings is that specific chromosome abnormalities have been detected in tissue well before cancer actually appears. If this finding is shown to occur also in more commonly occurring tumours (e.g. prostate cancer), then this could become an important tool in distinguishing tumours which have an increased likelihood of progression.

Selecting patients for special follow-up on the basis of changes in their chromosomal make-up would make sense if such techniques, as used in this study, were readily available, a project for the future, rather than for immediate application in Malta at present. ❄️

Reference

1. Li X, Galipeau PC, Paulson TG et al. Temporal and Spatial Evolution of Somatic Chromosomal Alterations: A Case-Cohort Study of Barrett's Esophagus. *Cancer Prev Res (Phila)* 2014;7(1):114-27.