

Requiem for the term 'carcinoid tumour' in the gastrointestinal tract?

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Use of the term 'carcinoid tumour' to describe a unique type of tumour in the gastroenteropancreatic system is endemic in the medical literature and in daily clinical and pathological parlance. However, it is a somewhat misleading moniker because a spectrum of histopathological changes and hence, biological outcomes may occur in these tumours. The World Health Organization classification scheme recommends the use of the terms neuroendocrine tumours or carcinomas, which may be stratified as well-differentiated neuroendocrine tumours with benign or uncertain behaviour, well-differentiated tumours with low-grade neuroendocrine carcinoma behaviour and high-grade neuroendocrine carcinomas. These categories may be applied within different sites in the gastrointestinal tract and pancreas, and convey a sense of biological behaviour. In addition, a recently suggested tumour-node-metastasis scheme has been proposed and awaits clinical validation and acceptance. Thus, the term 'carcinoid' has served its purpose well, but its use should be phased out in favour of 'neuroendocrine tumour' or 'neuroendocrine carcinoma'.

Key Words: *Carcinoid; Neuroendocrine; WHO classification*

The term 'carcinoid' or carcinoid tumour has become entrenched in both the pathology and clinical literature over the past 100 years. In 1907, Siegfried Oberndorfer's prescient observation of lesions resembling 'little carcinomas' of the small intestine led to the birth of an entity that has withstood a century of interrogation and fascination. Although he originally believed these lesions to be benign, he subsequently added that a more aggressive malignant behaviour may accompany these tumours. Despite the appearance of terms such as argentaffinoma and APUDoma, carcinoid tumours have remained a stock-in-trade for both pathologists and clinicians, and its widespread use continues unabated.

Oberndorfer's contribution to neuroendocrine pathology has rightfully and deservedly been venerated in recent publications (1,2). The term 'carcinoid' will always be an integral part of the history of neuroendocrine pathology. However, the appellation 'carcinoid tumour' does mean different things to different people. Many classify any neuroendocrine tumour occurring in the gastrointestinal tract as a carcinoid tumour. Others use the term almost exclusively to designate those serotonin-producing tumours that occur in the ileum, metastasize to the liver and result in carcinoid syndrome. Within this diverse application of the term, the most worrying connotation

Requiem pour le terme « tumeur carcinoïde » dans le tractus gastro-intestinal ?

L'utilisation du terme « tumeur carcinoïde » pour décrire un type unique de tumeur dans le système gastroentéropancréatique est endémique dans les publications médicales et dans le langage clinique et pathologique courant. Cependant, c'est une appellation plutôt trompeuse parce que tout un spectre de changements histopathologiques et, par conséquent, d'issues biologiques, peut découler de ces tumeurs. D'après le schéma de classification de l'Organisation mondiale de la santé, les termes tumeurs neuroendocriniennes ou carcinomes neuroendocriniens sont recommandés, et ils peuvent être stratifiés en tumeurs neuroendocriniennes bien différenciées au comportement bénin ou incertain, en tumeurs bien différenciées au comportement de carcinome neuroendocrinien peu différencié et en carcinomes neuroendocriniens bien différenciés. Ces catégories peuvent s'appliquer à divers foyers du tractus gastro-intestinal et du pancréas, et elles communiquent le sens d'un comportement biologique. De plus, un schéma de tumeur-nodosité-métastase a récemment été proposé et est en attente d'être validé et accepté. Ainsi, le terme « carcinoïde » a bien fait l'affaire, mais on devrait arrêter de l'utiliser au profit de « tumeur neuroendocrinienne » ou de « carcinome neuroendocrinien ».

of the use of the word 'carcinoid' is the belief that they all have benign clinical and biological behaviour.

As it stands, 'carcinoid' without any accompanying qualifying comment is somewhat meaningless and does not convey any indication of possible behaviour. There is an almost anecdotal interpretation of the term 'carcinoid tumour'. The need for refinement and consensus is heightened by the fact that neuroendocrine tumours in the gastrointestinal tract are rare and, despite the common cell of origin, are heterogeneous among tumours arising in the foregut, midgut and hindgut. For the same reasons, it is easy to see why all neuroendocrine tumours could be lumped under the rubric of 'carcinoid tumours', irrespective of clinicopathological characteristics.

In the last few years, there has been an increasing awareness that so-called carcinoid tumours span a range of morphological appearances and that they also have varied biological behaviours. This has culminated in the World Health Organization (WHO) classification scheme (3), which introduces a uniform approach to the diagnosis of neuroendocrine tumours within the gastroenteropancreatic tract. The basic tenets of this classification scheme are to consider well-defined pathological features (size, lymphovascular invasion, mitotic counts, Ki-67 labelling index, invasion of adjacent organs, presence of metastases and

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functional status) that could be applied across different sites within the gastrointestinal tract. Inherent in the WHO classification scheme, is the introduction of the terms 'neuroendocrine tumour' and 'neuroendocrine carcinoma' (3).

Neuroendocrine tumours are now stratified into three categories that could be applied across all sites within the gastrointestinal tract:

- well-differentiated neuroendocrine tumours with either benign or uncertain behaviour;
- well-differentiated neuroendocrine carcinomas with low-grade malignant behaviour; and
- poorly differentiated neuroendocrine carcinomas, which are the large cell neuroendocrine and small cell carcinomas.

Klöppel et al (4) have tabulated the application of this simple, yet reproducible classification scheme within the different sites in the gastroenteropancreatic tree. One of the most obvious advantages of the WHO classification scheme is that despite site-specific variations, terminology that reflects behaviour is applied, allowing for less confusion when considering and/or instituting appropriate therapeutic regimes. Several clinical studies (5-9) have applied the WHO classification and have demonstrated its usefulness in allowing for appropriate treatment among the lower grade neuroendocrine tumours.

A more recent development has been a tumour-node-metastasis (TNM) staging consensus proposal for gastrointestinal neuroendocrine tumours, under the auspices of the

European Neuroendocrine Tumor Society. A group of 62 experts on gastrointestinal neuroendocrine tumours from 20 countries gathered in Frascati, Italy, in November 2005. Emanating from their deliberations were two proposed TNM classifications for foregut, midgut and hindgut neuroendocrine tumours (10,11). The clinical validation of these proposed TNM classifications is awaited, but it does represent an excellent attempt to provide clinicians with a 'handle' to manage patients with gastrointestinal neuroendocrine tumours based on sound, reproducible pathological parameters. In the past seven years or so, much reflection and thought has gone into the classification of and approach to neuroendocrine tumours. Like most things in modern medicine, this entity has outgrown its historical roots and origins. We will forever be indebted to the astute observations of Oberndorfer and his legacy – the carcinoid tumour. Just as Mozart reinterpreted and reworked Handel's anthem into his own Requiem, perhaps the WHO and suggested TNM classifications 'borrow' heavily from Oberndorfer's seminal observation, augmenting and supplementing it with something that benefits patient management in the 21st century. It is advocated that the use of the noncommittal term 'carcinoid tumour' be avoided and the terminology of the WHO classification scheme – 'neuroendocrine tumour' or 'neuroendocrine carcinoma' – be used instead, when appropriate. While expunging or purging the term 'carcinoid' from the medical lexicon is by no means the object of the present commentary, it is believed that the pursuit of a reproducible classification of neuroendocrine tumours of the gastrointestinal tract is hampered by its continued shibbolethic use.

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