Early and Precursor Lesions in Endocrine Pathology: Innocent Lambs or Wolves in Sheep’s Clothing?

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In May 2006, a symposium was held at the interim meeting of the European Society for Pathology in Ioannina, Greece, organized by the Working Group Endocrine Pathology. During this symposium, the detection of early and/or precursor lesions of endocrine tumors in the major endocrine organs was discussed, as well as the clinical significance of these lesions and their relationship to the full-blown tumors. The basis for the various contributions was formed by the steadily increasing knowledge of hereditary endocrine tumor syndromes that permit early detection, expanded by more recent data from various fields of research.

The key problem in the identification of early or precursor lesions for endocrine tumors is their rarity, combined with the fact that every case forms a snapshot of an ongoing biological process, which is halted at the time of operation. Thus, it is not always clear what significance has to be attributed to such lesions and whether they are innocent processes that are detected by chance or the forerunners of well-recognized malignant tumors. At present, few relevant animal models exist that permit the evaluation of tumor development that is analogous to human tumor development [1–6]. Until these shed more light on the biological processes, careful analysis of patient series and unique experiments of nature form the basis of our present knowledge, as is exemplified by the contributions of Anlauf et al. [7] and van Nederveen et al. [8] in this volume of Pathobiology.

Without repeating the contents and messages of these papers, one can extract a number of overall conclusions that appear from their work and that of others.

- Classical histopathology consisting of careful observation and interpretation is still an important cornerstone for diagnosis and patient management. Papillary microcarcinomas and C-cell hyperplasia in the thyroid gland, microadenomatosis in the pancreas and adrenomedullary hyperplasia in the adrenal have thus been identified. With the exception of the first entity, the majority (but not all) of these lesions occur in the context of hereditary syndromes, but we may be biased because these patients are monitored more closely. Thus, it is not clear whether non-syndrome-related cases harbor the same genetic abnormalities and follow the same clinical course as their syndromic counterparts.

- Molecular studies have shown that precursor lesions carry the same genetic abnormalities as the eventual tumors they give rise to. In microadenomatosis in the context of MEN1, allelic deletion of the MEN1 gene has been found and it can be hypothesized that something similar is the case in adrenomedullary hyperplasia in the MEN2 syndrome or von Hippel-Lindau disease. The fact that these lesions are still polyclonal does not necessarily mean that they should not be regarded as tumors, as polyclonality may also be observed in larger lesions [9; Stobbe et al., unpubl. obser...
This seems to indicate that size-based criteria for the distinction of precursor lesions from tumors may not be sound and genetic abnormalities may be a better marker for biological behavior. Taken together, one must conclude that much remains to be done before we begin to understand the initiation of endocrine tumorigenesis and whether an early or precursor lesion is one inevitably leading to potentially life-threatening disease or an innocent lesion not requiring further treatment. Tissue banking, especially the storage of frozen tumor tissue and normal tissue samples, is a challenge that we should undertake to overcome the present shortness of suitable samples. Collaboration with our clinicians to have well-documented patient series and national and international collaboration are indispensable to make progress.

References


