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Innovations in Immunohistochemistry for Tumor-based Biomarker Detection

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Description

Immunohistochemistry is still a crucial tool in surgical pathology diagnosis. It has four main uses in parathyroid tumours: detecting (1) parafibromin loss, (2) other signs of an abnormal immunophenotype suggesting carcinoma, (3) histogenesis of a neck mass, and (4) pathogenetic events, such as characteristics of the tumour microenvironment and immune landscape. The novel entity known as parafibromin-deficient parathyroid tumour, as specified in the WHO classification, must be identified using parafibromin stain (2022). Loss of parafibromin should prompt the search for inherited or somatic *CDC73* mutations since it raises the likelihood of a malignant course. When compared to benign parathyroid disease, parathyroid cancer exhibits an aberrant immunophenotype marked by the loss, upregulation or downregulation. Aberrant immunophenotype should spur the search for the conclusive criterion for carcinoma even though it is not the ultimate proof of malignancy. The measurement of Para Thyroid Hormone (PTH), chromogranin A, TTF-1, calcitonin, or CD56 can be useful in determining if a cervical or intrathyroidal mass is of thyroid *vs.* parathyroid origin. Finally, because it can show both the presence and the tissue location of specific proteins, immunohistochemistry is helpful in pathogenetic studies. In light of the most recent WHO classification (2022) of parathyroid tumours, the key indicators and difficulties are presented here.

Primary hyperparathyroidism, the traditional presentation of parathyroid tumours, ranks as the third most prevalent endocrine disorder. Primary hyperparathyroidism and parathyroid gland neoplasms are closely correlated in both directions. Primary hyperparathyroidism is typically brought on by parathyroid tumours. The presence of primary hyperparathyroidism is a characteristic of practically all parathyroid neoplasms, despite the fact that a few case reports have revealed the possibility of non-functional parathyroid tumours, primarily carcinomas.

Due to the fact that the majority of cancer registries focus on malignant entities whereas adenomas predominate in parathyroid tumours, the epidemiological characteristics of parathyroid neoplasms are also largely obtained from the data on primary hyperparathyroidism. In fact, 80%–85% of patients with primary hyperparathyroidism have adenomas.

The World Health Organization (WHO) has changed the pathology to multiglandular parathyroid disease at this time. Between 0.1% and 5% of all primary hyperparathyroidism patients are accompanied by parathyroid cancer. Although a substantially larger frequency of 5.2% (16 cases) has been documented in an Italian study of 290 surgically treated patients, it is believed to account for less than 1% of all cases in the Western world. As the diagnosis of parathyroid cancer can occasionally only be made through morphological analysis of surgical specimens, it is possible to anticipate that malignancy will develop more frequently in operated individuals than in the general population of people with primary hyperparathyroidism. The diagnosis and treatment of parathyroid mass lesions have made significant strides. First, the diagnostic paradigm has changed from clinically based suspicion or even difficult diagnosis in symptomatic patients to almost incidental findings routine biochemical laboratory assessment of serum calcium and Para Thyroid Hormone (PTH) levels as a result of growing awareness of parathyroid pathology and increased accessibility to laboratory and radiological evaluation. In fact, after the development of routine serum calcium testing, the prevalence of primary hyperpara-

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thyroidism increased significantly. The subsequent increase in occurrence has been linked to screening and comprehensive examination of osteoporosis patients using measurements of bone density together with evaluations of calcium and PTH levels to detect secondary osteoporosis.

Second, the field of parathyroid surgery is currently in its prime. Through the use of intraoperative parathyroid hormone testing, the indications, technology, and processes of operational intervention have all been well described. Currently, 97%-98% of patients who undergo parathyroid surgery are thought to recover fully. Finally, immunohistochemistry is still a crucial tool in the diagnosis of surgical pathology, including parathyroid tumours. Immunohistochemistry has four main uses in parathyroid pathology. To recognise the new WHO-defined entity, parafibromin-deficient parathyroid tumour, parafibromin must first be found. Loss of parafibromin raises the risk of a malignant course and should prompt testing for inherited or somatic *CDC73* gene abnormalities. Second, a number of markers that are either up- or down-regulated in benign parathyroid illness or down- or up-regulated in parathyroid carcinoma might help raise the suspicion of malignancy and trigger the search for the conclusive criterion for carcinoma.