



Surgical management of parathyroid glands; has the role of pathologists become redundant?

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The diseases of parathyroid glands are common in clinical practice and the histopathologists have a crucial role in classifying the underlying pathological condition (1). Traditionally, the pathologists were supposed to give an intra-operative assessment of the surgically removed specimen(s), but this approach is gradually being superseded by advancements in other diagnostic modalities, including imaging techniques, biochemical assays of rapid intra-operative assessment of parathormone (PTH) levels and surgical techniques (2,3). The adoption of minimally invasive parathyroidectomy has revolutionized the standard practice and operative strategies of bilateral neck exploration during parathyroidectomy for primary hyperparathyroidism (4). The need for routine frozen section confirmation has also been challenged with the availability of quick PTH assays. A significant decline in PTH level after excision of a suspected parathyroid adenoma may be confirmatory of operative success and provides the operating surgeons indirect evidence of removal of all hyper-functioning parathyroid tissue and may overcome the need for frozen section (5). However, it is not uncommon for the operating surgeons to send the parathyroid tissue to the pathologist for histological confirmation by frozen section examination despite the use of quick PTH assay because they are concerned about false-positive results and want tissue confirmation. In addition to the use of quick PTH assay in blood samples to confirm surgical success during parathyroid exploration, aspirate from excised parathyroid tissues for quick PTH assay can be performed expeditiously (5).

The role of pathologists in frozen section assessment of parathyroid tissue is twofold. The diagnostic assessment includes confirmation that the tissue removed is parathyroid versus, most commonly, lymph nodes, skeletal muscle, thymic tissue or thyroid, and in clinically and biochemically established diagnosis of hyperparathyroidism, establishing whether excised parathyroid glands represent hyperplasia or neoplasia (1). The confirmation of parathyroid tissue is straight forward in majority of cases, but sometimes it imposes difficulty

■ Implication for health policy/practice/research/medical education

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in demarcation between thyroid and parathyroid tissue; even, sometimes, it may not be possible, due to a striking overlap in the clinical, gross, and microscopic features (6). The second role is more challenging and fraught with difficulties.

The primary goal for intra-operative recognition of hyper-functioning parathyroid tissue is its critical impact on the management of patients with hyperparathyroidism (7). Frozen section has been widely used during these surgeries; however, accuracy of this procedure has been questioned. Error resulting from frozen section diagnoses is one of the significant factors leading to surgical failure (6). There are several confounding factors which may lead to formulation of incorrect diagnosis or deferred frozen sections, like frozen section artifacts, sampling errors, judgmental errors due to the coexistence of parathyroid and nodular thyroid disease, intra-thyroidal parathyroid glands showing conspicuous follicle formations or abundant oncocyctic cells, and thyroid nodules with fatty stroma. A careful histopathological examination in combination with gross inspection of the parathyroid glands by an experienced eye should contribute to adequate surgical treatment and minimize errors in operative management in patients with hyperparathyroidism (6,7). Despite of all the shortcomings, reported controversies among frozen section and final diagnoses and technical difficulties faced by pathologists, intra-operative assessment on frozen section plays a pivotal role in management of these patients.

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The commonest neoplastic lesion encountered by a pathologist in parathyroid gland is an adenoma, followed by an atypical adenoma and least commonly parathyroid carcinoma. Parathyroid hyperplasia is the most common non-neoplastic pathology seen after adenomas (2). There is a lack of well defined, precise histological definition of major parathyroid gland abnormalities, hence input from surgeons on preoperative findings and preoperative imaging techniques are mandatory to reach accurate diagnosis. Some surgeons may be indecisive about the role of pathologists in intra-operative assessment, but the most appropriate diagnosis can only be achieved by multidisciplinary teamwork approach of surgeons, endocrinologists, radiologists and pathologists (7). Both the surgeon and pathologist assigned to involve in the management should have keen and thorough appreciation of wide variability among normal parathyroid glands in regard to location, size, weight and histological characteristics. Furthermore, in an ideal situation, pathologist should personally visualize the parathyroid gland in situ and in agreement with the surgeon decide, which tissue would be appropriate for histopathological assessment. This facility is not widely available; pathologist should be thoroughly informed regarding anatomical site of tissue removal, number of enlarged glands, size, consistency and colour. The pathological assessment entails gross examination including size, weight, colour and consistency of the removed gland followed by microscopic examination with hematoxylin and eosin (H&E) stained frozen and permanent sections in adjunct to special stains for assessment of parenchymal and intracytoplasmic fat (6,8).

The two important criteria suggested in delineating among most common pathologies: adenoma versus hyperplasia, for pathologist are: 1) the lesion to be solitary involving single gland or occasional involvement of two glands; and 2) the lesion to be surrounded by a rim of compressed normal parathyroid gland. Despite of these suggestions, majority of pathologists believe that parathyroid adenoma and hyperplasia cannot be histologically distinguished with certainty, if only one gland is submitted (2,3). The histological verification of at least one other normal parathyroid gland is crucial to exclude hyperplasia. However, the possibility of focal hyperplasia and remote probability of double or even multiple concurrent adenomas are still debatable (7).

There are several studies in international literature which concluded that solitary enlarged parathyroid gland does not exclude hyperplasia, since 30-75% of patients with hyperplasia have single enlarged gland (7,9). The second suggested criterion described above is the one to which many pathologists give importance to distinguish among adenoma and hyperplasia but unfortunately this feature is also demonstrable in approximately 50-60% of adenomas. When this possibility is under consideration, pathologist

must be careful in interpreting it because any expanding space occupying mass lesion in parathyroid gland, whether neoplastic or hyperplastic, may lead to compression of surrounding structures and even a condensed fibrous pseudocapsule may be formed (9).

The role of pathologists in making precise histopathologic diagnosis could not be accomplished completely with gross and microscopic evaluation with routine H&E and tinctorial stains alone, since in modern parathyroid pathology, immunocytochemical methods and DNA determination may be integrated as useful adjunctive diagnostic tools in fine tuning the diagnostic categorizations (10). The use of proliferation markers has attracted increasing interest and DNA determination may also be of value in assessing the growth potential of parathyroid tumors. Although, majority of parathyroid adenomas are monoclonal but the remarkable role of application of molecular and genetic techniques in improving and further developing diagnostics in parathyroid pathology still remains to be seen.

In summary, it can safely be concluded that the role of pathologists has not become redundant in the surgical management of patients with parathyroid diseases, but has rather assumed more importance with advancements in molecular and genetic tests, which should be integrated with the traditional methods to make an accurate diagnosis of the parathyroid pathologies.

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