The Microscopical Pathology of Primary Parathyroid Hyperplasia

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ABSTRACT

The microscopical pathology of the two types of primary parathyroid hyperplasia is reviewed. The importance of the differential diagnosis between chief cell hyperplasia and adenoma is stressed. The problems of the surgical pathologist in making this differential diagnosis of a biopsy, especially on a frozen section sample, are discussed.

Primary parathyroid hyperplasia was first described in 1934.1 The original descriptions were of the clear cell type. Chief cell hyperplasia was recognized in 1958⁴ and is now the type of hyperplasia that is of greatest importance. Primary hyperplasia accounts for approximately 15 percent of the cases of primary hyperparathyroidism.³ The majority of cases are caused by single parathyroid adenomas.

Clear Cell Hyperplasia

This entity is characterized by the relatively uniform replacement of all the parathyroid glands by large cells with vacuolated amphophilic cytoplasm (figure 1). The cells are usually in sheets and clusters, but ribbons can be seen (figures 1 and 2). Fat and chief cells are absent.

Chief Cell Hyperplasia

In this variant of hyperplasia there is a diffuse or nodular, complete or partial replacement of all glands by chief cells or oxyphil cells or a mixture of both (figure 3). The cells may be in follicles, sheets or trabeculae. A variable amount of fat may be present in a very irregular distribution (figure 4). The variability of the pattern and the residual fat and nodularity may simulate a “rim of normal tissue” (figures 5 and 6) on a given section. Cysts with colloid-like material may also be present.

Discussion

The microscopic pathology of parathyroid hyperplasia assumes its greatest importance when the pathologist is asked to perform an intraoperative frozen sec-
tion to make the differential diagnosis between hyperplasia and adenoma. As the treatment of adenoma is removal of the involved gland while the treatment of hyperplasia involves subtotal removal of the entire parathyroid apparatus, the importance of the distinction is obvious. If one is dealing with clear cell hyperplasia, the diagnosis usually can easily be made on a small biopsy and appropriate parathyroid exploration and extirpation carried out. Unfortunately, for unknown rea-
sons, the frequency of clear cell hyperplasia has declined sharply in recent decades and it is now a rare disease.\textsuperscript{3} One is therefore usually faced with making the distinction between chief cell hyperplasia and an adenoma.

It is usually not possible to distinguish between an adenoma and chief cell hyperplasia on a sample of a single gland.\textsuperscript{2,3,4,5} The irregularity of the pattern of hyperplastic involvement can simulate a rim of normal tissue about an adenoma.

\textbf{Figure 3.} Chief cell hyperplasia, high power, uniform replacement of gland by sheets of chief cells.

\textbf{Figure 4.} Chief cell hyperplasia with residual fat, low power. Biopsy taken from left would be correctly interpreted; biopsy from area at right would be called normal.
The biopsy of an additional gland is usually requested. Difficulties can arise even with the second biopsy because the presence of residual fat in a small biopsy of a hyperplastic gland can cause an erroneous diagnosis of normal gland to be made on the second gland and, therefore, a diagnosis of adenoma to be made on the first. The gross appearance of a gland at operation is usually of no help since normally appearing glands can be microscopically hyperplastic.\(^2\)

**Figure 5.** Chief cell hyperplasia with apparent "rim of normal" on top. Biopsy of this entire area could be interpreted as an adenoma.

**Figure 6.** Chief cell hyperplasia, low power, of same field as (figure 5) showing connection between "rim of normal" and hyperplastic tissue.
Because of these uncertainties in parathyroid pathology, it has been suggested that biopsy at the time of exploration is optional. A final definitive diagnosis may only be possible after samples of all available parathyroid tissue are examined with careful chemical follow-up. The importance of follow-up is emphasized by the fact that 50 percent of cases originally classified as double adenomas were reclassified as hyperplasia upon review.

On a frozen section, the pathologist should be able to establish the presence of parathyroid tissue and generally distinguish between a normal gland and a hyperfunctioning gland, either chief cell hyperplasia or adenoma. The surgical procedure can range between a meticulous exploration of the entire parathyroid apparatus with or without biopsy and terminating the surgery with the removal of the first hyperfunctioning gland,—a procedure which will be adequate for the 85 percent of cases which are adenomas or carcinomas of a single gland. Subsequent follow-up will reveal those patients that have been inadequately treated in either case.

References