A middle-aged woman presented with elevated calcium (10.7 mg/dL [0.28 mmol/L]) and parathyroid hormone (131 pg/mL [4,663.6 pmol/L]) levels. A sestamibi scan exhibited a right upper parathyroid lesion. Parathyroidectomy revealed a 3152 mg right upper parathyroid gland and the intraoperative parathyroid hormone level decreased by 90% (from 27.1 to 2.6 pmol/L; reference range, 1.3-6.8 pmol/L). The lesion was removed intact without any “spillage.” Histology revealed hypercellular parathyroid with intravascular tumor clusters at the periphery of the main lesion. No necrosis or marked nuclear atypia was identified, and mitoses were rare (only 2 seen in the entirely submitted specimen). Parafibromin stain exhibited partial loss of nuclear reactivity in the tumor cells. The Ki67 proliferative index was less than 5% (see Figure 1).

Serial calcium measurements performed over the next decade were always within the normal range and then increased (10.8 mg/dL). The repeat calcium level 2 months later was 11.0 mg/dL. The next month the calcium level was 10.9 mg/dL and the parathyroid hormone level was 20.4 pg/mL. Ultrasound revealed numerous extrathyroidal nodules in the right central neck and a hypervascular lymph node in the right supraclavicular region.

The patient then underwent right thyroid lobectomy and right central neck lymph node dissection. The intraoperative parathyroid hormone level decreased from 25.0 to 10.7 pg/mL. Pathology revealed...
multifocal deposits of cellular parathyroid tissue, consistent with recurrent parathyroid carcinoma. The tumor deposits involved perithyroidal adipose tissue and skeletal muscle with extensive venous invasion (as seen on factor VIII staining). The tumor did not invade thyroidal tissue. The tumor cells exhibited retained parafibromin expression. The Ki67 proliferative index was approximately 5%. A separate incidental papillary thyroid microcarcinoma was also found (see Figure 2).

This case illustrates the diagnostic difficulty of parathyroid carcinoma and serves as a reminder that parathyroid carcinomas can recur, even many years after the primary tumor is excised. In fact, late recurrence or late distant metastasis, even after 20 years, have been reported in around 40% of patients in a series from the University of Texas MD Anderson Cancer Center, Houston.1 Additionally, as most, but not all, parathyroid carcinomas exhibit an elevated Ki67 proliferative index, the low percentage seen in this recurrence is an unusual feature. In difficult cases, an immunohistochemical panel including the assessment of the loss of parafibromin, APC, e-cadherin, p27, BCL-2a, MDM2, 5-hmC and positivity for hTERT, PGP9.5, galectin 3, and p53 can be useful in determining the malignant nature of these lesions.2,3 Moreover, parathyromatosis, a condition associated with parathyroid hyperplasia and often seen after surgery in which multiple foci of parathyroid tissue are deposited within the neck, can be considered but, as mentioned above, the original tumor in this case was resected intact and the venous invasion identified in both specimens was consistent with parathyroid carcinoma.

POTENTIAL COMPETING INTERESTS
The authors report no competing interests.

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