Hürthle (oxyphille) cell carcinomas comprise about 4% of all thyroid cancers. Hürthle cells are follicular epithelial cells that are larger than normal, with a large amount of granular, eosinophilic cytoplasm that is filled with mitochondria. These cells are found in a wide range of both non-neoplastic and neoplastic processes, including Hashimoto’s disease, as well as benign and malignant Hürthle cell tumors. To be classified as a Hürthle cell neoplasm, at least 75% of the tumor must be composed of oxyphille cells. Hürthle cell carcinoma is distinguished from a benign Hürthle cell tumor in the same way the follicular carcinoma is distinguished from a follicular adenoma: by the finding of neoplastic cells invading the tumor capsule or blood vessels within the tumor capsule. Hürthle cell tumors are usually classified as a subtype of follicular adenoma or carcinoma by the World Health Classification of tumors, but a few are Hürthle cell variants of papillary carcinoma.

HÜRTHLE CELL VARIANT FOLLICULAR CARCINOMA

Hürthle cell variant follicular carcinoma constitutes approximately 3% of thyroid cancers and approximately 20% of follicular carcinomas. The mean age at the time of diagnosis is about 55 years with a slight female predominance. A comprehensive review of the literature prior to 1997 related to the prognosis of Hürthle cell variant follicular carcinoma is presented in the book chapter by Ain that is cited in the reference section of this chapter. Multiple reports claim that the Hürthle cell variant has a worse prognosis than classic histology follicular carcinoma based on
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a higher risk of distant metastasis (~30% versus ~20%) and a higher diseases specific mortality (35–40% in some series). However, two more recent studies contradict the concept that Hürthle cell carcinoma has a worse prognosis when other variables are taken into account.

In a study by Hundahal et al. (1998), the 10-year cancer-specific mortality rates for patients operated on between 1985 and 1995 in the U.S. were 15% for follicular cancer and 25% for Hürthle cell carcinoma but outcome was similar when these two groups where matched for age and tumor stage. Similarly, the studies by Sanders and Silverman (1998) and Bhattacharyya et al. (2003) report no difference in outcome of patients with Hürthle cell carcinoma with low or high risk features compared to classic histology follicular carcinoma when patient age and tumor stage were taken into account. Bhattacharyya used a national database and multivariate analysis to compare the overall survival of 555 patients with nonmetastatic Hürthle cell carcinoma to a group of patients with classic follicular carcinoma matched for age, sex, tumor size, and local disease extension. Overall survival for Hürthle cell carcinoma was similar to that of comparably staged follicular cell carcinoma. Increasing age, male sex, and increasing tumor size substantially diminish survival in patients with Hürthle cell carcinoma.

Hürthle cell carcinoma can be a very aggressive tumor. In a recent large recent study by Lopez-Penabad et al. (2003), about 8% of 89 cases of Hürthle cell carcinoma were complicated by concurrent anaplastic thyroid carcinoma. Patients with Hürthle cell carcinoma tended to be older (51.8 vs 43.1 years) and to have larger tumors (4.3 cm vs. 2.9 cm) than those with Hürthle cell adenoma. Forty percent of the patients with Hürthle cell carcinoma died of tumor during follow-up and the authors found no improvement in disease-specific mortality in the past 5 decades for patients with these neoplasms. They found that older age and larger tumor size predicted reduced survival, and that I-131 therapy conferred a survival benefit when it was used for adjuvant ablation therapy, but not when residual disease was present. The authors could not demonstrate a survival benefit for the use of extensive surgery, external beam radiation therapy, or chemotherapy.

Hürthle cell carcinomas usually produce thyroglobulin but are generally less likely to concentrate radioiodine than follicular carcinoma. There are reports that the rate of radioiodine concentration in Hürthle cell carcinoma metastases is as low as 10%, while others report that 30% to 40% of distant metastases take up radioiodine.

HÜRTHLE CELL VARIANT PAPILLARY CARCINOMA

Many publications do not distinguish between the Hürthle cell variant of papillary carcinoma and the more common Hürthle cell variant of follicular carcinoma. The article by Berho and Suster (1997) is one of the classic references on the pathologic features of Hürthle cell variant papillary carcinoma.

A survey of the literature suggests that this variant accounts for approximately 3% of papillary carcinomas. The mean age at the time of diagnosis is about 50 years and there is a female predominance. As with Hürthle cell variant follicular carcinoma, there is controversy about the prognostic importance of Hürthle cell features in a papillary
carcinoma. The largest series on this subject is that by Herrera et al. (1992) in which the tumor recurrence rate at 10 years was almost three times higher for patients with the Hürthle cell variant papillary thyroid carcinoma than with classic papillary carcinoma (28% versus 10%). There is no series with age or stage-matched comparisons limited to the Hürthle cell variant of papillary carcinoma.

A “WARTHOLIN-LIKE” SUBTYPE OF HÜRTHLE CELL VARIANT PAPILLARY CARCINOMA

An unusual subtype of the Hürthle cell variant of papillary carcinoma was first described in 1995 by Apel et al. The distinguishing feature of this Hürthle cell tumor was a papillary carcinoma growth pattern with lymphoid aggregates in the tumor stroma. The histologic features are similar to that of the Wartholin’s tumor that commonly occurs in the salivary glands. The 13 patients in this series where free of disease 3 months to 9 years after treatment, which suggests that the prognosis is similar to that of classic papillary carcinoma.

TREATMENT OF HÜRTHLE CELL VARIANTS OF FOLLICULAR AND PAPILLARY CARCINOMA

Our approach to patients with the Hürthle cell variant of follicular or papillary carcinoma is the same as for poorly differentiated thyroid carcinomas, such as insular carcinoma. While these variants probably concentrate radioiodine less well that the classic form of papillary carcinoma, the management strategy is to use radioiodine therapy until it is clear that this is not a useful approach. This means that the treatment guidelines that we present throughout this book for well-differentiated thyroid cancer apply to patients with Hürthle cell variant carcinomas.

The only aspect of management that is different for patients with Hürthle cell variant carcinomas is that the threshold should be low for using a CT, MR, or PET scan to rule out the presence of recurrent disease following ablation of the thyroid remnant. The chance that Hürthle cell variant carcinoma will not concentrate radioiodine is high enough that imaging that does not involve radioiodine should be done whenever it is important to rule out gross tumor recurrence. In patients with Hürthle cell variant carcinomas, we obtain a CT, MR, or PET scan if symptoms suggest the possibility of a distant metastasis, or in a patient with markedly elevated thyroglobulin.

As we do for other forms of differentiated thyroid cancer, we give external beam radiotherapy to patients with Hürthle cell carcinoma when local-regional control cannot be achieved with I-131 therapy alone. The study by Foote et al. (2003) documents the efficacy of external beam radiotherapy for Hürthle cell carcinoma.

REFERENCES

