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External Beam Radiotherapy for Hürthle Cell Carcinoma of the Thyroid

JG Brabham, CG Morris, RJ Amdur, WM Mendenhall

Department of Radiation Oncology, University of Florida College of Medicine, Gainesville, Florida, USA

ABSTRACT

Objective: *To analyse the efficacy of external beam radiotherapy in patients with Hürthle cell carcinoma of the thyroid treated with curative intent.*

Patients and Methods: *Five patients received postoperative radiotherapy for suspected subclinical (3 patients) or gross residual (2 patients) disease after surgery. Patients were followed up from 15 to 72 months (median, 33 months).*

Results: *All the cancers were locally controlled. At last follow-up, 1 patient was alive and disease-free, 3 patients were alive with distant metastases, and 1 patient had died of intercurrent disease. No patient experienced a severe complication.*

Conclusions: *Hürthle cell carcinomas of the thyroid are likely to be radiosensitive, and external beam radiotherapy should be considered for patients with likely subclinical or gross residual disease after surgery.*

Key Words: *Hürthle cell carcinoma; Radiotherapy; Thyroid; Treatment outcomes*

INTRODUCTION

Hürthle cell carcinomas are rare and aggressive tumours of the thyroid. They comprise 2% to 10% of differentiated thyroid carcinomas, and are generally categorised as subsets of follicular thyroid cancer, although this classification is not universally accepted.[1,2] Histologically, Hürthle cell carcinomas are of epithelial origin and resemble oncocytomas found elsewhere in the body, with abundant, granular, eosinophilic cytoplasm filled with mitochondria.

Clinically, Hürthle cell carcinomas are distinguished from follicular and papillary carcinomas by a greater propensity for metastasis (33% versus 22% and 10%, respectively) and decreased survival (81% 5-year and 65% 20-year survival, versus 87% 5-year and 81% 20-year survival for follicular carcinoma, and 94% 5-year and 87% 20-year survival for papillary carcinoma).[3] Most recurrences occur in the neck, while most distant metastases occur in the lungs. Hürthle cell carcinomas are typically treated with a combination of thyroidectomy and radio-iodine (^{131}I), although most do not take up ^{131}I in therapeutic quantities.[4,5]

Historically, Hürthle cell carcinomas have been viewed as being poorly responsive to radiotherapy (RT),[4,6] although recent evidence suggests that this premise may be incorrect.[7] In this series, we analysed the University of Florida's experience with high-dose external beam RT for patients with Hürthle cell carcinoma.

PATIENTS AND METHODS

Five patients with histopathologically documented Hürthle cell carcinoma received external beam RT between January 1997 and July 2002. Four patients were treated with curative intent and 1 patient with a local recurrence and asymptomatic pulmonary metastases was treated with aggressive palliative RT. Two patients were men and 3 were women. The ages at presentation ranged from 47 to 77 years, with a median age of 68 years. Patients were retrospectively staged using the American Joint Committee on Cancer (AJCC) staging system. The extent of disease was determined by reviewing radiographic reports, operative reports, pathologic

Correspondence: *Dr WM Mendenhall, Department of Radiation Oncology, University of Florida Health Science Center, PO Box 100385, Gainesville, Florida 32610-0385, USA.*
Tel: (1 352) 265 0287; Fax: (1 352) 265 0759;
E-mail: mendewil@shands.ufl.edu
Reprints are not available.

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Table 1. Treatment and outcomes.

Patient	Year	Surgical margin	^{131}I	Total radiation dose (Gy)	Fractions	Dose/ fraction (Gy)	Fractionation	Treatment time (days)	Local control	Follow-up (months)	Status at last follow-up
1	1997	Positive	No	76.0	60	1.3	Twice daily	56	Yes	33	DID
2	1998	Close	No	74.4	62	1.2	Twice daily	44	Yes	72	AWD-DM
3	2000	Gross	Yes	68.4	38	1.8	Once daily	54	Yes	52	AWD-DM
4	2002	Gross	No	70.0	35	2.0	Once daily	50	Yes	23	AWD-DM
5	2002	Positive	No	66.0	33	2.0	Once daily	47	Yes	15	NED

Abbreviations: positive = microscopically positive margin; gross = gross residual disease; DID = dead of intercurrent disease; AWD-DM = alive with distant metastases; NED = alive with no evidence of disease.

reports, and physical examination documentation. One patient presented with an AJCC stage IVa tumour; 4 patients were treated for locally recurrent cancers. The 4 patients with locally recurrent tumours had all previously undergone total thyroidectomy followed by ^{131}I for 3 of the 4 patients. One of the 4 patients with a locally recurrent tumour had asymptomatic pulmonary metastases.

Work-up included history, physical examination, and computed tomography scans for all patients. All 5 patients underwent surgical resection and 1 received postoperative 100 mCi ^{131}I therapy. Two patients underwent total thyroidectomy without neck dissection. Three patients underwent extended thyroid resections with bilateral neck dissection, with 1 patient undergoing additional mediastinal dissection. Two patients had gross residual disease, 2 had microscopically positive margins, and 1 had very close margins. No patients received chemotherapy. Three patients were irradiated using 3-dimensional (3-D) conformal techniques, and 2 patients received intensity-modulated RT (IMRT). Two patients received twice-daily RT in 1.2 Gy fractions. The remaining 3 patients received daily RT with 1.8 to 2.0 Gy per fraction. The mean postoperative dose to the tumour bed was 70.9 Gy (range, 66.0 to 76.0 Gy). The median treatment time was 50 days (range, 44 to 56 days). One patient had a 4-day unplanned break in therapy. Table 1 shows the treatment and outcomes of the patients.

RESULTS

The overall median follow-up duration was 33 months (range, 15 to 72 months). No patients were lost to follow-up. Four of 5 patients were alive at the last follow-up; 1 patient had died of other causes with no evidence of cancer. All tumours were locally controlled. One patient treated at the time of local recurrence had pulmonary metastases and 2 additional patients developed distant metastases (thorax and brain in 1 patient and spine and femur in 1 patient). There were no severe (grade 3 or higher) treatment complications.

DISCUSSION

This study adds to the body of evidence suggesting that Hürthle cell carcinoma may be controlled with external beam RT. Foote et al recently reported that adjuvant radiotherapy prevented local recurrence in 4 of the 5 patients treated.[7] We reported an additional 5 patients treated with RT, all of whom maintained local disease control, despite 2 patients having gross residual disease and the remaining 3 patients having positive or very close margins. Four patients developed a local recurrence after prior resection and ^{131}I (3 of 4 patients) and only 1 of 5 patients received adjuvant ^{131}I in conjunction with external beam RT.

Although ^{131}I and surgery will likely remain one of the mainstays of treatment for Hürthle cell carcinoma, external beam RT should be considered for patients with a high risk of residual local-regional disease after surgery. Based on our experience with external beam RT for thyroid cancer, IMRT techniques are ideal to adequately treat the primary site and regional lymphatics.

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