# Clinical THYROIDOLOGY

# NECROSIS IN THE PRIMARY TUMOR AND LACK OF <sup>131</sup>I UPTAKE IN METASTASES PREDICT PROGRESSION OF METASTATIC THYROID CANCER

Deandreis D, Al Ghuzlan A, Leboulleux S, Lacroix L, Garsi JP, Talbot M, Lumbroso J, Baudin E, Caillou B, Bidart JM, Schlumberger M. **Do histological, immunohistochemical, and metabolic (radioiodine and fluorodeoxyglucose uptakes) patterns of metastatic thyroid cancer correlate with patient outcome?** Endocr Relat Cancer 2011;18:159-169.

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## **BACKGROUND AND METHODS**

The prognosis for thyroid cancer patients with distant metastases is worse if they are over 45 or if the metastases do not take up radioactive iodine (<sup>131</sup>I). This 5-year retrospective study surveyed a variety of possible prognostic features in 80 such patients who were followed for approximately 4 years (mean age at diagnosis, 55 years). All had had a total thyroidectomy and 54 had undergone lymph-node dissection. The distant metastases were diagnosed by <sup>131</sup>I whole-body scan, by computed tomography (CT) and/or by magnetic resonance imaging (MRI) during the initial evaluation of one fourth of the patients, but the metastases were found approximately 2.5 years later in three fourths of the patients, most in lung and/or bone. The primary tumor showed nonmedullary thyroid cancer with no undifferentiated components. All patients had a whole-body postablation scan with 100 mCi of <sup>131</sup>I, and those showing uptake in metastases were given 100 mCi every 6 to 12 months. In approximately 80%, a positron-emission tomography (PET)-CT scan with 18F-fluorodeoxyglucose (18 F-FDG) was performed within a year after the diagnosis of distant metastases, whereas the first PET-CT was done 2 to 10 years later in 20%. Patients with positive FDG scans were then followed annually with a PET scan, a CT scan, and/or an MRI.

#### RESULTS

Four patients had complete remissions after approximately 3 years of treatment with <sup>131</sup>I; all had distant metastases that took up <sup>131</sup>I but not FDG. On the other hand there was progression within 1 year in 16 patients: 15 had FDG-positive lesions (3 also had <sup>131</sup>I uptake), while 1 had FDG-negative but <sup>131</sup>I-positive lesions. At 2 years, there was 100% survival of those who had FDG-negative metastases, whereas only 60% of those with FDG-positive lesions had survived (70 to 80% survived if they had 1 to 10 lesions, but only 50% survived if they had more than 10 lesions). Of the 14 patients who died (median survival, 2 years), all had had FDG-positive metastases.

### CONCLUSIONS

Based on multivariate analysis, only two factors were independently related to progressive disease: the presence of necrosis (both focal and diffuse, but not otherwise defined) and the absence of <sup>131</sup>I uptake. Age and necrosis were associated with FDG uptake, number of FDG-positive lesions and the maximum FDG uptake value in the most-avid lesion. Other factors previously associated with tumor aggressiveness—such as the histologic subtype of the primary lesion (papillary, follicular, poorly differentiated), extracapsular extension, vascular invasion, size, and the number of nodes affected, as well as immunohistochemical markers related to iodine and glucose metabolism, angiogenesis, and cell growth did not have independent prognostic value.

### COMMENTARY • • • • • • • • • • • • • • • • •

Necrosis is a factor taken into account when assessing the cytologic grade of thyroid cancers. The current study indicates that necrosis in the primary tumor is an independent factor of poor prognosis in patients who have distant metastases. However, spontaneous necrosis (defined as an area of degenerating cytoplasm and punctuate karyorectic nuclear debris without evidence of fibro-blastic stromal reaction, hemorrhage or identifiable needle track) is not invariably associated with a poor prognosis (1). In 14 patients (mean age, 50 years) who had encapsulated thyroid follicular-cell tumors that showed some necrosis, 1 died of disease at

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6 years, 1 died of other causes at 11 years, 2 were alive with disease after 5 and 13 years, and the remaining 10 were alive with no evidence of disease with a mean follow-up of 10 years (1).

The authors found that the FDG positivity or negativity of distant metastases was not affected by whether the scan was done under TSH stimulation or under TSH suppression. However, the delay between when the distant metastases were found and when the initial FDG-PET-CT scan was performed raises concerns. (There can be discrepancies between repeat FDG scans, with a spontaneous shift from positive to negative (2), and some data indicate that higher TSH levels can increase FDG positivity).

Only 5% of the patients in this study had a complete remission following therapy with <sup>131</sup>I. This could reflect a selection bias because patients with aggressive disease may have been preferentially referred to this center to obtain access to their advanced research protocols and technology.

#### - Stephen W. Spaulding, MD

### References

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