1. INTRODUCTION

Thyroid cancer, the most common endocrine malignancy, accounts for 1.1% of all the newly diagnosed malignancies in the United States (1). It occurs three times more commonly in women. Its annual incidence has increased over the last few decades, possibly in part owing to improved diagnosis and cancer registration (2). However, the mortality rates owing to thyroid cancer have decreased by 20% between the years 1973 and 1996, because of early diagnosis, and better surveillance and treatment.

The various types of thyroid cancers are listed in Table 1 (3). Differentiated thyroid cancers (DTCs), which include papillary and follicular thyroid cancers, comprise 90% of all thyroid cancers (4). They originate from the follicular cells of the thyroid. They are also responsible for 70% of the mortality owing to thyroid cancers. Because papillary and follicular thyroid cancers are the main types, and are treated in a similar fashion, most of the subsequent discussion will be centered on these, while highlighting the difference between the two.

1.1. METASTATIC BONE DISEASE

Thyroid cancer can spread to lymph nodes or metastasize to distant sites such as lungs, bones, liver, and brain. Only 1 to 3% of the patients have distant metastasis at the time of initial diagnosis (5). Seven to twenty-three percent of the patients develop distant metastasis during their lifetime. Bone metastasis occurs in 4 to 13% of the cases (5–7). Half of these patients have bone metastasis at the initial presentation. One-third to half of those with bone involvement have multiple bone metastases, and one-third have other site involvement (5,7,8). Bone involvement can be a risk factor for occurrence of cerebral metastasis (9). Vertebrae are the most commonly affected site for bone metastasis, occurring in nearly 50% of the patients, followed by pelvis, ribs, femur, skull, humerus, clavicle, and scapula (5).

Two-thirds to three-fourths of all bone metastasis are symptomatic. Symptoms usually include pain and/or swelling, but may also include fractures (in 5% of the patients) and cord compression (3.5%). The “visible” bone metastasis are invari-
ably osteolytic lesions (7), although osteosclerotic lesions have also been reported (10). Of patients with bone metastasis, 28–60% present with symptoms related to bone metastasis (5,7,8).

All symptomatic lesions are visible on radiographic studies (5,8). The remaining bone metastases may be picked up by other imaging techniques like radioactive 131I whole body scan, 99Tc bone scan and sestamibi scan. The majority of patients with bone metastasis (86–93%) have follicular thyroid cancer, with the rest being papillary thyroid cancer (7,8). However, Tickoo et al. (11) reported that among patients of thyroid cancer with bone involvement seen at a tertiary referral center, 28% were papillary, 22% follicular, 20% insular, 13% anaplastic, 11% Hurthle cell, and 6% were medullary cancer. Two-thirds of these patients had similarly differentiated and one-third had better differentiated metastatic tumor as compared to the primary tumor. The patients with bone metastasis also tend to be older at the time of diagnosis, 87% being older than 45 yr of age (5). Metastatic thyroid tumors may rarely synthesize thyroid hormone (12).

1.2. SPINE

As previously mentioned, the spine is a frequent site of bone metastasis for thyroid cancer. About 12% of consecutive patients with spinal metastasis were reported to be from thyroid cancer (13). However, in an autopsy review of 140 cases of vertebral metastasis reported in 1975, only 1 case of thyroid cancer was reported (14). The spinal metastasis can be asymptomatic; or can cause spinal cord compression (15,16), which can present as Brown-Sequard syndrome (17) or distal cord compression (18). DTC can also metastasize to the epidural space without vertebal involvement (19), or cause isolated enlargement of intervertebral foramen (20), or present as intramedullary spinal cord metastasis (21). Spinal metastasis can also present as paravertebral mass (22) or can extend extraspinally (23).

2. CLINICAL EVALUATION

The diagnosis of thyroid cancer is usually confirmed by fine-needle aspiration of the thyroid (24). Other evaluations include clinical assessment of the extent of lesion by palpation of the thyroid, carotids, sternocleidomastoids, and lymph nodes, and by ultrasound. Indirect laryngoscopy is performed to evaluate vocal cords and, thereby, recurrent laryngeal nerve involvement. If lymph nodes are present, needle aspiration of the lymph nodes may be carried out.

Staging of the thyroid cancer is important for risk-stratification and prognostication. Staging is based on the tumor-node-metastases (TNM) system (Table 2) (25,26). Age is an important part of staging as it is a significant factor in the determination of prognosis, prognosis being better in patients younger than 45 yr of age.

3. PROGNOSTIC FEATURES

The outcome of thyroid cancers can be assessed in terms of long-term survival and recurrence rate of the cancer with treatment. Mortality is higher in patients who are over 40 yr of age at the time of diagnosis. Recurrence rates are high when age of diagnosis is less than 20 yr or more than 60 yr (26,27). Although men develop thyroid cancer less frequently, they have twice the mortality as compared to women. In fact the decline in mortality over the last couple of decades has been seen only in women (2). Other poor prognostic factors include: a family history of thyroid cancer, tumors less than 4 cm in diameter, bilateral disease, extrathyroidal extension, vascular invasion, regional lymph node involvement, presence of nuclear atypia, tumor necrosis, and distal metastasis (26). Tumors that do not or poorly concentrate radiiodine have poorer prognosis. Follicular thyroid cancers seem to have more distant metastasis as well as higher mortality as compared to papillary thyroid cancers (28). Hurthle cell, tall cell, columnar cell, diffuse sclerosis, and insular variants do poorly, as opposed to encapsulated papillary, papillary microcarcinoma, and cystic papillary variants, which have moderate to low risk. Other types such as undifferentiated, anaplastic, and medullary carcinomas have worse outcomes.

3.1. PROGNOSTIC VARIABLES AMONG PATIENTS WITH METASTASIS

Among the patients of thyroid cancer with distant metastasis, patients with bone metastasis have worse prognosis (29). Long-term, patients with lung metastasis do better than patients with bone involvement (30). Patients who had metastatic tissue with radioactive iodine uptake had better survival as compared to those with metastatic tissue that did not take up iodine (5,29). Among the subgroup of patients with metastatic disease, older patients and follicular tumors had poorer prognosis.

Among the patients with bone metastasis, detection of metastasis as a revealing symptom of thyroid carcinoma, absence of nonosseous metastases, radiiodine uptake, and Hurthle cell subtype seemed to be associated with improved prognosis (5,6). There seems to be no difference in survival in patients with single bone lesion compared to those with multiple bone lesions (5).