3. THYROID LYMPHOMAS

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INTRODUCTION AND HISTORICAL ASPECTS

Primary thyroid lymphomas have been recognised for many years and have been documented from the 1940s and 1950s. It was deemed to be important to recognise this entity "for it seems that about a third of the cases may be treated successfully with X-rays, followed by maintained thyroid medication" (1). Thus, the importance of separating lymphomas from its mimics, namely, chronic thyroiditis and small cell carcinoma, was evident at an early stage because of the therapeutic implications. Indeed, the histological difficulty in separating lymphoma from chronic thyroiditis and small cell carcinoma, no doubt led to the under-diagnosis of lymphoma. Even 50 years and more ago, certain peculiarities of thyroid lymphoma were apparent to pathologists: the predilection for elderly women, long survival and the tendency for similar lesions to occur in the gastrointestinal tract. These lymphomas were so characteristic that Brewer and Orr coined the term "struma reticulosa" to describe them (2). The fact that primary and secondary lymphomas could occur in the thyroid was accepted and sporadic papers on the subject, including the occasional large review, appeared in the literature (3). It was not until the early 1980s that primary lymphomas of the thyroid gland came under scrutiny again and was the centre of intense research. The introduction of the mucosa associated lymphoid tissue (MALT) concept led to the critical examination of primary thyroid lymphomas and similar appearing lymphomas with the seminal work of Isaacson and Wright responsible for the crystallization and clarification of the pathogenesis and morphology of these lymphomas (4–6). It is now clear that MALT

and lymphomas arising from these sites share morphological, immunophenotypic and molecular features to the extent that MALT-lymphomas can metastasize from one MALT site to another.

INCIDENCE

Lymphomas occurring primarily in the thyroid are decidedly uncommon, accounting for about 5% of all thyroid malignancies (7–10). This figures increases to 10% of thyroid malignancies in certain geographic locales where antecedent chronic thyroiditis is common (10, 11). Primary thyroid lymphomas constitute 2.5 to 7% of all extranodal lymphomas (12–14).

It is stated that 25 to 100% of thyroid lymphomas arise against a background of thyroiditis, either chronic lymphocytic or Hashimoto's thyroiditis (15–18). This association is so strong that the relative risk of a patient with chronic thyroiditis developing lymphoma of the thyroid is 40 to 80 times greater than the general population (14, 19, 20). The lymphomas evolve after a prolonged period, usually 20 to 30 years after the onset of chronic lymphocytic thyroiditis (14).

CLINICAL PRESENTATION

Women are more frequently affected than men with a ratio of 2.5 to 8.4: 1. Most patients are in the 50 to 80 year age range. There is usually rapid enlargement of an already existing goitre, and the mass may extend extra-thyroidally. The rapid growth and extent of invasion may result in dysphagia, hoarseness and dyspnoea (3, 16, 21). Thyroid function is usually normal but hypothyroidism has been documented in a minority of cases (11, 22). If hypothyroidism is present, it is usually due to the pre-existing thyroiditis and not due to the obliteration of thyroid parenchyma by the lymphomatous infiltrate. Very rare cases of hyperthyroidism have been encountered where rapid destruction of thyroid follicles with release of colloid and thyroid hormone into the circulation, have been implicated as causative (23, 24).

NOMENCLATURE AND TERMINOLOGY

In the last 10 or so years lymphoma classification has undergone a major revision with the appearance of the Revised European-American Lymphoma (REAL) classification (25–27) and the subsequent World Health Organization (WHO) update, refinement and minor modification of the REAL classification (28–34). After Isaacson and Wright brought the concept of MALT and lymphomas arising therefrom to prominence, the terms MALT lymphoma or lymphoma arising in MALT or "MALT-oma" have been used. The advent of the REAL/WHO classifications led to a re-appraisal, and these peculiar and characteristic lymphomas were categorized as: extra-nodal marginal zone B-cell lymphomas (MZBL) of MALT-type. This is the prototype lymphoma occurring primarily in the thyroid. Variants and other common related lymphomas will be discussed.

TYPES OF PRIMARY THYROID LYMPHOMA

As mentioned above the most morphologically distinctive and recognizable (but not necessarily the commonest variant encountered) primary lymphoma is MZBL of