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Angiocentric T-cell lymphoma: an extensive lesion involving the posterior tongue, hypopharynx and supraglottis

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Abstract
Angiocentric T-cell lymphoma, which in the past has been grouped with a variety of granulomatous diseases, occur uncommonly as a destructive condition of the posterior nasal space and midface. We report on a patient with a chronic granular ulcerative lesion involving the posterior tongue, hypopharynx and supraglottis.

Key words: Lymphoma, T-cell; Hypopharynx; Larynx

Introduction

Previously progressive ulcerative and destructive diseases of the midface and nose have been called a variety of names. These midline granulomatous conditions can be subdivided into aetiological groups. They include infective diseases (tuberculosis, syphilis, fungal infections, etc.), vasculitides in particular Wegener's disease and neoplastic conditions. Lesions not classifiable in this framework were considered idiopathic. Technological advances have allowed more accurate diagnosis causing this idiopathic group to progressively diminish or disappear (Barker and Hosni, 1996). A number of these lesions are now regarded as angiocentric lymphomas (Norton, 1994).

Previously reported angiocentric lymphomas in this area are rare. Ho *et al.* (1984) in the largest series of 294 patients from Hong Kong described six lesions involving the tonsil. Borisch *et al.* (1993) describe a single lesion of the hypopharynx while Smith *et al.* (1996) noted a laryngeal lesion in a patient with acquired immunodeficiency syndrome (AIDS).

Case report

A 68-year-old female had been in the care of a private ENT surgeon for six months with a granulomatous ulcer of the left posterior tongue. The lesion had been examined under anaesthesia, biopsied and treated with oral steroids to which it showed an initial response. The biopsy had shown a chronic inflammatory infiltrate of plasma cells, lymphocytes and histiocytes with no evidence of malignancy. The patient, who was a non-smoker and had no medical history of note, was then referred to the Department of Otolaryngology, Groote Schuur Hospital, to establish a diagnosis and to continue management.

When the patient was first seen in our department, an infected ulcer at the base of the left tonsil was identified and a small ipsilateral jugulodigastric lymph node was palpated. The white cell count was normal, but the ESR was elevated to 37 mm/hr. Serological testing for syphilis and HIV were negative and a chest X-ray and urinalysis were normal. Examination under anaesthesia revealed a granular punched-out ulcer involving the base of the left tonsil, the lateral pharyngeal wall and the left base of tongue extending into the left vallecula. Tissue biopsies and an excision biopsy of part of the posterior faucial pillar were sent for histological and bacteriological analysis. Histology showed inflammatory changes with no evidence of malignancy and tissue culture for tuberculosis was negative.

The lesion gradually settled, but the patient presented again six months later with similar symptoms and an ulcerative lesion in the left posterolateral tongue. Biopsy again revealed nonspecific inflammatory infiltrate without evidence of malignancy. A Mantoux skin test for tuberculosis was negative. The patient was treated with short courses of steroids and antibiotics over the following four months with intermittent improvement. In this period the antineutrophil cytoplasmic antigen (ANCA), rheumatoid factor and collagen vascular screens were repeatedly negative.

Three months later the patient presented with weight loss, hoarseness and mild stridor. The lesion was re-examined under anaesthesia and was found to have extended to involve the left piriform fossa and the left supraglottis and had destroyed most of the epiglottis. Thyroid function tests were normal but the ESR was now 60 mm/hr. Deep biopsies of the supraglottic larynx showed inflammatory changes without tuberculous or fungal involvement. The stridor initially settled on steroid therapy, but six weeks later a tracheostomy became necessary. Further biopsy with specific culture excluded both histoplasmosis and toxoplasmosis. Microscopy showed non-specific inflammation with overlying ulceration the appearance of which did not suggest a lymphoproliferative disorder. Protein electrophoresis showed no abnormal proteins and normal levels of specific immunoglobulins.

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The patient was given a trial of cytotoxic therapy using cyclophosphamide, but whilst under physician care she developed pneumonia and died. The diagnosis of angiocentric T-cell lymphoma was made from tissue obtained at postmortem. Previous sections submitted for histology were reviewed, revealing necrotic ulceration with inflammatory infiltrate only. The time period from initial presentation to death was two years.

Pathology

Post mortem examination of the hypopharynx revealed a large ulcerative and destructive lesion. It extended from the base of the tongue to the level of the vocal folds. The epiglottis was completely destroyed (Figure 1). Apart from an extensive bronchopneumonia which was responsible for the demise of the patient, the remainder of the autopsy was essentially non-contributory. No prominent lymph nodes or metastatic carcincoma was identified.

Routine haemotoxylin and eosin stained paraffin sections showed surface ulceration with underlying necrosis admixed with an inflammatory infiltrate. A vasculitis with nuclear dust and fibrinoid necrosis was identified with numerous atypical lymphoid cells located around these vessels (Figure 2).

Selected slides were subjected to immunohistochemical analysis. The pleomorphic angiocentric lymphoid population stained positive to an antibody to the CD3 antigen, identifying these cells as being of T-lymphocyte lineage. Other lymphoid markers, including the natural killer (NK) cell antigen (CD 56) were negative. T-cell receptor gene rearrangement studies failed to confirm clonality.

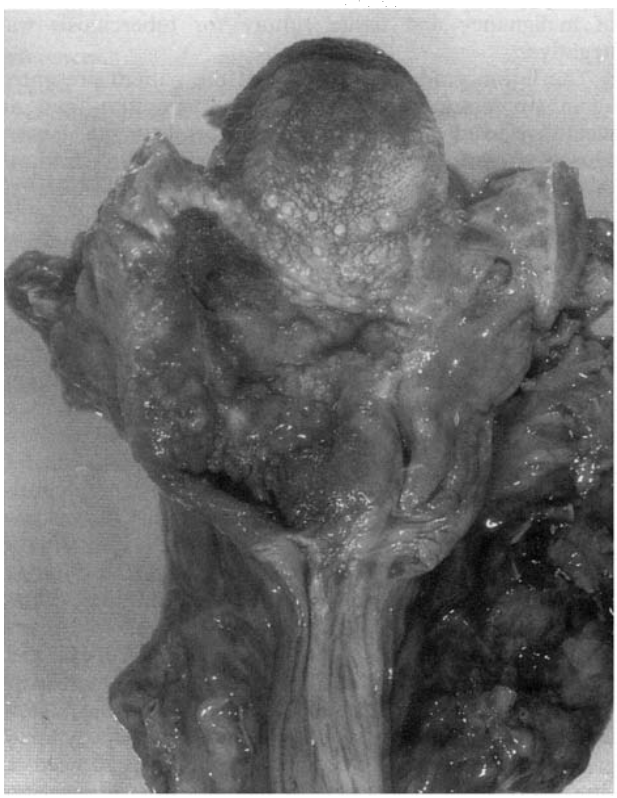

FIG. 1

Posterior view of larynx, hypopharynx and posterior tongue showing a large destructive ulcer (post mortem)

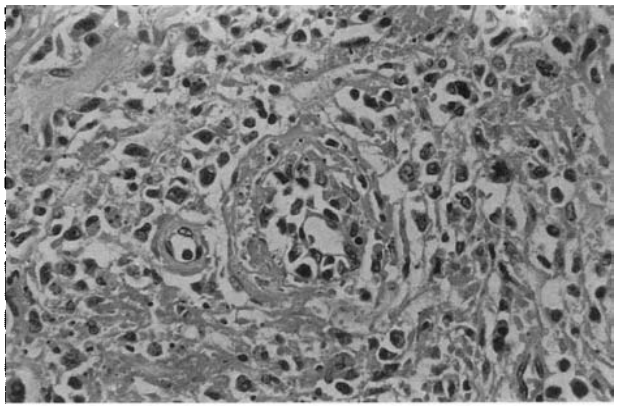

FIG. 2

Routine haemotoxylin and eosin stained paraffin section of tumour showing atypical lymphoid cells infiltrating a vessel (200 × magnification, ZEISS microscope – camera).

Discussion

The diagnosis proved to be elusive despite having excluded most of the possible differentials. Normal chest radiography, repeatedly normal urinalysis and the lack of histological granulomata made conditions such as Wegener's granulomatosis, sarcoid, syphilis, tuberculosis and mycotic conditions unlikely. Syphilis and tuberculosis, which occur commonly in Cape Town, were further excluded by serology and skin testing. Collagen vascular diseases were considered but, in the light of negative screening tests and lack of histological evidence, were also excluded. Midline granuloma had been considered, although the unusual location and unconvincing histological picture made this a dubious choice. A scenario of treating a condition without a diagnosis arose.

Historically, as early as 1897 McBride described the first case of rapid destruction of the nose, but the syndrome of relentless ulceration and destruction of the nasal and midfacial structures was first recognized by Stewart in 1933. The pathology of Stewart's original 10 cases was heterogeneous and it is now clear that a number of different disorders cause midfacial destruction, particularly vasculitic, granulomatous and inflammatory conditions. The term 'polymorphic reticulosis' was used by Eichel *et al.* (1966) to describe primary nasal lymphoma in which the histological features were similar to those described by Stewart. Notable features were a mixed inflammatory infiltrate with perivascular accumulations of atypical lymphoid cells typically angiocentric and often angiodestructive. Developments in immunophenotypic and molecular analysis showed that the cells in the polymorphic reticulosis group of disorders were of T-cell origin (Ishii *et al.*, 1982). Other malignancies can also however cause midfacial destruction, viz. epithelial carcinomas, melanoma or B-cell lymphoma (Grange *et al.*, 1992). The collective term angiocentric immunoproliferative lesions (AIL) was proposed by Jaffe (1984) and Medeiros *et al.* (1992). A spectrum exists in AIL with increasing atypia including polymorphic reticulosis and lymphomatoid granulomatosis progressing to overt lymphoma at the malignant end of the continuum.

Recent work has also shown that these lesions have a deficient T-cell phenotype (Ho *et al.*, 1990). They frequently fail to express the β-heterodimer-CD3-antigen complex and do not show molecular gene rearrangement of the T-cell receptor (Kanavaros *et al.*, 1993). There can, however, be expression of other markers including; HLA-DR, CD25 and CD56 or the natural killer (NK)

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cell antigen (Ng *et al.*, 1987). This suggests that these lesions are of NK origin rather than of T-cell lineage as previously thought (Borisch *et al.*, 1993). Using polymerase chain reaction (PCR) amplification the Epstein-Barr virus (EBV) genome, particularly the subtype 2, and gene products have been found in neoplastic cells in the majority of upper airway lesions (Borisch *et al.*, 1993). Minarovits *et al.* (1994) isolated a single terminal EBV DNA fragment in six angiocentric lymphomas tested, representing clonal proliferations of cells infected with EBV on a single occasion.

Angiocentric T-cell lymphoma does occur outside the posterior nasal region, as in this case. Representative biopsy material and good interaction with the pathologist is important. Although not always possible, a diagnosis should be sought prior to commencing a treatment course.

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