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Pathology in Focus

Laryngeal involvement by cutaneous lymphoma

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Abstract
Laryngeal involvement by cutaneous lymphoma is rare; it may be isolated or part of systemic spread. We report a case of cutaneous T-cell lymphoma with isolated extracutaneous spread to the larynx, confirmed by the polymerase chain reaction in addition to histology. Awareness of this association may allow early recognition of symptoms heralding laryngeal embarrassment.

Key words: Lymphoma, T-cell, Cutaneous; Laryngeal neoplasms

Introduction

Primary cutaneous T-cell lymphomas represent a heterogeneous group of T-cell lymphoproliferative disorders that originate in the skin and, after a variable period of time, may progress to involve lymph nodes, peripheral blood and/or visceral organs (Scheffer *et al.*, 1986). Lymphoproliferative infiltration of the larynx is rare (Wells *et al.*, 1995). It may occur as a primary extranodal disease or as a feature of multifocal disease. When the primary site is skin, subsequent laryngeal involvement may be either part of a widespread systemic disease or it may be the first manifestation of subsequent systemic spread.

The incidence of cutaneous lymphomas is about one to two per cent of lymphomas (Kim and Dorfman 1974). Documentation of isolated subsequent laryngeal involvement is rare and review of the English-language literature reveals only six previous case reports citing this occurrence. Five of these case reports are of the commoner variant of cutaneous T-cell lymphoma, mycosis fungoides (MF)/Sézary syndrome (SS) (Hood *et al.*, 1979; Agarwal *et al.*, 1982; Fertilo *et al.*, 1986; Gordon *et al.*, 1992; Kuhn *et al.*, 1992). There is only one report of cutaneous B-cell lymphoma spreading to the larynx in isolation (Wells *et al.*, 1995). This association between cutaneous lymphoma and laryngeal involvement is worth documenting, since symptoms referable to the larynx may be easily overlooked. We report a case in which the laryngeal involvement was the first sign of visceral manifestation of the disease.

Case report

A 69-year-old woman who had a history of ischaemic heart disease with atrial fibrillation and psoriasis presented in December 1995 with a lesion on her left shin. This was subsequently diagnosed as a high-grade pleomorphic T-cell lymphoma of the skin (peripheral T-cell lymphoma, unspecified-REAL classification). Computed tomography (CT) scan showed no evidence of any lymphadenopathy or spread to other organs. Because of her heart disease she was treated with a chemotherapy regime that was less cardiotoxic than usual. Her treatment consisted of six courses of C-NOP (cyclophosphamide, nitrozanterone, vincristine and prednisolone) over the next five months. The initial response to the chemotherapy was brisk and complete, but she soon had a recurrence of smaller maculopapular lesions in the adjacent skin, which surprisingly regressed spontaneously. Her lesions over the left tibia reappeared three months later. She was treated with two courses of ifosfamide/MESNA/etopside followed by local radiotherapy. After receiving 3500 cGy in 20 fractions the lesion over her left tibia regressed, but she developed multiple lesions over her right leg and left forearm. During her admission for the recurrence of the skin lesions she developed stridor and was referred to the ENT department. On examination of her larynx, there was a swelling over the right supraglottic region obscuring visualization of the vocal fold. A bronchoscope could not be passed beyond the tumour. CO_2 laser excision of the lesion revealed extension into the subglottic region, but no inferior extension into the trachea. An emergency tracheostomy was done. A palliative dose of radiotherapy was given. She received 2000 cGy in five fractions over seven days to the anterior neck. The condition of the patient deteriorated over the next three months and she died in June, 1998, approximately two and a half years after the initial diagnosis.

Pathology

Biopsy of the initial skin lesion showed an intense multifocal lymphoid infiltrate within the dermis (Figure 1) extending into subcutaneous fat. The epidermis was not involved by the infiltrate. The infiltrate was forming diffuse sheets although in areas it was accentuated around vessels and appendage structures. The infiltrate for the most part was composed of irregularly shaped blast cells admixed with intermediate and smaller convoluted cells (Figure 2).

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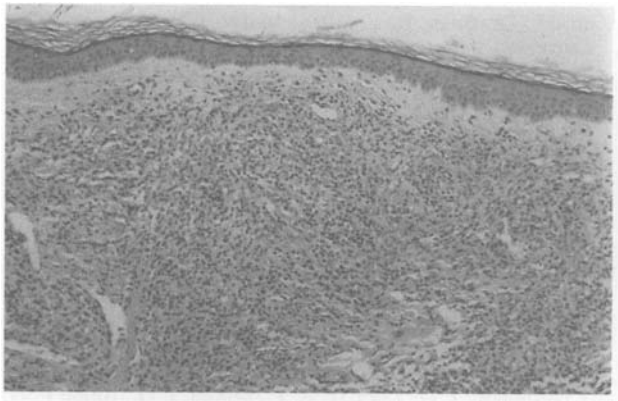

FIG. 1

Skin biopsy. There is diffuse infiltration of the dermis by lymphoid cells (H&E; × 100).

Mitotic activity was high with up to five mitoses per single high power field. In the deeper part of the biopsy within the subcutaneous tissue confluent sheets of large blast cells were present. A histiocytic reactive population was also present within the lesion. Immunocytochemistry showed the cellular infiltrate to be predominantly T-cell in type. A small number of B-cells and plasma cells were present. The tumour cells were negative for the Ki 1 antigen (CD30). The features were that of a high-grade pleomorphic T-cell lymphoma (peripheral T-cell lymphoma, unspecified-REAL classification). The subsequent laryngeal biopsy showed that pleomorphic large lymphoid cells, which stained immunocytochemically as T-cells, infiltrated the lamina propria (Figure 3). There was focal infiltration of the squamous epithelium. The infiltrate was similar to that seen in the previous skin biopsy. The polymerase chain reaction showed a similar T-cell gene rearrangement in both the cutaneous tumour and the laryngeal recurrence (Figure 4).

Discussion

For many years, MF and SS were the only well known entities in the group of cutaneous T-cell lymphomas. The application of monoclonal antibodies to the diagnosis of cutaneous lymphomas has resulted in the recognition of an increasing group of cutaneous T-cell lymphomas that do not meet the criteria for classical MF, SS or related conditions (Willemze *et al.*, 1994). Cutaneous T-cell lymphomas other than MF/SS represent approximately 30 per cent of all cutaneous T-cell lymphomas. Non-MF/SS

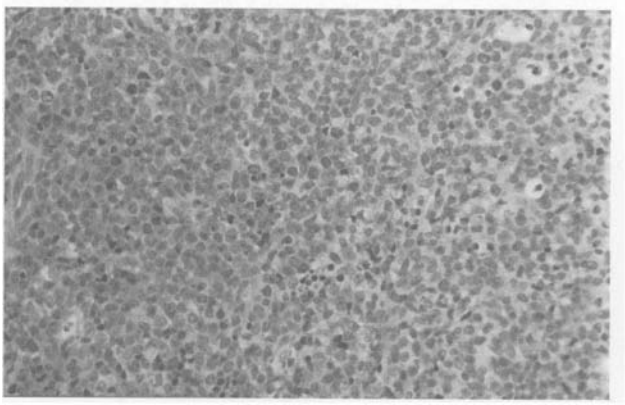

FIG. 2

Skin biopsy at higher magnification. This shows the pleomorphic nature of the lymphoma cells, with many blast forms (H&E; × 250).

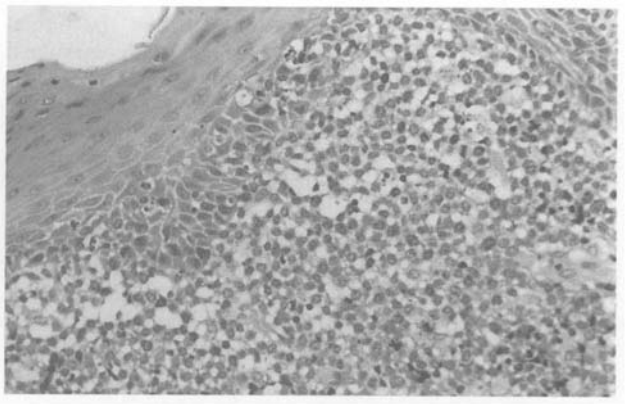

FIG. 3

Laryngeal biopsy. Lymphoma cells similar to those in the skin biopsy diffusely infiltrate the lamina propria. (H&E; × 250).

lymphomas include CD30 positive anaplastic lymphomas, which have a more favourable prognosis despite being classified as high grade (Willemze *et al.*, 1994).

Hood *et al.* (1979) reported the first case of primary laryngeal MF, initially interpreted as an undifferentiated malignant neoplasm. After two years and three months the cutaneous lesions appeared, and MF was diagnosed. Another case of primary laryngeal MF was reported by Agarwal *et al.* (1982) without follow up. Ferlito and Recher (1986) reported the laryngeal tumour as the first visceral manifestation of the disease, with later widespread dissemination to lung, liver, and lymph nodes. Kuhn *et al.* (1992) presented two cases of laryngeal MF, one of whom presented with vocal fold paresis (progressing to paralysis). Gordon *et al.* (1992) reported a case of laryngeal involvement of MF as the earliest extracutaneous manifestation. The patient later developed evidence of leptomeningeal MF. Wells *et al.* (1995) described the only case of a cutaneous B-cell lymphoma with isolated relapse in the larynx. Complete remission of the primary lesion was attained with local radiotherapy, and a second complete remission with chemotherapy.

There are few published reports on cutaneous T-cell lymphomas other than MF, SS and the group of CD30 positive lymphomas. The prognosis of MF and CD30 negative cutaneous lymphomas is poor once dissemination has occurred (Block *et al.*, 1963; Merlo, 1987; Suasville *et al.*, 1988; Willemze *et al.*, 1994). In all six cases of cutaneous T-cell lymphoma presenting in the larynx that were followed up (Hood *et al.*, 1979; Ferlito and Recher, 1986; Gordon *et al.*, 1992; Kuhn *et al.*, 1992), the patient

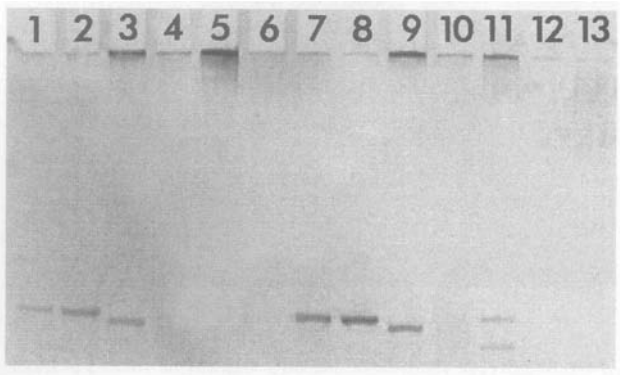

FIG. 4

Polymerase chain reaction results. Lanes 1 and 7 correspond to the skin biopsy, lanes 2 and 8 correspond to the laryngeal biopsy and lanes 3 and 9 are the positive control. Both the biopsies show a similar T-cell gene rearrangement.

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died between a year and six years after the initial diagnosis. The only reported patient with laryngeal involvement by cutaneous B-cell lymphoma had been followed for only a year at the time of reporting (Wells *et al.*, 1995). It was suggested that survival in this case was due to a difference in the behaviour of T- and B-cell lymphomas, but it may simply reflect the short follow-up period.

The incidence of laryngeal involvement in patients with cutaneous lymphoma is low, as a result of which symptoms referable to the larynx may be easily overlooked in the early stages. The mildest of symptoms should be treated with a high index of suspicion in order to prevent embarrassment of the airway.

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