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Tumour regression predicts higher risk of sentinel node involvement in thin cutaneous melanomas

SIR, Metastatic involvement of regional lymph nodes is one of the most important prognostic factors in cutaneous malignant melanoma (CMM).[1,2] The sentinel lymph node biopsy (SNB) has become widely established in several countries as a technique for prognostic assessment. The surgical procedure is not complicated and carries relatively low morbidity; however, the indications for SNB are still a matter of debate.

Although metastatic involvement in patients with very thin primary melanoma is rare, there have been several reported cases.[3,4] Melanomas showing histological evidence of regression are in some cases associated with a worse clinical course than similar but nonregressing tumours.[5–7] We therefore examined the correlation of primary melanoma regression and sentinel node positivity in patients with thin melanomas.

One hundred and thirty-four patients with melanoma with a primary tumour thickness of 2·0 mm or less underwent SNB at the Department of Dermatology, University of Szeged, between 1 January 1999 and 31 December 2000. Following preoperative lymphoscintigraphy (Tc-99m nanocoll) and lymphatic mapping, sentinel nodes were successfully identified in all cases using both blue dye and radiolabelled colloid with a gamma probe.[8–10] Both primary tumours and sentinel nodes were analysed histologically in serial sections of paraffin-embedded specimens using haematoxylin and eosin staining and immunohistochemistry for HMB-45 and S-100 antibodies by two well-trained dermatopathologists independently.[10] For the definition of regression we used the criteria suggested by the Pathological Group of the World Health Organization Melanoma Programme. This includes the presence of a zone of tumour-free epidermis and dermis in which there is fibrosis, often along with inflammation and dilated vessels, flanked on one or both sides by tumour.[11]

Among the 134 patients with melanoma, 31 (23%) had positive SNB. There were 89 patients with CMM < 1 mm thick, of whom 12 (13%) had positive SNB. The false-negative rate was 3·1% and the specificity 97%. The false-negative rate is defined as the number of false-negative sentinel node procedures (SNB negative with disease progression) divided by the sum of true-positive (SNB positive) and false-negative procedures: $[1/(31 + 1)] \times 100\%$. The sensitivity is defined as the number of true-positive procedures divided by the sum of true-positive and false-negative SNB cases: $[31/(31 + 1)] \times 100\%$. The patients in our study underwent follow-up visits every 3 months. The median follow up was 36 months (range 24–48).

Sentinel node metastases were found in a significantly greater proportion among patients with primary tumours showing histological evidence of regression: 14 of 22 (64%) vs. 17 of 112 (15%) positive cases in patients with regressing and nonregressing melanomas, respectively. The relative risk of SNB positivity for patients with regressing tumours was 9·779 (95% confidence interval 3·56–26·862) compared with patients with nonregressing tumours. Furthermore, of the 14 SNB-positive patients with regressing melanomas, 11 had tumours thinner than 1·0 mm (mean ± SD 0·682 ± 0·20; range 0·380–0·912), and none of these were ulcerated or had infiltrated deeper than the papillary dermis (Clark level II).

These findings indicate that early in their disease course, patients with relatively thin but regressing melanomas are at an almost 10 times higher relative risk of developing regional lymph node metastases than are patients with nonregressing melanomas. It is possible that histological regression results in a decreased Breslow thickness measurement, and thus in some cases an erroneously more favourable prognostic estimate. Although melanoma regression has been reported to be associated with higher metastatic potential,[4] to date no direct evidence has been published to the effect that histological regression predicts an increased risk of nodal involvement. Currently, for patients with primary melanoma < 1·0 mm thick, SNB is only indicated if ulceration or deep infiltration (Clark level IV–V) is present.[10,12] Our results suggest that patients with thin melanomas showing histological signs of regression should be considered as potential candidates for SNB.

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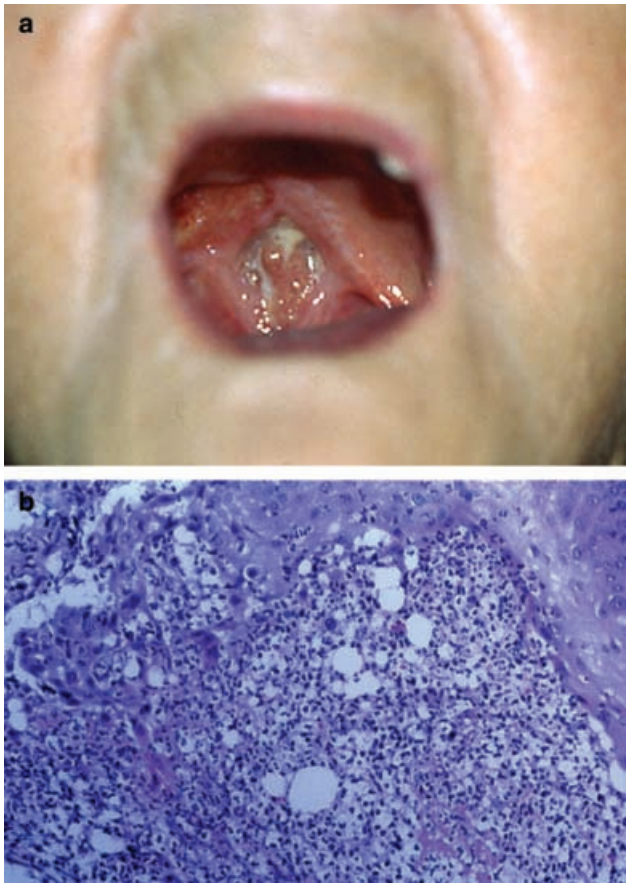

Figure 1. (a) Extensive, 4 × 2·5 cm ulceration of the hard and soft palate and right tonsil. (b) The inflammatory infiltrate within the lamina propria showed a conspicuous neutrophilic component with no signs of vasculitis (haematoxylin and eosin; original magnification × 40).

Oral pyoderma gangrenosum

Sir, Pyoderma gangrenosum (PG) is an uncommon disease characterized by the occurrence of chronic ulcerations on the skin. This condition is associated with a systemic illness in approximately 50% of cases, with rheumatoid polyarthritis, inflammatory bowel disease and haematological disorders being the most frequent related diseases. Oral PG is rare and is associated with cutaneous lesions in the vast majority of cases. We report a patient with PG affecting exclusively the oral mucosa.

An 84-year-old woman presented with a painful, extensive oral ulceration first noticed 3 months previously. She had a history of high blood pressure and osteoarthritis. She had no other cutaneous lesions. Examination showed an extensive ulceration affecting the right soft and hard palate and right tonsil (Fig. 1a). Several biopsy specimens revealed a dense neutrophilic infiltrate in the lamina propria of the mucosae and a mixed inflammatory cell infiltrate in the deeper area without signs of vasculitis (Fig. 1b). Periodic acid-Schiff and Gram stains were negative. Direct immunofluorescence study was not performed. Laboratory tests were as follows. Full blood cell count: erythrocytes $2{\cdot}9 \times 10^{12}$ L^{-1}; haemoglobin 9·7 g dL^{-1}; mean corpuscular volume 101·2 fL; leucocytes $5{\cdot}92 \times 10^{9}$ L^{-1} (78·4% neutrophils, 17·5% lymphocytes, 2·4% monocytes); platelets 165×10^{9} L^{-1}; erythrocyte sedimentation rate 91 mm in the first hour (normal < 30). Biochemistry: albumin 29 g L^{-1}; aspartate aminotransferase 45 U L^{-1} (normal < 37); alanine aminotransferase 52 U L^{-1} (normal < 40); γ-glutamyl transferase 1507 U L^{-1} (normal < 50); alkaline phosphatase 2859 U L^{-1} (normal < 279); glucose, urea, creatinine and the remaining parameters were normal. Antinuclear and antimicrosomal antibodies were negative, as was viral hepatitis serology. Ultrasonography excluded macroscopic biliary causes of cholestasis. The patient was on amiloride and hydrochlorothiazide, two antihypertensive drugs that have not been reported to cause cholestasis. The family of the patient refused any further studies, such as liver biopsy, to clarify abnormal liver function