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Value of Elective Lymph Node Dissection in the Management of Malignant Melanoma

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A total of 23 patients who underwent elective lymph node dissection for malignant melanoma were included in this study to evaluate the role of elective lymph node dissection in the management of malignant melanoma with clinically negative lymph nodes and there predictive value in prognosis of the disease. Seven patients has tumor thickness <0.75 mm, 6 patients has tumor thickness >0.75 mm but less than 1 mm, 10 patients has tumor thickness 1-4.6 mm. The excision margin was based on preoperative clinical assessment of tumor thickness and histological type. Histological status of lymph nodes was 6 (26%) positive and 17 (74%) negative and number of excised lymph nodes ranging between 5-14 mean 8 and number of positive lymph nodes were ranging between 2-7 mean 5 lymph node metastases correlate with thickness of the primary tumor, whereas lesions <0.75 mm shows no lymph node metastases, while lymphatic invasion occur in patients with thick tumor >0.75 mm. Also lymph node metastases correlate with local recurrence whereas 75% of patients with local recurrence has positive lymph nodes. Moreover lymphatic metastases correlate also with regional recurrence where 33% of regional recurrence occur in positive lymph nodes. From this study we conclude that elective lymph node dissection can predict local and regional recurrence in patients with clinically negative lymph node.

Key words: Elective lymph node dissection, malignant melanoma, predictive value, excision margin, local recurrence and regional recurrence

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INTRODUCTION

Cutaneous malignant melanoma is highly aggressive neoplasm. Regardless of the efforts of primary prevention and of the recent advances in systemic multimodality therapies, its incidence and mortality rates are alarming (Cruz *et al*., 2003).

Melanoma incidence has increased dramatically over the last decades and the regional lymph nodes are the most common first sites of melanoma progression. The prognosis for patients having melanoma with lymph node involvement has depended on the number of metastatic nodes, whether nodal metastases were palpable and the presence or absence of primary tumor ulceration (Philippe *et al*., 2005).

The effective management of metastatic melanoma remains a formidable challenge. Estimate of median survival ranges from 6-9 months, with a 5 years survival of less than 5% (Boasberg *et al*., 2003). Multivariate evaluation revealed tumor thickness, histological subtypes, body site, sex and age as significant prognostic factors, whereas ulceration, regression and Clark' s level of invasion did not seem to have an independent significant effect on the prognosis of cutaneous melanoma (Leiter *et al*., 2004).

The management of the draining nodal basin in patients with clinically node-negative melanoma traditionally has been a source of controversy. Two management options were available: (1) observation and (2) elective lymph node dissection. A third option, sentinel lymph node biopsy, is now available. The likelihood of having occult nodal disease is directly related to the thickness of the primary melanoma. Proponents of elective lymph node dissection argue that it is a useful procedure and that removal of metastasis nodal disease before it becomes palpable may prevent systemic spread in some patients. Proponents of observation contend that elective lymph node dissection subjects many patients to potentially morbid procedure without benefit and that no prospective, randomized trial to date has shown a survival benefit after routine elective lymph node dissection (Reeves and Coit, 2000).

An elective lymph node dissection is required in the treatment of intermediate-thickness (1-4 mm) cutaneous malignant melanoma of the head and neck (Myers, 1999). This study evaluates the prognostic value of elective lymphadenectomy in malignant melanoma patients with clinically negative lymph nodes.

MATERIALS AND METHODS

Between March 1998 and June 2003, at Sayed Galal, Alazhar University Hospital 23 patients (14 men and 9 women; age rang 28 to 72 years mean 53.5) underwent elective lymphadenectomy for malignant melanoma (5 in the head and neck, 3 in the upper limb and 1 in the perianal region and 14 in lower limb) with impalpable lymph nodes and Table 1 shows clinical details of patients.

The histological type was superficial spreading in 8 patients, nodular melanoma in 9 patients and lentigomaligna in 6 patients (Table 2). Patients with clinically positive lymph nodes were excluded from the study (they submitted to radical block dissection). Lymph nodes were not palpable in all patients. Preoperative assessment of tumor thickness was possible for all lesions; where 10 were judged as impalpable (thin lesion) and 13 considered as palpable (thick lesion).

Treatment policy: All patients underwent histological diagnoses preoperatively. Eleven patients underwent preliminary excision biopsy, 7 incision biopsy and 5 intraoperative frozen section biopsy. The excision margin was based on preoperative clinical assessment of tumor thickness. Impalpable lesions were excised with 1 cm margin (6 patients); lentigomaligna was excised with a 0.5 cm (6 patients), palpable but not overtly nodular tumors with a 2 cm margin (2 patients) and overtly nodular lesions with a 2-3 cm margin (9 patients). It was occasionally necessary to sacrifice adherence to this margin policy to preserve important anatomical feature, while trying to observe adequate clearance in the direction of the draining lymphatic.

Elective lymph node dissection was done for all patients. The histological status of the lymph nodes is shown in Table 3. Follow up period ranged between 21-43 months with mean of 31 months.

The number of excised lymph nodes ranging between 5-14 lymph node, mean 8 and number of positive lymph nodes ranging between 2-7, mean 5, there is no extra capsular invasion.

Table 1: Clinical details of 23 patients with melanoma

Sex ratio male: female	61:39
Mean age	53.5
Site	
Head and neck	5 cases
Upper limb	3 cases
Perianal	1 case
Lower limb	14 cases

Table 2: Histological type and tumor thickness

Superficial spreading	8 lesions
Nodular melanoma	9 lesions
Lenttigomaligna	6 lesions
Tumor thickness	
≥0.75 mm	7 patients
0.76-1 mm	6 patients
1.1-4.6 mm	10 patients

Table 3: Histological status of lymph nodes

Histological status	No. of patients
Positive	6 patients (26%)
Negative	17 patients (74%)

RESULTS

Preoperative clinical assessment: The clinical estimate of tumor thickness correlated well with histological measurement. Of the 12 lesions considered impalpable, 6 were ≤0.75 mm on histological assessment and 6≥0.75 mm but less than 1 mm of the 11 palpable lesions, 1 was ≤0.75 mm thick and 10 has tumor thickness ranged between 1 and 4.6 mm with the mean 2.9 mm. No patients, therefore, had an inappropriately wide excision as a result of clinical overestimation of tumor thickness.

Also tumor thickness is correlated well with histological lymph node invasion, as 6 patients with histological lymph node invasion 4 of them were have tumor thickness more than 1 mm 40% and 2 have tumor thickness less than 1 mm 15% (Table 4).

Local recurrence: Four patients 16.5% had local recurrence; these all had thick (1.1 and 4.6 mm) tumors of poor prognosis. Three patients with positive lymph node had local recurrence. In one case, which has negative lymph node, re-excision was followed by prolonged survival, in the remaining three patients, systemic or nodal recurrence either preceded local recurrence or supervened within 3 months, suggesting that more radical primary surgery would have made little difference. One of them died with uncontrolled symptomatic locall regional disease (in the form of ulceration bleeding and infection). Reduction of maximum excision margin to 3 cm did not lead to an increase in the rate of local recurrence. Also elective lymph adenectomy could not prevent local recurrence where 50% of patients with positive lymph node have local recurrence. Whoever positive lymph node can predict local recurrence (75% of patients with local recurrence had positive lymph node).

Regional recurrence: All patients underwent elective lymph node dissection as a part of initial treatment, (Table 5) of whom 6 shows lymphatic invasion by malignant cells 6/23 (26%) (Occult metastases) all of them with tumor thickness more than 0.75 mm.

Regional recurrence was seen in 3 patients (13%) 2 of them shows histological lymph node invasion (2/6 33%). All has tumor thickness more than 1.5 mm. Patients with regional recurrence fared better than those with local recurrence; in particular, 2 patients who had regional recurrence in the absence of local recurrence remain alive at 31 and 37 months.

Adjuvant therapy: Four patients received local radiotherapy as part of the initial treatment all with thick tumor more than 3 mm rapidly growing melanoma and all has histological positive lymph node. Three of these patients is alive without recurrence at 29 months and the one died at 19 months from uncontrolled symptomatic local regional disease.

Table 4: Influence of tumor thickness on recurrence rate

Thickness (mm)	No. of patients	Patients with recurrence
≤0.75	7	0
0.76-1	6	0
≥1	10	4

Table 5: Type of recurrence in 6 patients with positive lymph nodes

No. of patients	State of recurrence
2	Local recurrence
1	Regional recurrence
1	Local regional recurrence
2	No recurrence

DISCUSSION

The minimum adequate excision margin for melanoma is unknown, but extremely wide clearance is unnecessary. One-stage definitive excision based on clinical estimation of tumor thickness can be safely applied to tumors of the head and neck (Orr *et al*., 1993). Impalpable (≤ 0.75 mm thick) lesions should be excised with a 1 cm margin. For palpable tumors (≥ 0.76 mm thick), a 2 cm margin results in no increase in local or distant recurrence rate compared with wider excisions; this can safely be reduced to 1 cm in one direction to spare important anatomical features while taking a wider margin in the direction of draining lymphatic. All patients underwent preliminary biopsy and none had an excessive clearance because of clinical overestimation of depth. Where local recurrence occurred, it was generally preceded by (or was simultaneous with) regional or systemic disease, suggesting that recurrence was more a marker of aggressive disease than the result of inadequate surgery. This results are supported by results of Orr *et al.* (1993) who stated that a policy of selective excision margins, 1 cm for impalpable and 2 cm for palpable lesions, was found to be safe. Tumor thickness is directly correlated with local recurrence as shown by occurrence of local recurrence in four out of ten patients with tumor thickness more than 1 mm (40%) with no recurrence in patients with tumor thickness less than 1 mm. Myers (1999) found that tumor thickness and ulceration provide the most useful prognostic information in patients with node-negative melanoma and that tumor thickness forms the basis of the American Joint Committee on cancer staging system for this disease. Also lymph node metastases correlate with the thickness of the primary lesions. Whereas lesions thinner than 0.75 mm shows no lymph node metastases. Moreover tumor thickness not only correlates with lymph node

metastases but also with the rate of occult nodal metastases. Where the 6 patients with occult nodal metastases shows tumor thickness of more than 1 mm, these results are coincident with results of Medina and Canfield (1996) who decide that the incidence of cervical metastases in cutaneous malignant melanoma of the head and neck correlate with the thickness of the primary lesions. Whereas lesions thinner than 0.76 mm rarely metastasize, melanomas from 0.76-4.0 mm in thickness metastasize to regional lymph nodes in 14-44% of patients. For lesions thicker than 4.0mm the rate of regional nodal disease is 50 to 60% (Medina and Canfield, 1996). Also Kane *et al.* (1997) found that tumor thickness correlates with the rate of occult nodal disease in patients with intermediate thickness lesions as demonstrated by the pathologic analyses of specimens from 424 patients who underwent elective lymph node dissection for stage 1 and II melanoma. Also lymph node metastases correlate with local recurrence whereas 75% of patients with local recurrence have positive lymph node and only 6% (1/17) of patients with negative lymph node shows local recurrence. The role can applied also on regional recurrence where 2 patients with positive lymph node has regional recurrence (33%) while only one patient with negative lymph node has regional recurrence. So, elective lymph node excision can predict local and regional recurrence in clinically negative lymph node. The rational for elective lymph node dissection is based on the hypothesis that cutaneous malignant melanoma spreads, in a stepwise manner, from the primary to the regional nodes and then to distant sites. The aim of elective lymph node dissection is, therefore, to provide definitive surgical treatment at an early stage in the natural history of the disease (Balch, 1988). Unfortunately, this is not always the case and even when local-regional control is achieved, distant disease develops in some patients. It seems more likely that the presence of lymph node metastases is a biological marker of aggressive behavior (Buzaid *et al.*, 1997).

Although elective lymph node dissection discovers lymph node metastases early in clinically negative patients (occult metastases). And a regional lymph node metastasis is a major determinant of outcome for patients with melanoma and the presence of regional lymph node metastasis has been commonly used as an indicator for systemic, often intensive adjuvant therapy does not affect local or regional recurrence (White *et al.*, 2002). Opponents of elective lymph node dissection believe that because 80% of patients with clinical stage 1 disease have histological negative nodes at the time of resection of the primary tumor, prophylactic excision of the regional nodes is unnecessary (Lawton and Ariyan, 2000).

Kane *et al.* (1997) elucidate that elective lymph node dissection did not appear to have a significant impact on regional recurrence or overall survival. However, the procedure is useful in determining a patient's prognosis and finding those patients who might benefit from the use of adjuvant radiation therapy (Myers, 1999). Balch *et al.* (1985) contend that the Breslow thickness of the primary melanoma is the major indicator of the group of patients who might benefit most from elective lymph node dissection. They argue that primary melanoma of Breslow thickness 0.76-4 mm has a high risk of occult regional metastases, up to 60% in patients with lesions 1.5-4.99 mm thick and a low risk of systemic metastases and those patients should benefit from lymphadenectomy (Scott and McKay, 1993).

Major arguments against elective lymph node dissection include the following: (1) surgical morbidity that is not offset by a survival benefit; (2) sentinel lymph node mapping may provide the same information as elective lymph node dissection with a more limited, less morbid procedure and (3) radiation therapy provides excellent rates of local-regional control (Myers, 1999). Intraoperative lymphatic mapping and sentinel lymphadenectomy are rapidly becoming the standard of care for management of the regional lymphatic in patients with melanoma of the trunk or extremities greater than 1 mm in thickness (Morton, 1997).

These data suggest that in the absence of other methods to determine occult nodal metastases (as lymphatic mapping and sentinel lymph node biopsy) in patients with cutaneous malignant melanoma, elective lymph node dissection can identify those patients who may derive a survival benefit from subsequent treatment with adjuvant therapy, also lymphadenectomy can predict local and regional recurrence. Moreover patients with histological positive lymph nodes (occult metastases) benefit from elective lymph node dissection more than histological negative patients.

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