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Biopsy procedures, primary wide excisional surgery and long term prognosis in primary clinical stage I invasive cutaneous malignant melanoma

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Summary

281 patients managed for primary clinical Stage I invasive cutaneous malignant melanoma at one Plastic Surgery Unit were followed up to a minimum of 10 years after primary surgical treatment. Sixty-three (23%) had received an initial biopsy procedure prior to definitive wide margin excisional surgery. One third of all lesions initially treated by so called incisional biopsy were rendered histologically unassessable on current histopathological criteria. Incisional biopsy significantly interfered with the accurate histopathological staging of the tumours. Of the assessable incisional biopsy specimens the majority were >4.0 mm thick. When the incidences of local tumour recurrence and mortality were related specifically to maximal tumour thickness of the primary lesion, prognosis at minimum follow up of 10 years was not significantly different between patients treated initially by either incisional biopsy, minimal margin excisional biopsy or primary wide excisional surgery.

Whether or not incisional biopsy adversely affects prognosis in cutaneous malignant melanoma, the technique should be avoided since it compromises accurate histopathological microstaging which represents one of our most valuable prognostic guides. Clinical doubt over the diagnosis of cutaneous malignant melanoma should be resolved by a total excisional biopsy of the lesion in question.

Introduction

Biopsy procedures have been claimed to adversely affect the prognosis in cutaneous malignant melanoma *(1,2,3)*, although the evidence for this is conflicting and inconclusive *(4,5,6,7,8,9)*. The advent of an objective method of quantifying the size of the primary tumour—measurement of maximal tumour thickness with an ocular micrometer *(10)* has allowed an attempt to resolve the controversy. As primary tumour thickness is widely regarded as the dominant single most important prognostic variable in cutaneous malignant melanoma *(11,12,13,14)*, we have sought to relate long term prognosis to both maximal primary tumour thickness and initial treatment in patients treated for clinical Stage I invasive cutaneous malignant melanoma at one Plastic Surgery Unit.

Materials and methods

All patients treated for clinical Stage I invasive cutaneous malignant melanoma at the Plastic Surgery Unit, Frenchay Hospital for whom there were complete minimum 10 year follow-up records were reviewed for the 6 year period 1967–1972. Patients dying of causes other than malignant melanoma during this follow-up period were excluded. Patients with in situ (Clark level I) lesions and lentigo maligna melanomas were also excluded because these forms of the disease are widely recognised to be much less aggressive than invasive malignant melanoma of the superficial spreading or nodular types. All case notes and microfilm records were studied and all available histological material was classified according to current histopathological criteria *(10, 15)*. Patient follow-up was facilitated by using a computerised data base constructed from the above information. In addition to the records of the Melanoma Registry and outpatient annotations, general practitioners also provided information on the nature of first tumour recurrence (local, nodal, or visceral), dates of first tumour recurrence and death from the disease. Local recurrence was classified as either within the scar or graft(IG), at the edge of scar/graft(EG) or in the skin or subcutaneous tissues outside the scar or graft area but not involving the regional lymph nodes—in transit (IT). During the period under review central block tissue sections had been taken through all lesions and it is likely that measurements recorded do represent maximal tumour thicknesses for the vast majority of patients *(16)*.

The surgical policy throughout the review period was standard. When patients were referred with the lesion intact, a primary wide margin excision was usually performed on the basis of the clinical appearance alone *(17)*. Margins varied from 1 to 2 cm on the head and neck, to 5 cm on the limbs and 10 cm on the trunk. When patients underwent definitive wide excision after an initial biopsy procedure, the biopsy site was excised in a similar fashion (patients were considered to have undergone incisional biopsy if the margins of the initial histological specimen were recorded as containing tumour; if all resection margins were clear of tumour the procedure was designated minimal margin excision biopsy). Split thickness skin grafts were usually then used to re-surface the resultant defects, although occasionally

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direct wound closure was possible. Deep fascia was not excised nor were prophylactic (elective) lymph node dissections performed.

Statistical analyses utilised the Chi square test with Yates correction to study differences in the availability of histological material between groups and rates of tumour recurrence and mortality. Student's *t*-test and a one way analysis of variance were used to study differences in tumour thicknesses between groups.

Results

During the 6 year review period 281 patients were managed for primary clinical Stage I invasive cutaneous malignant melanoma. The management in 218 (77%) patients was by definitive primary wide excision without an initial biopsy, whilst 63 (23%) patients were subjected to wide margin excision of a biopsy site (usually after referral from other clinicials). For 23/281 (8%) patients histological material was either unassessable or unavailable (Fig.).

Six out of 19 patients initially treated with an incisional biopsy had unassessable histological specimens and tumour thickness could not be accurately measured; for one further patient the histology was unavailable (Table I). This 37% (7/19) unassessable or unavailable specimens following incisional biopsy compares with 14% (6/44) for those undergoing initial minimal margin excision biopsy, and 5% (10/218) for those treated with an initial wide excision. These differences were even more obvious if unassessable specimens alone were considered. These differences were statistically significant ($p < 0.001$).

Therefore maximal tumour thickness measurements and minimum 10 year follow-up were available for 258 determinate patients. Twelve patients treated by incisional biopsy initially (1/12 treated primarily by this Unit), 38 patients treated with an initial minimal margin excisional biopsy (9/38 treated primarily by this Unit), and 208 patients subjected to a primary wide margin excision by this Unit (11/208 had intra-operative excisional biopsy and frozen section histological examination proceeding to definitive wide margin excision at the same operation are considered as primary wide margin excisions).

Twenty-six patients developed local tumour recurrence (Table II) with the local recurrence rate after primary wide excision of 9.6% contrasting with a 12.0% local recurrence rate when wide margin excision followed an initial biopsy procedure. Although the mean maximal tumour thickness was less for those undergoing an initial biopsy, the tumour thicknesses of the two groups did not show a statistically significant difference. The relationship between type of initial treatment and long term mortality is shown in Table III. There were no significant differences here between the groups.

Table IV details those patients referred after incisional biopsy (including the one patient who underwent an incisional biopsy on this Unit) for whom the maximal tumour thickness could be measured. Only 2/12 patients were found to have histological evidence of residual tumour in their re-excision specimens. The mean maximal tumour thickness for these 12 patients was 4.2 mm, a much higher figure than the 2.8 mm mean maximal tumour thickness for the 50 patients comprising the whole group who had initial biopsy procedures. Indeed all but 3 of these 12 patients had maximal tumour thicknesses in excess of 4.0 mm. Therefore, dependent upon initial treatment, all patients with tumours 4.0 mm thick or greater (55 patients) were compared for both incidence of local recurrence and long term mortality (Table V). The differences between tumour thicknesses for the three groups were not statistically significant, neither were the rates of mortality. No local tumour recurrences were seen when minimal margin excisional biopsy was followed by wide margin excision, and the incidence of local tumour recurrence in the incisional biopsy and primary wide excision groups was the same.

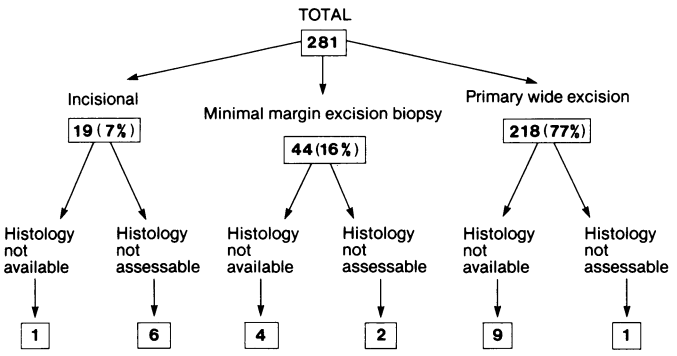

FIG. Schema illustrating the initial management of 281 patients presenting with clinical Stage I invasive cutaneous malignant melanoma, and numbers with unassessable or unavailable histological material.

TABLE I *Details of histological material unassessable or unavailable in the 3 groups studied*

Type of primary surgical treatment	*n*	*Unassessable*	*Unavailable*	*Total*
Incisional biopsy	19	6 (32%)	1 (5%)	7/19 (37%)
Minimal margin excisional biopsy	44	2 (5%)	4 (9%)	6/44 (14%)
Primary wide excision	218	1 (0·5%)	9 (4%)	10/218 (5%)

TABLE II *Relationship of initial treatment and other variables to the rate of local recurrence of tumours. 26 patients*

	Initial biopsy ($n = 6$)	*Primary wide excision* ($n = 20$)	*Difference*
Male : Female	1 : 5	6 : 14	
Mean age (years)	53	54	ns
Mean maximal tumour thickness (mm)	2.8	3.8	ns
Incidence of local tumour recurrence	6/50 (12.0%)	20/208 (9.6%)	ns

TABLE III *Mortality from malignant melanoma 10 years or more after primary treatment for 258 determinate clinical Stage I patients*

	Initial biopsy procedure		*Primary wide excision*		*Total*	
	n	*Mortality*	*n*	*Mortality*	*n*	*Mortality*
	50	22/50 (44%)	208	82/208 (39%)	258	104/258 (40%)
Mean maximal tumour thickness (mm)	2.6	3.1	2.7	3.6	2.7	3.5

TABLE IV *Details of 12 patients treated initially by incisional biopsy for whom maximal tumour thickness was measurable*

Age (years)	*Site*	*Maximal tumour thickness (mm)*	*Residual tumour seen in wide excision specimen*	*Interval (months) to first recurrence and site*	*Outcome Alive at 10 years or Dead of melanoma (months after primary treatment)*
52	calf	0.68	NO	—	Alive at 10 years
68	foot	1.35	YES	24 m node	Dead 48 m
58	toe (sub-ungual)	1.8	NO	24 m node	Alive at 10 years
58	calf	4·0	NO	12 m node	Dead 84 m
60	trunk	4.0	NO	12 m node	Dead 26 m
75	cheek	4.0	NO	—	Alive at 10 years
39	scalp	4.4	YES	5 m skin	Alive at 10 years
54	leg	5.6	NO	44 m skin	Alive at 10 years
32	neck	5.8	NO	5 m node	Dead 17 m
64	heel	5.8	NO	10 m node	Dead 31 m
71	heel	6.2	NO	5 m node	Dead 20 m
43	leg	6.8	NO	—	Alive at 10 years

TABLE V *Data for patients with lesions >4.0 mm thick (55 patients)*

Type of primary surgical treatment	*n*	*Mean maximal tumour thickness (mm)*	*Incidence of local recurrence*	*Mortality from melanoma at 10 years*
Incisional biopsy	9	5.2	2/9 (22%)	5/9 (56%)
Minimal margin excisional biopsy	6	4.8	0/6 (0%)	3/6 (50%)
Primary wide excision	40	6.1	9/40 (22%)	26/40 (65%)

Although the numbers are small, percentage figures have been used for clarity.

Discussion

The incidence of biopsy of cutaneous malignant melanomas prior to definitive surgical excision varies widely *(3,5,6, 7,9,17)*. Whether or not such biopsy procedures adversely influence rates of local tumour recurrence or mortality, they can interfere with subsequent attempts to accurately microstage the tumour *(18,19,20)*. It would appear that when excision biopsy is followed by definitive wide margin excision the prognosis does not differ significantly from patients treated by primary wide excision *(21,22)*. Our experience reported here would confirm this.

In the present study patients referred with a histological report of incomplete tumour excision were classified as having had an incisional biopsy. Compared with the other groups studied, those specimens resulting from incision biopsy produced a significantly greater proportion of unassessable histological preparations. The incidence of incisional biopsy in patients referred to this Unit was 19/281 (7%), a much lower figure than the 41% given by Roses *et al. (19)*. Only 2/12 patients had histological evidence of residual tumour in the re-excision specimens performed after initial incisional biopsy. Therefore although these have been considered to have had an initial incisional procedure, it is possible that the whole tumour was in fact totally excised (albeit with no clear margin of normal tissue) at the initial operation. Nevertheless such initial treatment has been classified as incisional biopsy throughout this report. Whilst Bagley *et al. (9)* considered that dermal punch biopsy gave both accurate staging information and carried no increased risk of local recurrence or death from the disease, Rampen *et al. (4)* concluded that survival was reduced after incisional biopsy. However some patients reported in that study were treated by prophylactic regional lymph node dissection in addition to excision of the primary tumour, and maximal tumour thickness measurements were not available for all the patients they detailed. It is therefore difficult to clearly assess the significance of their data in relation to ours. But they did find, as have we, that incisional biopsy rendered many histological specimens unsuitable for accurate measurement of tumour thickness. In view of the small number of cases of incisional biopsy in the present series and the large proportion of these for which inadequate pathological materials was available, we would be cautious in the conclusions we might draw.

Within the constraints of the available, assessable histological material in our study it appears that the majority of patients subjected to incisional biopsies have advanced primary tumours (>4.0 mm maximal tumour thickness). The finding might in part explain the comments of earlier writers that patients have a poorer prognosis after such 'inadequate procedures' *(1,2,3)*. But our most significant conclusion must be that whilst initial biopsy procedures did not appear to adversely affect long term prognosis, so called incisional biopsy resulted in an unacceptably high incidence of tumour distortion which precluded measurement of maximal tumour thickness in almost 1/3rd of cases. For this reason alone incisional biopsy should be regarded as wholly unacceptable as a diagnostic procedure for skin lesions suspected clinically of being malignant melanomas.

It is likely that the optimal resection margins for malignant melanomas of the skin are considerably less than have been previously described *(23,24)*, but if definitive resection margins are to be based on the measured maximal tumour thickness (as many workers have suggested), then an initial adequate total excisional biopsy is essential. In any studies which relate primary surgical or adjuvant treatments to prognosis in cutaneous malignant melanoma, long term direct follow-up to 8–10 years or more would appear to be critical *(25)* if the effect of late mortality is to correctly influence data analysis.

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