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Original Article

Cutaneous Carcinoma of the Head and Neck with Clinical Features of Perineural Infiltration Treated with Radiotherapy

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Abstract

Aims: To review the outcome of patients with non-melanomatous carcinoma of the skin of the head and neck with perineural infiltration (PNI) with clinical features treated with radiotherapy.
Materials and methods: Between 1991 and 2004, 56 patients with non-melanomatous skin carcinoma with PNI with clinical features were identified from the institution's oncology database. All patients had radiotherapy as either definitive or adjuvant treatment. The factors that affected outcome were analysed. The primary end point was the 5 year relapse-free survival (RFS) from the time of diagnosis of PNI.
Results: The overall 5 year RFS for the whole group was 48%. Squamous histology had a more unfavourable outcome than basal cell histology (5 year RFS: 39% versus 80%; $P = 0.07$). Tumours located in the distribution of the cranial nerves V1 and V2 had a worse outcome than tumours at other sites (5 year RFS: 33% versus 72%, $P = 0.056$). Those with multiple cranial nerve involvement did worse than those with single nerve involvement (27% versus 62%, $P = 0.1$). The pattern of relapse was predominantly local (87%), with a low rate (15%) of successful salvage.
Conclusion: Radiotherapy with or without surgery is curative in about half head and neck cutaneous non-melanomatous carcinomas with clinical PNI. The frequent local failure suggests that improvements in local treatment are required.

Key words: Perineural infiltration; radiotherapy; skin carcinoma; surgery

Introduction

Skin cancers are common, and nearly 2% of the Australian population are treated for non-melanomatous skin cancer every year [1]. Perineural infiltration (PNI) of such cancers is the phenomenon where tumour extends along the perineurium to involve branches or the trunk of a nerve. Its presence is associated with an increased risk of relapse. For non-melanomatous skin carcinoma, the reported incidence of PNI is in the order of 2–3% [2].

PNI has been categorised into two groups: those where on microscopic examination there is evidence of tumour extending to the adjacent nerve with no clinical or radiological features; and a second group with the pathological features as well as clinical features and/or positive imaging findings secondary to involvement of the nerve. Symptoms may include pain, formication, sensory or motor loss or diplopia. With PNI, magnetic resonance imaging (MRI) may show nerve enlargement or enhancement, or obliteration of the normal fat plane surrounding a nerve. Computer tomography can complement the MRI scan by detecting and defining the extent of any associated bone erosion. These incidental and clinical PNI groups vary in outcome [3,4]. The latter group of clinical PNI was the subject of this study, particularly analysing the factors that affect the outcome of treatment.

Materials and Methods

Patients with cutaneous carcinomas of the head and neck who had PNI and were treated between 1991 and 2004 were identified from the cancer care services database at

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our institution. Squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) histological types were included, whereas melanoma, Merkel cell and skin appendage tumours were excluded from the study. Patients were excluded from the analysis if the intent of treatment was palliative or if they did not receive radiotherapy. From the database, 278 patients with PNI treated with curative intent were identified; 222 patients had no clinical features and 56 had clinical features or abnormal imaging of PNI. The outcome of the former group has been reported in a separate study [5]. The latter group of 56 patients with PNI with clinical features is analysed in this study. The study had institutional human research ethics committee approval.

Statistical Methods

The primary end point was 5 year relapse-free survival (RFS) from the date of diagnosis of PNI. The rates of 5 year RFS were calculated actuarially using the Kaplan–Meier product limit method. Differences between curves were calculated using the Log-rank test using a two-sided test.

Results

Patient and Disease Characteristics

The baseline characteristics were summarised in Table 1. The associations between various factors and outcomes are listed in Table 2. PNI was identified histologically in 43 patients (77%), either in the primary tumour or in the biopsy of the involved nerve. The 5 year RFS for the whole group was 48%. Most patients had SCC. Those with SCC had a worse outcome than those with BCC, with 5 year RFS of 39% compared with 80% in the BCC group ($P = 0.07$; Figure 1). Nodal involvement was present in nine patients, all in the SCC group.

The site of the primary skin cancer was recorded in 48 patients. Sites included forehead, eyebrow, inner canthus, nose and nasolabial sulcus, upper lip, lower lip, mandible, cheek, temple, pre-auricular, pinna, post-auricular/mastoid, scalp and neck. They were further grouped according to the sensory distribution of that site. Fifteen patients had primary tumours within the distribution of the first branch of the trigeminal nerve (V1), 22 in V2 and seven in V3; the remaining 12 patients were categorised as 'other' locations, which included the vertex and posterior scalp, pinna, mastoid and neck. The differences between these groups were not statistically significant. However, by grouping V1 plus V2 and comparing that with V3 plus others, the difference was significant ($P = 0.056$; Figure 2). In some patients, skin cancer and clinical features of PNI were diagnosed at presentation (the *de novo* group), whereas others previously had skin cancer and presented subsequently with clinical features of PNI (the recurrent group). There was no difference between those groups ($P = 0.94$).

Fifty patients reported symptoms of nerve involvement; including pain (15), paraesthesia (19), formication (four), facial weakness (11) and blurred vision (one). Abnormal signs were present in 45 patients. The most commonly involved nerves were branches of the trigeminal nerve (40 patients) and the facial nerve (21 patients); three had

Table 1
Baseline patient and treatment characteristics

Perineural infiltration confirmed on histology	
No	13
Yes	43
Gender	
Male	40
Female	16
Age	63 (41–84)
Magnetic resonance imaging	
Positive	28
Negative	9
Not done	15
Unknown	4
Histology	
Squamous cell carcinoma	44
Basal cell carcinoma	12
Nodal involvement	
No	47
Yes	9
Chemotherapy	
No	52
Yes – concurrent	3
Yes – other	1
Radiotherapy dose, Gy, median (range)	60.0 (48–74)
Number of fractions	30 (20–38)
Duration of radiotherapy in days	42 (13–56)
Radiotherapy to the skin	
Local	4
Wide	51
Unknown	1
Radiotherapy to the orbit	
Partial	21
Whole	9
No	26
Radiotherapy to cavernous sinus	
No	45
Yes	8
Unknown	3
Radiotherapy to internal auditory meatus	
No	41
Yes	14
Unknown	1
Radiotherapy to base of skull	
No	34
Yes	20
Unknown	2
Radiotherapy to regional nodes	
No	29
Yes	25
Unknown	2
Photons	
No	7
Yes	48
Unknown	1
Electrons	
No	26
Yes	28
Unknown	2