Lymph node and distant metastases in patients with sinonasal carcinoma

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Abstract

A retrospective analysis of 34 cases of sino-nasal squamous cell or undifferentiated carcinoma in patients admitted between 1984 and 1992 was undertaken. Multimodality therapy incorporated radiation, surgery and chemotherapy. The five-year survival rate was 53 per cent. The local control rate was 82 per cent. Patients died of local failure (six), distant metastases (six), lymph node metastases (one) and other causes (three). Twenty-eight patients with local control were separated into groups: G1–2 (well and moderately differentiated) and G3–4 (poorly differentiated and undifferentiated) and evaluated to find the association between differentiation and metastasis. Lymph node metastasis was not related to the degree of differentiation. Distant metastasis was significantly related to the degree of differentiation (Fisher's exact test: $p = 0.007$). The result of the combination therapy is poor for patients with poorly differentiated or undifferentiated carcinoma because of distant metastases. Adjuvant chemotherapy may be necessary for them to prevent distant metastasis.

Key words: Paranasal sinus neoplasms; Carcinoma, squamous cell; Neoplasm, metastasis

Introduction

The method of treatment for paranasal sinus carcinoma is controversial. The methods range from surgery to radiation therapy to a combination therapy (surgery, irradiation, and/or chemotherapy). Recent literature appears to support the concept that the combination therapy can provide the best survival rate. The five-year survival rate was 54 per cent (Sakai *et al.*, 1983a, b), 52 per cent (Knegt *et al.*, 1985), and 49 per cent Sisson *et al.*, 1989. The results are still poor. To improve the survival rate, local recurrence and metastasis have to be controlled. Local recurrence rate after the combination therapy depended on the tumour stage (Kondo *et al.*, 1984). Therefore, diagnosis must be made at the early stage. However, a search of the literature revealed no report correlating histopathological differentiation with metastasis in patients with sinonasal carcinoma.

The aim of the present retrospective study was to investigate the association between histopathological differentiation and metastasis of sinonasal squamous cell and undifferentiated carcinomas.

Materials and methods

Between 1984 and 1992, 34 cases of sinonasal squamous cell carcinoma or undifferentiated carcinoma were treated at Kagawa Medical School Hospital. Six patients had recurrence at the primary site which could not be controlled. Twenty-eight patients with local control were evaluated. Because we excluded the idea, that the T stage could have influenced the development of distant disease we did not differentiate between distant diseases which occurred during the initial treatment from those which had occurred before the initial treatment but we did exclude distant diseases which occurred after the initial treatment.

There were 18 males and 10 females (age range, 48 to 84 years; median, 64 years). Eighteen patients who were still alive had a minimum follow-up time of 19 months (range, 19 to 125 months; median, 60 months). The primary sites were maxillary sinus (17), ethmoid sinus (eight), frontal sinus (one), nasal cavity (two). Maxillary sinus carcinoma was staged according to the 1987 UICC TNM classification (UICC, 1987).

Patients were treated according to the treatment policy which has been reported previously by Sakai *et al.* (1983 a, b). The treatment method for maxillary sinus carcinoma is a combination of Lineac irradiation (50 Gy), continuous intra-arterial infusion of 5-fluorouracil during radiotherapy (to a total dose of 2000 mg), and an extensive Denker's operation for partial maxillectomy. Treatment consisted of the combination therapy (radiation, chemotherapy and surgery) in 22 patients, radiation and chemotherapy

TABLE I

THE PRIMARY SITES, TUMOUR STAGE, DISTANT METASTASIS AND DIFFERENTIATION OF 28 PATIENTS WITH LOCAL CONTROL

Site	M_0 (n = 21)	M_1 (n = 7)	G1–2 (n = 17)	G3–4 (n = 11)
Maxillary sinus	12	5	9	8
T_1	0	0	0	0
T_2	6	0	5	1
T_3	3	5	3	5
T_4	3	0	1	2
N_0	10	5	7	8
N_1	1	0	1	0
N_2	1	0	1	0
Stage I	0	0	0	0
II	4	0	3	1
III	4	5	4	5
IV	4	0	2	2
Ethmoid sinus	6	2	5	3
Frontal sinus	1	0	1	0
Nasal cavity	2	0	2	0

M_0 = no distant metastasis; M_1 = distant metastasis.
G1–2 = well and moderately differentiated carcinoma.
G3–4 = poorly differentiated and undifferentiated carcinoma.

in four patients, radiation and surgery in one patient, and surgery alone in one patient. Five patients had cervical lymph node metasases at diagnosis and two patients developed lymph node metastases later. Therefore, seven patients had neck dissection. No patients had distant diseases at diagnosis and seven patients developed distant diseases later.

Results

Overall local control was achieved in 28 out of 34 (82 per cent) patients. Six patients with local recurrence died of their disease 4, 11, 12, 21, 22 and 31 months after diagnosis. The primary sites for the six patients were maxillary sinus (four) and nasal cavity (two). The degree of differentiation of the six patients was well differentiated (one), moderately differen-

TABLE II

THE ASSOCIATION BETWEEN DIFFERENTIATION AND LYMPH NODE AND DISTANT METASTASES

	G1–2	G3–4	Fisher's exact test
Lymph node metastasis	5	2	$p = 0.67$
Non-lymph node metastasis	12	9	
Distant metastasis	1	6	$p = 0.007$
Non-distant metastasis	16	5	

tiated (three), poorly differentiated (two). The five-year survival rate for the 34 patients was 53 per cent.

Twenty-eight patients with local control were evaluated to find the association between metastasis and histopathological grading. Out of 28 patients with local control, five patients had only distant metastases, five patients had only cervical lymph node metastases and two patients had both. The histopathological grading was well differentiated (eight), moderately differentiated (nine), poorly differentiated (six), undifferentiated (five). The degree of differentiation was separated into two groups: G1–2 (well and moderately differentiated) and G3–4 (poorly differentiated and undifferentiated). The primary sites, tumour stage at diagnosis, distant metastasis and degree of differentiation of 28 patients with local control are shown in Table I.

The association between differentiation and lymph node and distant metastases is shown in Table II. Lymph node metastasis was not related to the degree of differentiation. However, distant metastasis was significantly related to it (Fisher's exact test; $p = 0.007$).

Eighteen out of 28 (64 per cent) patients were alive and disease-free after a minimum of 19 months follow-up (range, 19 to 125 months). Seven patients died of metastases without local recurrence 3, 7, 8,
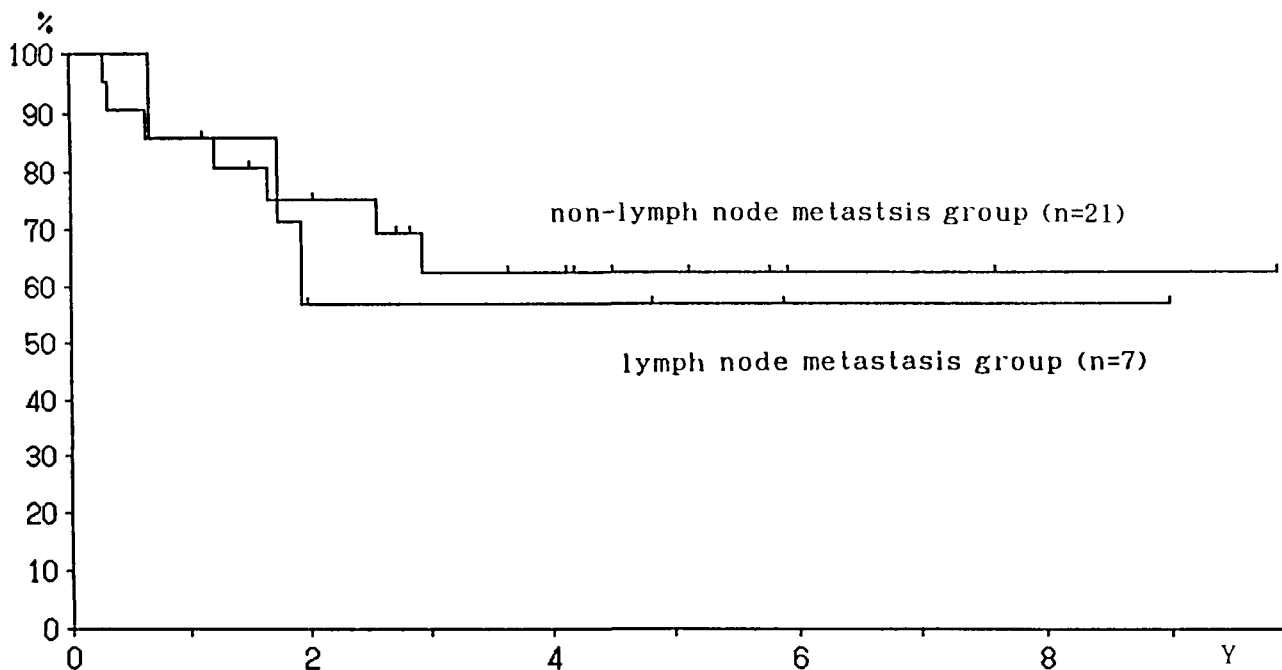

FIG. 1
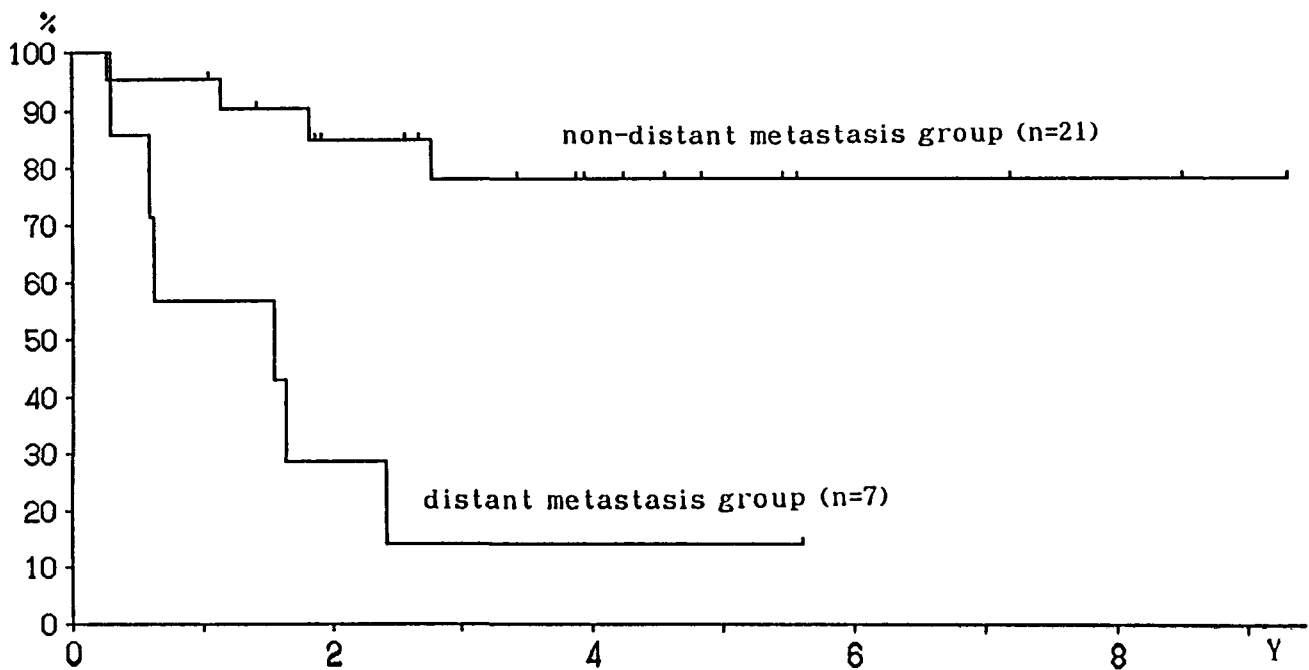Kaplan–Meier survival curves in patients with local control in relation to lymph node metastasis.

FIG. 2

Kaplan–Meier survival curves in patients with local control in relation to distant metastasis (logrank test; $p = 0.0004$).

19, 21, 23 and 31 months after the initial treatment. Three patients died of other causes (disease-free) 3, 14 and 35 months after the initial treatment. Kaplan-Meier survival curves were obtained for the lymph node (n = 7) and non-lymph node metastasis (n = 21) groups, distant (n = 7) and non-distant metastasis (n = 21) groups, and G1–2 (n = 17) and G3–4 (n = 11) groups (Figures 1, 2, 3). These five-year survival rates were 57 and 63 per cent, 14 and 78 per cent (logrank test; $p = 0.0004$), and 72 and 44 per cent (logrank test; $p = 0.061$), respectively.

Discussion

The five-year survival rate was 53 per cent which was almost the same as other reports with the combination therapy (Sakai *et al.*, 1983 *a, b*; Knegt *et al.*, 1985; Sisson *et al.*, 1989). The local control rate was 82 per cent which was better than that in other reports (Knegt *et al.*, 1985; Kondo *et al.*, 1984; Giri *et al.*, 1992). Local failure was not related to differentiation. Therefore, it is not necessary to change the treatment method for the primary site according to tumour differentiation. The most important factor
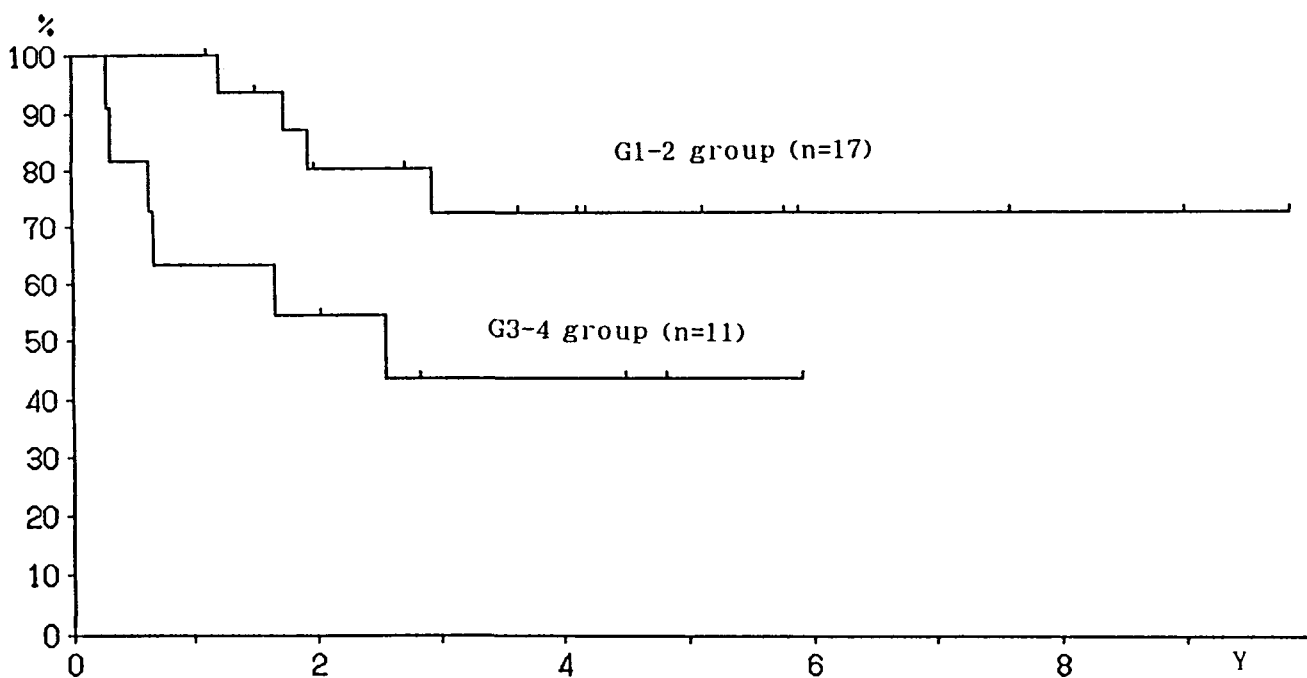

FIG. 3

Kaplan–Meier survival curves in patients with local control in relation to differentiation (logrank test; $p = 0.061$). G1–2 = well and moderately differentiated carcinoma; G3–4 = poorly differentiated and undifferentiated carcinoma.

for survival was reported to be local control (Sisson *et al.*, 1989). However, in our series, six patients died of local failure and seven patients died of metastases. Metastasis is as important as local control. A new protocol may be necessary to prevent metastases.

Although Lindeman *et al.* (1987) reported that patients with glandular involvement had a poor prognosis despite additional surgery and radiotherapy, and Giri *et al.* (1992) also reported that neck node metastasis correlated negatively with survival (Cox model; $p = 0.01$), four out of five (80 per cent) patients with only lymph node metastasis were cured by neck dissection and only one patient died of neck metastasis in our series. Lymph node metastases occurred in five out of 17 (29 per cent) patients in the G1–2 group and two out of 11 (18 per cent) patients in the G3–4 group (Fisher's exact test; $p = 0.67$). The five-year survival rate was 63 per cent in the non-lymph node metastasis group with local control and 57 per cent in the lymph node metastasis group with local control (logrank test; $p = 0.77$). These results suggested that lymph node metastases were not correlated with histopathological differentiation and did not influence the prognosis. Therefore, if patients have no palpable lymph node at diagnosis, treatment for the neck is not necessary. A neck dissection is performed when a palpable lymph node is found during initial treatment or at follow-up.

Although one patient with lung metastasis was cured by radiotherapy and is still alive, six out of seven (86 per cent) patients with distant metastases and all six (100 per cent) patients with local recurrence died of their disease. The five-year survival rate was 78 per cent in the non-distant metastasis group with local control and 14 per cent in the distant metastasis group with local control (logrank test; $p = 0.0004$). These results suggested that distant metastases and local failure should be recognized as not curable. Sakai *et al.* (1983 a, b) reported that distant metastases were more often found in the combination therapy with sinus curetting group than in the cryosurgery group. Sinus curetting could increase the local control rate, but mechanical irritation by the sinus curetting might cause distant metastases. However, they did not mention histopathological differentiation of patients with distant metastases. In our local control series, one out of 17 (six per cent) patients in the G1–2 group had distant metastases. However, six out of 11 (55 per cent) patients in the G3–4 group had distant metastases. This difference was statistically significant (Fisher's exact test: $p = 0.007$). The five-year survival rate was 73 per cent in G1–2 group and 44 per cent in G3–4 group. This statistical difference (logrank test; $p = 0.06$) did not correlate with lymph node metastasis but correlated with distant metastasis. Giri *et al.* (1992) also reported that patients with well differentiated tumours fared better than those with poorly differentiated tumours (Cox model; $p = 0.005$). Therefore, patients with poorly differentiated or undifferentiated carcinoma have a worse prognosis and distant metastasis might occur in about half of them.

Conclusions

The results of the combination therapy is poor for patients with poorly differentiated or undifferentiated carcinoma. Other methods of treatment should be explored to improve their survival rate. We recommend that adjuvant chemotherapy should be added to the combination therapy for patients with poorly differentiated or undifferentiated carcinoma of the nasal cavities and paranasal sinuses.

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