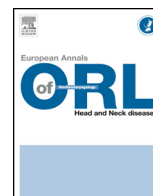




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Original article

## Prognostic factors for parotid metastasis of cutaneous squamous cell carcinoma of the head and neck

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### ABSTRACT

**Background:** Cutaneous squamous cell carcinoma (CSCC) develops on the head in 80% of cases. Parotid metastasis (PM) is rare, but treatment, which associates surgery and radiation therapy, is heavy and prognosis poor.

**Material and methods:** All cases of parotidectomy for PM of CSCC of the head and neck between 2005 and 2015 were studied retrospectively. Epidemiologic, oncologic and therapeutic data were analyzed. Overall and specific survival were calculated following Kaplan-Meier. Log-rank and Cox models were used to identify prognostic factors for PM.

**Objectives:** The principal study objective was to identify factors for survival in PM from CSCC of the head and neck.

**Results:** Thirty-five patients were included. Mean time to onset of PM was 13 months. Overall 1-, 2- and 5-year survival was respectively 70, 66 and 59%. Independent prognostic factors comprised immunodepression, age at treatment, positive CSCC margins, macroscopic facial nerve involvement, and metastatic cervical adenopathies.

**Conclusion:** The study confirmed an association of several independent prognostic factors at the stage of parotid lymph-node metastasis, related to patient, primary CSCC and PM. Complete primary resection is essential to reduce the risk of PM. Intensified radiologic and clinical surveillance should enable early diagnosis.

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### 1. Introduction

Cutaneous carcinoma is the most frequent human malignancy [1]. Squamous cell carcinoma accounts for 20–30% of non-melanoma skin cancer, and 80% show head and neck location [2].

Unlike upper airway squamous cell carcinoma, cutaneous squamous cell carcinoma (CSCC) seldom shows metastasis. Regional, parotid and/or cervical metastasis rates are 4–5% [3,4]. Although incidence is low, however, prognosis is poor, with 5-year survival of 30–60%, whatever the stage [5]. Diagnosis is often late, in elderly patients with multiple comorbidity, leading to heavy surgical and radiation treatment. Parotid location increases surgical morbidity, with parotidectomy and neck dissection. Treatment at

the lymph-node metastasis stage is a therapeutic challenge, requiring multidisciplinary management.

The main objective of the present study was to identify factors for survival in parotid metastasis (PM) from CSCC of the head and neck.

### 2. Material and methods

A retrospective study, conducted between January 2005 and June 2015, included all patients in a single center treated by parotidectomy for PM from CSCC of the head and neck. The study used data from the university hospital database, ENT, dermatology and oncology consultation records, and community physicians. All patients had been assessed in a multidisciplinary oncology-dermatology team meeting.

The inclusion criterion was parotidectomy for one or more parotid metastases from CSCC of the head, with identified primary.

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**Table 1**  
Prognostic classification of CSCC according to the 2009 guidelines of the French Society of Dermatology Risk area (R+): peri-orificial area (nose, lip, external ear, eyelid) and scalp; dermatitis, burn scar, chronic inflammation or ulceration..Low risk area (R-): other localizations of the cephalic extremity.

Criteria	Group 1: low risk	Group 2: significant risk
<b>Clinical</b>		
Primary vs. recurrence	Primary	Recurrence
Degree of clinical infiltration	Absent	Adherence to deep plane
Symptoms of neurologic involvement	No	Yes
Immune status	Immunocompetent	Immunodepressed
Diameter according to location	< 10 mm in zone R+ < 20 mm in zone R-	≥ 10 mm in zone R+ ≥ 20 mm in zone R-
<b>Pathologic</b>		
Perineural invasion	No	Yes
Degree of cell differentiation	Good	Moderate to undifferentiated
Histologic forms	Common, verrucous, fusiform (except radiation zone), mixed or metatypic CSCC	Desmoplastic > muco-epidermoid > acantholytic CSCC
Depth (Clark level)	≤ III	≥ IV
Thickness	≤ 3 mm	> 3 mm

For each patient, data were analyzed concerning epidemiology (age, gender, immune status), primary CSCC (number of tumors, location, size, recurrence, differentiation, thickness and depth of invasion, perineural invasion or vascular emboli, resection margins, any complementary treatment), PM (discovery circumstances, time to onset after primary treatment, parotid location, size and number of affected nodes, capsule rupture, perineural invasion, vascular emboli, resection margins) and treatment (superficial/total parotidectomy, need for facial nerve resection due to macroscopic invasion, neck dissection, adjuvant treatment). CSCCs at significant risk of metastasis were identified using the clinical and pathologic criteria of the French Society of Dermatology (SFD) [6] to classify the primaries (Table 1).

Overall and specific 1-, 2- and 5-year survival were calculated following Kaplan-Meier, with comparison on log-rank test. Survival was calculated between the date of parotidectomy and that of death or last follow-up. Prognostic factors for PM were explored in the epidemiologic and oncologic data. Quantitative variables were analyzed on univariate analysis by log-rank and on multivariate analysis by Cox model. Continuous variables were analyzed on association tests. 95% confidence intervals and P-values were calculated. Results were reported only when  $P \leq 0.10$ .

### 3. Results

Thirty-five patients were included: 30 male, mean age 75.4 years (range, 55–93 years), and 5 female, mean age 81.2 years (range, 64–92 years): i.e., sex-ratio=6. Four (11.4%) showed immunodepression, 3 had had kidney graft, and 1 was under immunosuppression for skin lymphoma.

All but 2 pathology reports for the primary were available, and resection margins were known for 1 or these 2. Primaries were single, except in 3 patients: i.e., 38 primaries in all (Table 2).

On the SFD classification, 35 of the 36 primaries with pathology data were at significant risk of metastasis. Only 1 lesion (15 mm, temple) was at low risk.

Primary treatment was surgical in all cases:

- 67.6% of the 37 tumors for which margins were known showed complete resection;
- 41.7% of the 32.4% with microscopically positive margins were located in the outer ear;
- 33.3% of those with microscopically positive margins showed local recurrence, treated independently of PM treatment, with onset at a mean interval of 19 months.

Mean time to onset of PM was 13.1 months (median, 8 months; range, 0–63 months). In 2 patients, PM was diagnosed

**Table 2**  
Epidemiological and oncologic data.

	Total	%
<i>n</i> patients	35	100
M/F	30/5	85.7/14.3
Mean age (years)	76.3	
Immunodepression	4	11.4
<i>n</i> lesions	38	100
Size (mean diameter) mm	26.3	
Anatomic site		
Ear	12	31.6
Temple	12	31.6
Scalp	6	15.8
Recurrent lesion	6	15.8
Size		
≥ 10 mm R+	18/33	54.5
≥ 20 mm R-	10/33	30.3
Differentiation		
Moderate or poor	17/35	53.1
Invasion depth		
≥ Hypodermis	25/34	73.5
PNI+	5/36	13.9
VE+	1/36	2.8
R1	12/37	32.4

*n*: number; M: male; F: female; R+: at-risk zone; R-: low-risk zone; PNI+: perineural invasion; VE+: vascular emboli; R1: positive microscopic margins.

**Table 3**  
PM characteristics.

PM	Total	%
Mean diameter (mm)	31.1	
CR+	26	74.3
PNI+	9	25.8
VE+	8	22.9
R1	12	34.3
ND+	15/32	46.9
NDCR+	10/15	66.7

CR+: PM capsule rupture; PNI+: perineural invasion in PM; VE+: vascular emboli in PM; ND+: ≥ positive adenopathies in ipsilateral neck dissection specimen; NDCR+: capsule rupture in neck dissection.

simultaneously to the primary. Mean time to onset of PM in case of microscopically positive margins was 9.5 months.

PM was diagnosed by palpation on clinical examination in all cases except for 1 revealed by peripheral facial palsy. Fine-needle aspiration was performed in 11 cases, and systematically found malignancy-suspect cells.

Superficial parotidectomy was performed in 25.8% of cases, total parotidectomy sparing the facial nerve in 60%, and total parotidectomy sacrificing the facial nerve in 14.2%.

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