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## Case report

# Nasopharyngeal carcinoma with cutaneous metastases

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## ARTICLE INFO

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## ABSTRACT

**Introduction:** Cutaneous metastases from nasopharyngeal carcinoma are extremely rare and associated with a poor prognosis.

**Case reports:** We retrospectively reviewed 820 patients with nasopharyngeal carcinoma treated over a 20-year period in the radiotherapy department of Farhat Hached hospital in Sousse and Ibn Khaldoun Medical centre, Hammam Sousse. Two of these patients presented cutaneous metastases. The skin lesions appeared during radiotherapy and 3 months after treatment of the primary tumour. Cutaneous metastases present as multiple painless nodules and erythematous plaques. Cutaneous metastases were associated with other metastatic sites (liver, bone). One patient received chemotherapy. Both patients died in a context of rapidly progressive disease.

**Discussion:** Nasopharyngeal carcinoma with cutaneous metastases is a rapidly fatal disease. In the light of these two cases and a review of the literature, patients with this disease are aged between 30 and 63 years with a marked male predominance. Cutaneous metastases are correlated with a more advanced primary tumour. The main sites are the trunk and scalp. There is no standard treatment modality for this disease and survival does not exceed 9 months.

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## 1. Introduction

Undifferentiated carcinoma of nasopharyngeal type (UCNT) is a malignant disease related to Epstein-Barr virus (EBV) infection predominantly observed in Southern China, Southeast Asia and Northern Africa. Tunisia is a zone of intermediate risk with a prevalence of about 3 to 4/100,000 [1]. UCNT is characterized by a high potential for visceral metastases, especially involving bone, liver and lung. Cutaneous metastases are exceptional and are associated with poor prognosis. We report two cases of cutaneous metastases and a review of the literature.

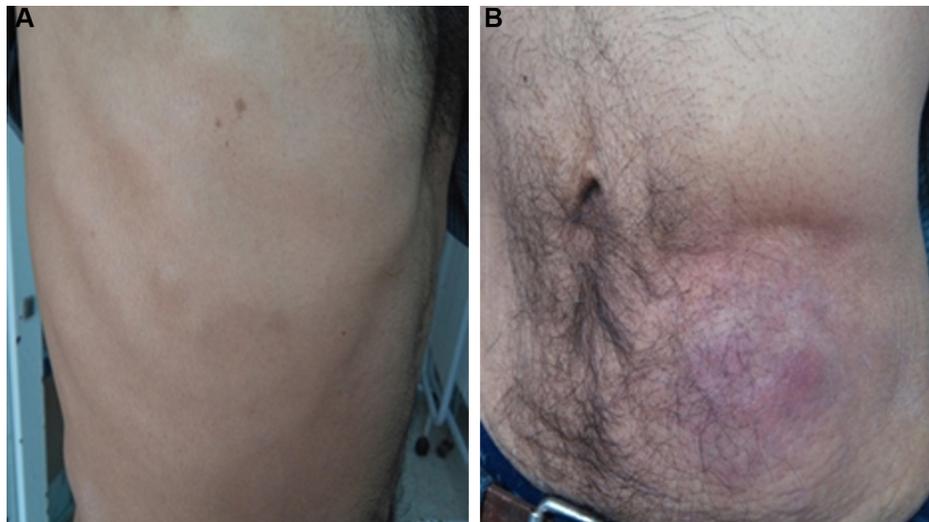
## 2. Case 1

A 54-year-old man with stage T3N3aM0 UCNT diagnosed in a context of cervical lymph nodes and earache was treated with 3 cycles of neoadjuvant chemotherapy, followed by head and neck radiotherapy at a planned dose of 70 Gy in 35 fractions. During the fourth week of radiotherapy, he presented disseminated cutaneous nodules on the trunk measuring 1 to 2 cm (Fig. 1). Biopsy revealed cutaneous metastases of UNCT.



Fig. 1. Multiple erythematous nodules on the back.

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**Fig. 2.** A. A subcutaneous nodule on the trunk. B. Erythematous plaques on the abdomen.

**Table 1**

Table summarising the 8 cases reported in the literature and the two patients in this article.

Reference	Age (years)	Sex	Sites of metastases	Time to progression	Presentation	Other metastasis	Treatment	Follow-up
Fatihli et al. [5]	50	M	Scalp, abdomen, back	At diagnosis	Nodules	Lymph nodes, bone	RT-CT	D, 9 months
Caluglo et al. [6]	40	M	Chest, arm	During treatment	Erythematous nodules	Liver, lung	CT (5FU), RT 30 Gy in 10 fractions	D, 3 months
Luk et al. [7]	63	M	Chest, axilla, epigastrium, nipple	6 months	Painful nodules	Bone	RT	D, 8 months
	47	F	Chest	12 months	Painful nodules	Local recurrence, bone, lung	CT (5FU, CDDP)	D, 8 months
	32	M	Buttocks	18 months	Painful nodules	Local recurrence, bone	No treatment	D, 1 months
Yucel et al. [8]	30	M	Back	48 months	Nodules	Lung	CT (5FU, CDDP)	D, 9 months
	34	M	Scalp, forearm	At diagnosis	Painless erythematous nodules	None	Resection, CT (5FU, CDDP)	D
	40	M	Abdomen	At diagnosis	Erythematous nodules	Bone	Excision	D, 4 months
Our cases	54	M	Back	During treatment	Painless erythematous nodules	Liver	No treatment	D, 2 months
	53	M	Trunk, lower limb	3 months	Painless nodules Erythematous plaque	Bone	CT (5FU, CDDP)	D, 3 months

M: male; F: female; RT: radiotherapy; CT: chemotherapy; D: deceased.

Radiotherapy was stopped after a dose of 44Gy due to general physical health deterioration. Repeat staging assessment showed liver metastases. The patient died after two weeks of radiotherapy.

### 3. Case 2

A 53-year-old man was treated in 2016 for stage T4N2M0 UCNT by 3 cycles of neoadjuvant chemotherapy (5FU-CDDP) followed by concomitant chemoradiotherapy at a dose of 70 Gy. Clinical examination at three-month follow-up revealed painless subcutaneous nodules varying in size between 1 and 3 cm on the trunk and lower limbs and a large erythematous plaque on the abdomen (Fig. 2). Excision-biopsy of one of the nodules demonstrated cutaneous metastasis of UCNT. Magnetic resonance imaging did not reveal any signs of local recurrence, but bone scan demonstrated disseminated bone metastases. The patient received a first cycle of chemotherapy and died two weeks later.

### 4. Discussion

Cutaneous metastases of UCNT are exceptional, as they are observed in only 0.7–9% of all cancers [2]. The primary site is essentially the lung and kidney in men and the breast in women [2]. Cutaneous metastases from head and neck cancers are very rare, estimated to account for 9.1% of all cutaneous metastases [3,4]. A review of the literature revealed only 8 cases published to date [5–8] (Table 1).

Two mechanisms of cutaneous metastases have been described: “clonal expansion” due to genetic and epigenetic modifications, suggesting that cutaneous metastases represent the last step of tumour progression; and “the rare variant model”, which suggests that metastases arise by selecting rare, highly aggressive variants from the primary tumour [4]. Cutaneous metastases occur as a result of haematogenous spread for sites situated away from the primary tumour and lymphatic spread for sites adjacent to the primary tumour [6].

The mean age of the cases reported in the literature was 42 years (range: 30–63 years), with 7 men for one woman. Our patients were two men aged 54 and 53 years.

Cutaneous metastases were often diagnosed in patients with a known cancer (5 patients) and were correlated with advanced disease. These metastases were present at the time of diagnosis of UCNT or occurred during treatment in 4 cases. In the other patients, the time to onset of cutaneous metastases ranged from 6 to 48 months with a mean of 21 months. In our cases, cutaneous metastases appeared during treatment and 3 months after treatment.

In the study by Saeed et al. concerning 77 cases of cutaneous metastases, the lesions involved the trunk in 40% of cases, the head and neck in 28% of cases, the extremities in 18% of cases and several sites in 14% of cases [3]. Cutaneous metastases tend to arise close to the primary tumour. Cutaneous metastases from primary head and neck tumours are predominantly situated in the head, neck and trunk [3]. The predominant sites of cutaneous metastases from UCNT were the scalp, trunk, axilla, buttocks and limbs.

Cutaneous metastases mostly present in the form of single or multiple rapidly growing subcutaneous nodules [2–4]. The clinical presentation of cutaneous metastases depends on the histology of the primary tumour and the route of dissemination [4,9]. These lesions may present in the form of cellulitis or erysipelas in the case of lymphatic spread and in the form of telangiectasia in case of haematogenous spread [9]. All metastases from UCNT consisted of nodules, which were painful in 3 cases. The two patients reported here presented painless erythematous nodules on the trunk.

Staging must be performed in the presence of cutaneous metastases, as the majority of patients present other metastatic sites [3,4]. Seven patients with UCNT had distant metastases, essentially bone metastases and two patients presented local relapse. In our two cases, cutaneous progression was accompanied by bone and liver metastases.

Surgical resection is impossible in most cases due to the presence of disseminated metastases. However, Yucet et al. showed that isolated cutaneous metastases can be treated surgically and that concomitant systemic therapy improved survival [8]. Chemotherapy (5FU-CDDP) achieved a partial response [7]. Radiotherapy can be proposed to patients ineligible for chemotherapy or who progress on chemotherapy [6,7]. One of our patients did not receive any further treatment due to marked deterioration of his general state of health and the other patient received one cycle of chemotherapy.

Cutaneous metastases have a very poor prognosis, but the clinical course varies considerably according to the primary tumour [4]. Cutaneous metastases from breast cancer are associated with better survival than metastases from other cancers, with a median survival of 42 months versus 6 months, respectively [9,10]. Median survival was 6 months (range: 1–9 months) for patients with UCNT, and 2.5 months for our two patients.

## 5. Conclusion

The diagnosis of cutaneous metastases from UCNT is essential in order to adapt treatment and determine the prognosis. Cutaneous metastases indicate the presence of disseminated metastatic disease associated with high mortality. An effective treatment is necessary in order to improve the prognosis.

## Disclosure of interest

The authors declare that they have no competing interest.

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