

CASE REPORT

## Skin metastasis: an unusual localization from laryngeal carcinoma

Cilt metastazı: Larenks karsinomundan kaynaklanan nadir bir lokalizasyon

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Skin metastasis from laryngeal carcinoma is rare and indicates a poor prognosis. A case of laryngeal carcinoma with unusual metastasis to the skin of the hand is reported. The patient had undergone total laryngectomy, left radical neck dissection and right functional neck dissection. After the operation, the patient received radiotherapy. On the postoperative 18th month, a mass on the left hand was observed. It was found to be a metastatic tumor from laryngeal carcinoma, histopathologically as well as immunohistochemically. Metastatic potential in malignant neoplasm is generally correlated with reduced cellular adhesiveness. We investigated the expression of the vascular endothelial growth factor (VEGF), matrix metalloproteinase-9 (MMP-9), E-cadherin. Interestingly the immunohistochemical expression characteristics of such an aggressive tumor are not positive.

**Key Words:** Carcinoma; squamous cell/pathology; laryngeal neoplasms/pathology; neoplasm metastasis; skin neoplasms/pathology/secondary.

Larenks kanserinde cilt metastazı, kötü prognozu gösteren nadir bir durumdur. Bu makalede ele cilt metastazı yapan bir larenks kanseri olgusu sunuldu. Hastaya total larenjektomi, sol radikal boyun disseksiyonu ve sağ fonksiyonel boyun disseksiyonu yapıldı. Hastaya ameliyattan sonra radyoterapi uygulandı. Ameliyat sonrası 18. ayda sol elinde metastatik kitle gözlemlendi. Histopatolojik ve immünohistokimyasal olarak kitlenin larenks kanserinden kaynaklanan metastatik bir tümör olduğu saptandı. Malign neoplazilerde metastaz potansiyeli genellikle "cellular adhesiveness" ile korelasyon gösterir. Bu olguda vascular endothelial growth factor (VEGF), matrix metalloproteinase-9 (MMP-9), E-cadherin ekspresyon paternleri araştırıldı. Böylesine agresif seyirli bir tümörde, immünohistokimyasal ekspresyon karakteristiklerinin pozitif olmaması ilginçtir.

**Anahtar Sözcükler:** Karsinom; yassı epitel hücreli/patoloji; larengeal neoplaziler/patoloji; neoplasm metastazı; cilt neoplazileri/patoloji/ikincil.

Although development of distant metastasis from laryngeal squamous cell carcinoma (SCC) is a rare condition, the most encountered distant

metastatic site is the lung.<sup>[1,2]</sup> However, distant metastasis from laryngeal carcinoma to the extremity skin is extremely rare. We report a case of laryn-

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geal carcinoma with unusual metastasis to the skin of the hand.

### CASE REPORT

A 61-year-old man visited our clinic complaining of dysphagia, hoarseness and hemoptysis. He was a heavy smoker and alcohol consumer for 30 years. In indirect laryngoscopy, there was a mass destructing the epiglottis on the left, extending into left aryepiglottic plica, left ventricle, left arytenoid, interarytenoid region and caused fixation. Laryngeal biopsy revealed squamous cell carcinoma (SCC). Total laryngectomy, left radical and right functional neck dissection were performed. He underwent postoperative radiotherapy as he had bilateral nodal metastasis with extracapsular spread in the neck and thyroid cartilage invasion.

On the postoperative 18th month, he presented with a 3x2 cm fixed mass on the left submandibular region. Fine needle aspiration biopsy revealed SCC. He rejected the therapy and two months later applied to our clinic with an ulcerated and haemorrhagic mass on the palmar surface of metacarpophalangeal joint of the left fifth finger (Fig. 1). The chest computed tomography (CT) was unremarkable. Biopsies from the hand lesion showed poorly differentiated SCC (Fig. 2). The patient underwent an exploration of the left submandibular region. During the operation, the cervical mass was found to have prevertebral fascial invasion passing deep through the carotid artery and considered to be inoperable. The metastatic haemorrhagic mass on the left hand was resected. Palmar mass showed poorly differentiated SCC, but there was no epidermal involvement despite the large ulcerated surface.

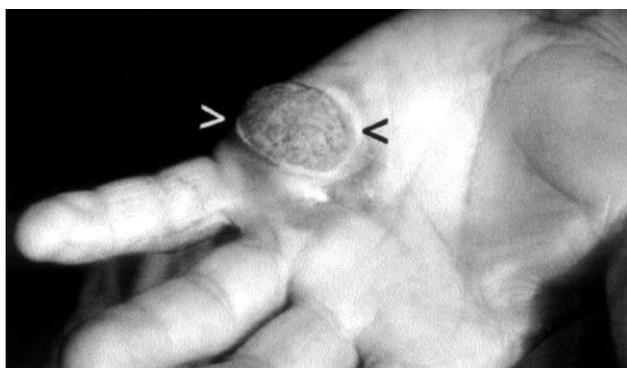


Fig. 1 - Cutaneous mass on the palmar surface of metacarpophalangeal joint of the left fifth finger.

To get a further insight into this highly aggressive carcinoma, we examined the immunohistochemical expression of vascular endothelial growth factor (VEGF) (Takara, Japan; 1:250), E-cadherin (Takara, Japan; 1:150) and matrix metalloproteinase-9 (MMP-9) (Neomarker, Fremont CA, USA; prediluted). Tumor samples from larynx and hand were stained with these antibodies. All the specimens revealed the same expression pattern. MMP-9 and VEGF were negative and E-cadherin was mildly positive (Fig. 3).

Two months later lung metastases and disseminated skin metastases were detected. He died five months after the detection of the mass on the left submandibular region.

### DISCUSSION

Metastasis to the upper extremity skin is relatively uncommon. The most frequent primary tumors are malignant melanoma and breast carcinoma, respectively.<sup>[3]</sup> Upper extremity cutaneous metastasis from laryngeal carcinoma is an extremely rare condition. To our knowledge, only a few cases have been reported so far.<sup>[4-5]</sup>

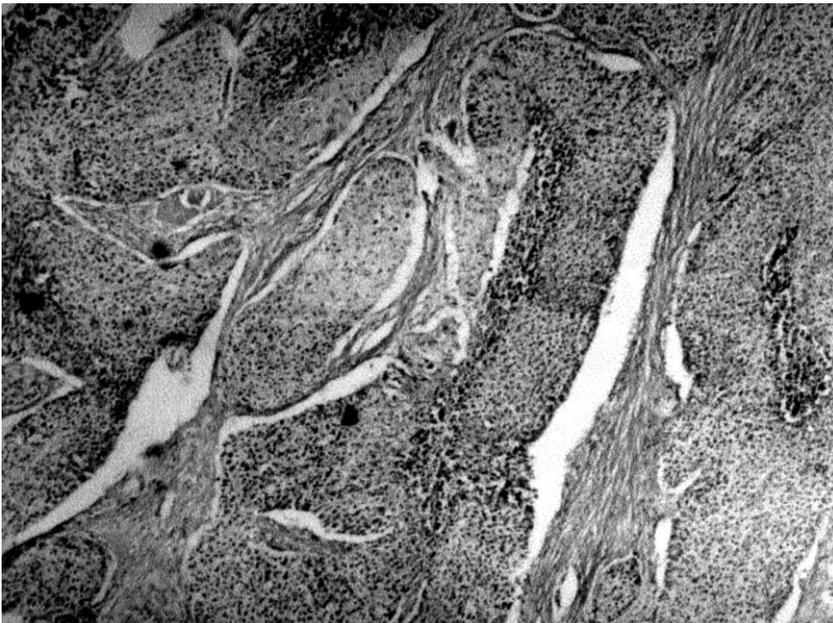
In laryngeal carcinoma, the metastasis, except from regional cervical lymph nodes are considered to be distant metastasis. Cutaneous neck metastasis via superficial cervical lymphatics is also categorized as distant metastasis. Skin metastasis of laryngeal carcinoma is mostly due to the direct extension of metastatic cervical nodes to the skin or peristomal regional recurrence.<sup>[3,6]</sup> In our patient, skin of the hand metastasis was considered to be hematogenous spread, which is a rare pattern of distant metastasis.

Distant metastasis from laryngeal carcinoma is not a common condition if any primary or secondary lesion does not exist.<sup>[6,7]</sup> The common concept about distant metastasis is that the lungs are involved prior to the other organs.<sup>[7,8]</sup> In our patient, hand mass preceded lung metastasis by two months. However, pulmonary metastatic lesion may not be large enough to be via recognized at the same time. In lungs any lesion smaller than 3 mm cannot be evaluated by imaging systems.<sup>[7,9]</sup> Another postulate is that this unusual metastatic process in our patient could have disseminated through the paravertebral venous plexus of Batson before pulmonary metastasis was present.

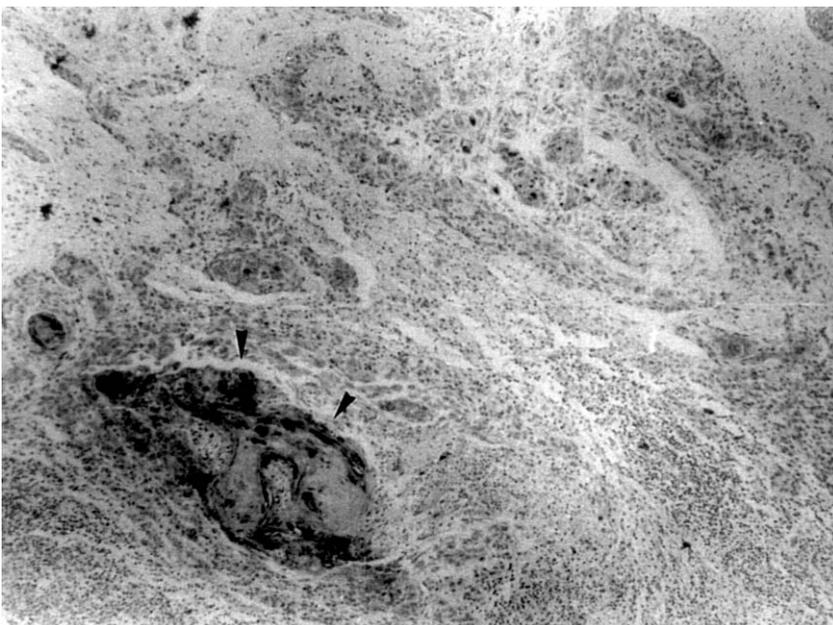
Pitman and Johnson<sup>[10]</sup> stated that the development of skin metastasis was most closely related to the presence of two or more cervical nodal metastases and/or extracapsular spread of tumor in the cervical metastases. Advanced stage is also considered as a predicting factor for distant metastasis.<sup>[11]</sup> Besides, the most common site in patients with distant metastases from laryngeal carcinoma is the supraglottic region.<sup>[1,2,7,8]</sup> Our patient had several poor prognostic factors such as advanced stage supraglottic tumor,

multiple nodes with extracapsular extension and regional recurrence that may have played a role in occurrence of distant skin metastasis. In addition, we hypothesize that postoperative radiotherapy may have contributed to this unusual metastatic process.

Cutaneous metastasis of the head and neck carcinoma is a poor prognostic factor. It has been reported that the expression of vascular endothelial growth factor (VEGF), E-cadherin and matrix metalloproteinases (MMPs) are correlated with metastasis



*Fig. 2 - The histopathologic appearance of the cutaneous mass. Poorly differentiated solid areas of squamous cell carcinoma (H-E x 200).*



*Fig. 3 - Reduced expression of E-cadherin in invasive squamous cell carcinoma (H-E x 40).*

of various tumors.<sup>[11,12]</sup> Tumor samples from larynx and thenar region were stained with these antibodies. All the specimens revealed a similar expression pattern. MMP-9 and VEGF were negative. E-cadherin was mildly positive. In normal stratified squamous epithelium E-cadherin and MMP-9 were stained positively and VEGF was consistently negative. These results, that showing the expression of the VEGF, MMP-9 and E-cadherin of such an aggressive tumor are very interesting.

The average survival period is three months after diagnosis of skin metastasis in ninety percent of patients.<sup>[10]</sup> Chemotherapy, external beam radiation, brachytherapy, excision, indomethacin and immunotherapy were carried out as the treatment modalities.<sup>[5,8,10]</sup> Surgical resection of the hand lesion in our patient was being considered for palliation.

In the development of distant skin metastasis from laryngeal carcinoma, it was thought that advanced stage supraglottic tumor, regional metastasis with extracapsular extension are negative factors. Treatment should be palliative since the prognosis is poor.<sup>[6-9]</sup>

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