



Unusual metastasis of esophageal cancer

Neobična metastaza karcinoma jednjaka

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Abstract

Introduction. Carcinoma of the esophagus is in the eighth place by the frequency of malignant diseases and the sixth cause of death from cancer worldwide. It usually metastasizes to regional lymph nodes, liver, lungs, central nervous system, and bones, but metastases can appear to unusual locations such as facial skin and lips. **Case report.** We presented a 56-year-old man who reported to his physician because of upper lip swelling. A physical checkup of the patients also showed a lesion on the skin of the left temporal region and both lesions were biopsied. Based on the results of histopathological and immunohistochemical analyses of the samples a diagnosis of metastatic adenocarcinoma to the skin was established. Additional diagnostic procedures, including esophagogastroduodenoscopy, detected the infiltration into the distal part of esophagus, which was histopathologically confirmed as adenocarcinoma of esophagus. The results of positron emission tomography/computed tomography (PET/CT) examination showed the invasion of the disease. Because of the disease expansion, a multidisciplinary oncology team suggested chemo- and radiotherapy treatment. The patient has received 4 cycles of platinum-based chemotherapy so far. **Conclusion.** The physicians should always consider unusual skin lesions as the first sign of cancer spreading.

Key words:

esophageal neoplasms; neoplasm metastasis; lip; diagnosis; adenocarcinoma; histological techniques; immunohistochemistry.

Apstrakt

Uvod. Karcinom jednjaka je osmi karcinom po učestalosti i šesti uzrok smrti od karcinoma u svetu. Najčešće metastazira u regionalne limfne čvorove, jetru, pluća, centralni nervni sistem, kosti, ali se sreću metastaze i na neuobičajenim mestima kao što su koža lica i usne. **Prikaz bolesnika.** Prikazali smo bolesnika starog 56 godina koji se javio lekaru zbog oteklina u predelu gornje usne. Pregledom je viđena i promena u predelu kože slepoočnog predela glave sa leve strane te su u istom aktu ekstirpirane obe promene. Patohistološkim pregledom, uključujući imunohistohemijsku analizu, postavljena je dijagnoza metastatskog adenokarcinoma u koži. Dopunskom dijagnostikom, uključujući ezofagogastroduodenoskopiju viđena je infiltracija distalnog dela jednjaka, čiji je patohistološki nalaz potvrdio dijagnozu adenokarcinoma jednjaka. Pozitronska emisija tomografija-kompjuterizovana tomografija (PET/CT) je ukazala na proširenost bolesti. S obzirom na proširenost bolesti multidisciplinarni onkološki tim je predložio hemioterapiju i radioterapiju. Bolesnik je do sada primio četiri serije hemioterapije po protokolu sa platinom. **Zaključak.** Lekari moraju imati na umu da neuobičajene promene na koži mogu biti prvi znak proširenosti karcinoma.

Ključne reči:

jednjak, neoplazme; neoplazme, metastaze; usna; dijagnoza; adenokarcinom; histološke tehnike; imunohistohemija.

Introduction

Carcinoma of the esophagus is sixth cause of death from cancer worldwide (fifth cause from cancer among men and eighth among women). China, countries of Central Asia, and certain parts of America are the regions with the highest incidence. In Europe, carcinoma of the esophagus is a rare malignant disease¹. In Serbia about 460 newly diagnosed patients are registered annually². The highest incidence is in the region of Vojvodina and it ranges 7 new cases *per* 100,000 yearly.

Mostly it affects older population in the sixth decade of life. Adenocarcinoma of the esophagus most frequently metastasizes to regional lymph nodes, liver, lungs, central nervous system, bones and rarely to facial skin and scalp.

Case report

A 56-year-old male patient visited the physician because of the skin lesion on his upper lip and skin of the left temporal region. Both lesions were biopsied and the samples were

histopathologically analyzed. Based on routine hematoxylin and eosin staining (Figure 1) the diagnosis of metastatic adenocarcinoma was established. Because of the immunoprofile of tumor cells [cytokeratin (CK) 7 positive (Figure 2), epithelial membrane antigen (EMA) positive (Figure 3 and

4), carcinoembryonic antigen epithelial membrane antigen (CEA) positive, CK20, and thyroid transcription factor-1 (TTF-1) negative] additional immunohistochemical analysis of tumor tissue was done. The results presented as adenocarcinoma metastasis to skin.

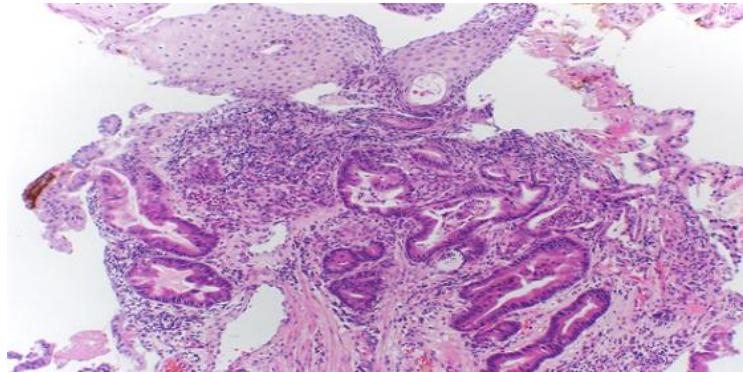


Fig. 1 – Mucosa and submucosa of the esophagus infiltrated by tumor tissue (hematoxylin and eosin staining, $\times 10$).

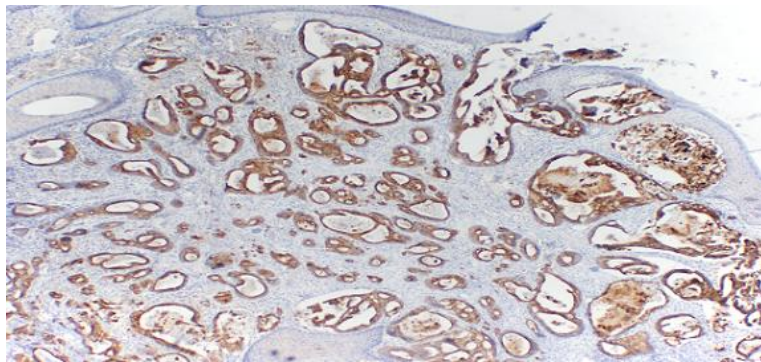


Fig. 2 – Tumor tissue infiltration into the skin of the upper lip (Cytokeratin7+, $\times 4$).

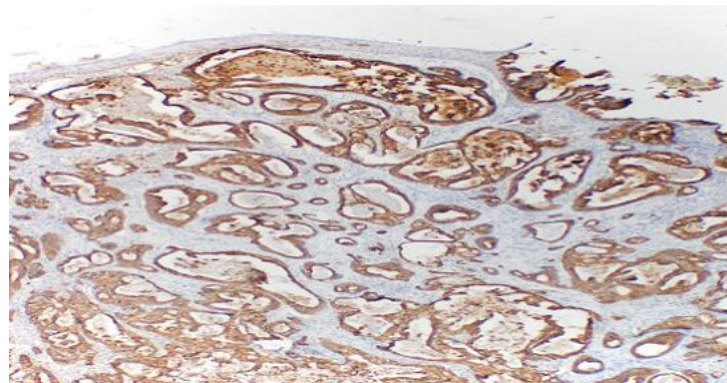


Fig. 3 – Tumor tissue infiltration into the skin of the upper lip (Epithelial membrane antigen +, $\times 4$).

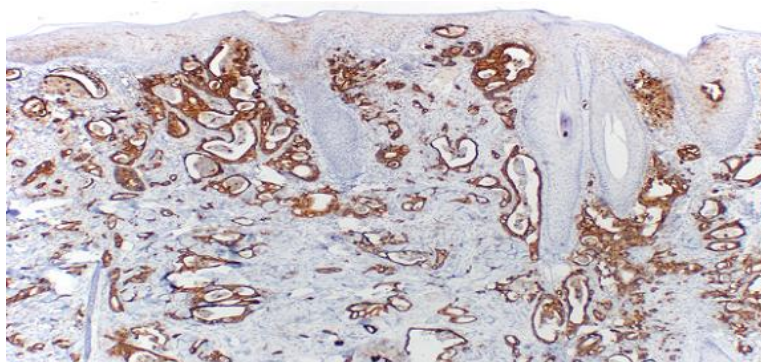


Fig. 4 – Tumor tissue infiltration into the skin of the left temporal region (Epithelial membrane antigen +, $\times 4$).

Differential diagnosis procedure referred to primary adenocarcinoma of gastrointestinal tract. The patient has been suffering from rheumatoid arthritis for 10 years. He consumes alcohol moderately and quit smoking 27 years ago. He smoked about 15 years on the average 30 cigarettes *per* day. As he complained of swallowing difficulties esophagogastroduodenoscopy was performed. The examination results showed an infiltrative stenosis of esophagus at 38 cm of its length, which was impassable for the tip of the instrument. The lesion was biopsied and the sample was histopathologically analyzed. The result showed a well-differentiated adenocarcinoma. The findings of computed tomography (CT) examination of the chest and abdomen indicated the presence of single lymph nodes in mesentery up to 6 mm in size and one small lymph node conglomerate of 14 × 8 mm. Bilateral diffuse nodular lesions found in lung parenchyma were most probably secondary deposits. In addition, CT findings evidenced lesion infiltration into the distal part of the esophagus and cardia. The patient was referred to positron emission tomography (PET)-CT examination by the surgeon to evaluate the expansion of the primary disease. The findings of the examination showed metabolic activity of lymph nodes in the axilla, bronchopulmonary segment right, preaortic space, and bilaterally in mesentery. The active focuses were also detected in the liver right lobe, skeleton (left arm, right shoulder blade, rib 9 right, cervical vertebra 7, lumbar vertebrae 1, 2, and 4, pelvic bones bilaterally, and proximal ends of both femur. Thyroid gland was polynodally changed and enlarged. A multidisciplinary oncology team indicated the treatment with chemotherapy (adriamycin 40 mg/m² at the day 1; 5-fluouracil 300 mg/m² at the day 1–5; cisplatin 20 mg/m² at the day 1–5, every four weeks) and radiotherapy. So far, the patient was administered 4 cycles of chemotherapy, not associated with any significant side effects. The patient reported smaller swallowing problems. Radiotherapy has not been initiated yet.

Discussion

The incidence of esophageal adenocarcinoma is significantly increasing^{3,4}. Most patients present at the advanced

stage where therapeutic measures with a curative intent are not feasible⁵. Carcinoma of the esophagus characterized with biologically aggressive course, local infiltration, involvement of adjacent lymph nodes, and distant metastases by means of hematogenous routes⁶. Most frequently it metastasizes to lymph nodes (45%), liver (35%), lungs (20%), skeleton (10%), peritoneum (2%), and brain (1.5%)⁷. In total of 4,000 cases of metastatic esophageal carcinoma skin metastases were found in about 10% of patients⁷. Squamous cell carcinoma and adenocarcinoma of the esophagus metastasize to the skin with an equal frequency in less than 1% of cases. Similar to our case, Nisi et al.⁸ report a case of esophageal carcinoma with upper lip metastases. The patient was confirmed to be affected with adenocarcinoma of the gastroesophageal junction with secondary deposits. Iwanski et al.⁹ describe a patient with disseminated and extensive skin lesions. Histopathological analyses of these lesions show the presence of esophageal carcinoma. Maheshwari et al.¹⁰ report a case of a female patient with skin lesions and difficulties in swallowing. Adequate diagnostic procedures and histopathological analysis of the lesions confirm skin metastases. Herbella et al.⁷ describe a case of a patient with dysphagia and painless but rapidly advancing ulcerations on nose and neck, which all were histopathologically verified as metastases from squamous cell carcinoma of the esophagus. There is also a report on a patient presented with skin lesions two years after the operation of adenocarcinoma of the gastroesophageal junction; the lesion was histopathologically verified as adenocarcinoma⁷. Metastasizing of esophageal adenocarcinoma to the upper lip is rare and with poor prognosis because of the high probability of secondary localization of the disease⁸. In total a 4-year survival of patients affected with carcinoma of the esophagus, regardless the stage of the disease, is lower than 10%, and 21% after the surgical treatment¹¹.

Conclusion

Physicians should always consider unusual lesion of the skin, which may be the first sign of disease expansion.

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