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A- Conception and study design; B - Collection of data; C - Data analysis; D - Writing the paper; E- Review article; F - Approval of the final version of the article; G - Other (please specify)

ABSTRACT

Introduction: The most common neck masses in adults are neoplastic in nature, so they should be treated as neoplasms until the diagnosis turns out otherwise.

Case presentation: A 72-year-old man was admitted to the hospital to remove a suspicious lesion in the neck area on the right side. The patient's right lymph node was removed and taken for histopathological evaluation which showed the metastasis of non-keratinized squamous cell carcinoma to the lymph node, without any signs of crossing the nodal capsule. It was suspected that the most likely primary tumor location might be in the nasopharynx and middle pharynx area. PET examination revealed foci of increased uptake in the right palatine tonsil and the lateral wall of the oropharynx on the right. Due to its results doctors decided to collect the suspected right palatine tonsil and a section from the right side of the pharynx. The collected material was sent for histopathological examination in which the right palatine tonsil was covered by normotypic epithelium with extensive fibrosis in the stroma; a section of a lateral throat stenosis on the right side with normotypic epithelium and high expression of the Ki67 antigen in the reproductive center. The Real-Time PCR test of the previously removed lymph node revealed the presence of HPV DNA of the genotype with high oncogenic potential - HPV-16.

Conclusions: In recent years, there have been a significant increase in the importance of infection with oncogenic types of HPV, mainly HPV-16, as the etiology of head and neck cancers, including SCCUP. For this reason, diagnosis for highly oncogenic HPV may be considered when SCCUP is suspected. Treatment should be determined by multidisciplinary committee and focused on finding the primary tumor location which, according to the literature, have the most relevant impact for further treatment and prognosis.

Keywords: squamous cell carcinoma, SCC, SCCUP, OPSCC

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INTRODUCTION

The most common neck masses in adults are neoplastic in nature, so they should be treated as neoplasms until the diagnosis turns out otherwise. The vast majority of the neck masses are the metastasis of the baseline tumors located in the oral cavity, pharynx or larynx. SCC is spread through the lymphatic system, starting with the local and regional lymph nodes. SCC metastases to the neck lymph nodes of unknown primary site (SCCUP) account for about a few percent of all head and neck cancers [1].

CASE PRESENTATION

A 72-year-old man was admitted to the hospital for the removal of a suspicious lesion in the neck area on the right side which turned out to be a right lymph node. After the lymphadenectomy doctors performed the evaluation of the node and found inside of it a cyst 1.7 cm in diameter with visible damage in the area of 0.5 cm. Macroscopically, the cyst walls were smooth. The material was sent for the histopathological evaluation. The microscopic image revealed the metastasis of non-keratinized squamous cell carcinoma to the lymph node, without any signs of crossing the nodal capsule (Fig. 1a,b). It was suspected that the most likely location of the primary tumor might be in the nasopharynx and middle pharynx area. The patient was referred to positron emission tomography (PET) using the 18FDG marker to find the primary focus of the lymph node lesion. PET imaging revealed foci of increased uptake in the right palatine tonsil and the lateral wall of the oropharynx on the right (SUV max 7.3) and in the along 55mm in the greater curvature of stomach (SUV max 5.7). Due the examination results, suspected right palatine tonsil (dimensions 3x2x1 cm) and a 0.3 cm section from the right side of the pharynx were collected. The material was sent for histopathological examination, in which revealed that the right palatine tonsil was covered by normotypic epithelium with extensive fibrosis in the stroma; a section of a lateral throat stenosis on the right side with normotypic epithelium and high expression of the Ki67 antigen in the reproductive center and outside this center the expression was at the level of 1-2%. It was decided to commission the evaluation of the previously removed lymph node for HPV DNA. The Real-Time PCR test showed the presence of HPV DNA of the genotype with high oncogenic potential - HPV-16.

DISCUSSION

The European Cancer Patient Coalition described head and neck cancers were the sixth most common cause of human malignancies in 2017. Most often, these neoplasms are located in the epithelial line in the upper respiratory and digestive system. Mainly are head and neck squamous cell carcinomas (HNSCC) [2]. The key factors causing head and neck cancers are tobacco and alcohol, however, in recent years, an increasing importance of oncogenic HPV infection as an etiological factor of head and neck cancers, in particular oropharyngeal squamous cell carcinoma (OPSCC), can be observed [3]. These tumors are more common in men than in women, with a ratio of 2: 1 to 4: 1 [4]. Patients with HNSCC mainly present symptoms of a local-regional disease with enlarged neck lymph nodes [2]. However, there are cases with of only the neoplastic lymph node in the neck [5]. Diagnostic process of SCCUP is based on the search for a primary tumor that may be a source of metastasis. It is recommended to perform endoscopy of the upper respiratory and digestive tract, esophagoscopy, tracheobronchoscopy and imaging tests (CT, MRI,
FDG-PET and others) [5]. The key issue seems to be a complete, operational diagnosis of the upper part of the respiratory tract in suspicious places of the mucosa, including targeted biopsy. Biopsies from random areas should not be performed due to low efficiency. In patients with unilateral lymphadenopathy, in whom the diagnosis does not identify suspicious primary location, the surgeon should consider ipsilateral tonsillectomy of the palatine tonsils, followed by ipsilateral tonsillectomy of the lingual tonsil and bilateral tonsillectomy of the palatine tonsils [6]. The chance of finding a primary lesion in operative endoscopy with or without targeted biopsy ranges from 20% to 30% [7]. Therefore, complete and complicated diagnostics should be carefully and carefully performed. Considering the growing importance of HPV etiology in oropharyngeal squamous cell carcinoma (OPSCCs) and in SCCUP, it seems reasonable to extend diagnostics in this direction. Highly oncogenic HPV is detected in approximately 80% in the USA and 18%-90% in Europe of OPSCCs [2]. HPV type 16 is responsible for more than 90% of HPV DNA positive for OPSCCs. Cystic degeneration is a frequent find in the metastatic lymph node of the neck in HPV positive OPSCCs and HPV positive SCCUPs [8]. Due to the lack of randomized controlled trials towards SCCUP, optimal regional therapy is controversial. Treatment of unilateral neoplasms with small neck volume should be determined based on surgery or radiotherapy [6]. Due to the increased importance of HPV as the etiology of head and neck cancers, including SCCUP, older retrospective studies are less useful in the current therapy. Recent studies do not show therapeutic difference between surgery and radiotherapy as the first choice of treatment [9]. Patients with unilateral SCCUP in the neck lymph node, HPV positive, initially treated with radiotherapy should simultaneously undergo radiotherapy of the presumed primary lesions. In patients with removed lymph nodes with neoplastic extranodal infiltration, adjuvant chemoradiotherapy treatment should be offered [6].

CONCLUSION

In the course of diagnostics, a primary focus can be established in approximately 20-30% of patients [7]. In recent years, there have been a significant increase in the importance of infection with oncogenic types of HPV, mainly HPV-16, as the etiology of head and neck cancers, including SCCUP [8]. For this reason, diagnosis for highly oncogenic HPV may be considered when SCCUP is suspected. Surgical treatment and radiotherapy play a key and equal role in therapy. The described patient was diagnosed with metastasis of a non-keratinized squamous cell tumor to the right neck lymph node with an undetermined primary tumor with the presence of highly oncogenic HPV-16 in metastasis. The advanced age of the patient is surprising, especially in the light of the statistical data which showing that the occurrence of this type of neoplasms is so much common in young men. We believe that treatment should be determined by multidisciplinary committee and focused on finding the primary tumor location which according to the literature have the most relevant impact for further treatment and prognosis.

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