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CASE SERIES AND REPORTS

Papillary squamous cell carcinoma of the palatine tonsil: a rare cancer of the head and neck

Carcinoma squamoso papillare della tonsilla palatina: un raro tumore della testa e del collo

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SUMMARY

Papillary squamous neoplasms of the upper respiratory tract are rare variants of squamous cell carcinomas. They are characterised by an exophytic, papillary growth and generally have favourable prognosis. The tumour has been described in the upper aerodigestive tract. In this context, most common sites of involvement are the larynx and hypopharynx, and rarely the oral cavity and oropharynx. The limited studies and small number of published cases of papillary squamous cell carcinoma of the palatine tonsil led us to make a complete analysis of this tumour by analysing the clinical, histological, radiological, virological and therapeutic aspects that are not always present in the literature. A case of papillary squamous cell carcinoma of the palatine tonsil is reported. The lesion (T2N0M0) was located into the left ~~palatal~~ tonsil that hung towards the oral cavity. Both HPV 16 DNA and E6/E7 mRNA were detected in the lesion. The clinicopathological profile of the neoplasm is presented and a comprehensive review of recent literature was made by analysing all aspects of interest of this neoplasm.

KEY WORDS: Squamous neoplasm • Human papillomavirus • Upper aerodigestive tract • Blot hybridization analysis

RIASSUNTO

Le neoplasie squamose papillari delle vie aeree digestive superiori sono una rara variante del carcinoma a cellule squamose. Sono caratterizzate da una crescita esofitica papillare e hanno una prognosi generalmente favorevole. Il tumore è già stato descritto a livello delle vie aeree digestive superiori. In tale contesto, le localizzazioni più frequenti sono la laringe e l'ipofaringe, mentre raramente sono interessati la cavità orale e l'ipofaringe. Gli studi limitati unitamente all'esiguo numero di casi pubblicati di carcinoma squamoso papillare a localizzazione tonsillare, ci hanno indotto a una completa analisi di questo tumore, analizzando gli aspetti clinici, istopatologici, radiologici, virologici e terapeutici, non sempre presenti in letteratura. Un case report di carcinoma squamoso papillare della tonsilla palatina è pertanto riportato. La lesione (T2N0M0), localizzata a livello della tonsilla palatina sinistra, si aggettava verso la cavità orale. HPV DNA 16 e mRNA E6/E7 erano rilevati nella lesione. Un profilo della neoplasia è pertanto presentato unitamente a una completa revisione della recente letteratura, analizzando tutti gli aspetti di interesse di tale neoplasia.

PAROLE CHIAVE: *Neoplasia ~~squamosal~~ • HPV • Vie aeree digestive superiori • Ibridizzazione blot*

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Introduction

Papillary squamous cell carcinoma (PSCC) is a variant of squamous cell carcinoma, recently identified and classified separately in the World Health Organization (WHO) classification [1]. It is characterised by an exophytic, papillary growth and has favourable prognosis [1].

PSCC occurs predominantly in males (male-female ratio of 2:1) and most patients are more than 50 years old [2-4].

The tumour has been described in the upper aerodigestive tract [3]. In this context, most common sites of involvement are the larynx and hypopharynx [1], and rarely the oral cavity and oropharynx [5]. Tonsil involvement, as in our case, is very uncommon, and only very few cases are reported in the literature [6 7].

Major predisposing factors of PSCC are smoking and alcohol abuse [1], and immunosuppression is believed to be a risk factor [8]. A subset of head and neck squamous cell carcinomas are caused by the human papillomavirus (HPV). This HPV related form of head and neck squamous cell carcinoma (HPV-HNSCC) has captured the attention of the oncology community for its rising incidence, its connection to non-traditional risk factors and its divergent clinical behaviour. This virus is associated with approxi-

mately 40% of head and neck squamous cell carcinomas, but the role played in the oncogenesis of papillary lesion is unclear [7]. The presence or absence of stromal invasion is important for the diagnosis. It is not always easy in particularly in cases of biopsy considering the scarcity of the tissue, which is often superficial. If no stromal invasion is found, the lesion is called atypical papillary hyperplasia or PSCC *in situ* [1].

Case report

A 59-year-old man, afflicted with benign prostate hyperplasia, presented at the ENT Clinic of the Department of Medical Sciences, Surgical and Advanced Technologies "G.F. Ingrassia, University of Catania (Sicily, Italy), with the complaint of foreign body sensation in his throat for one month, with no aggravating and relieving factors.

The medical history of the patient was not significant and he did not report any history of alcohol or tobacco use and he was not immunosuppressed. Physical examination found no significant abnormalities.

Laboratory examination revealed an elevated erythrocyte count (6.21 x 10^6/μL) and RDW-CV (15,5%); the total count of white blood cells (WBC) was decreased (4.32×10^3/μL), as well as MCH (23.1 pg). Blood glucose was increased (134 mg/dL); other haematological and biochemical parameters were within normal limits.

The intra-oral examination and fiberoptic endoscopy revealed a papillomatous lesion of the left palatal tonsil that hung towards the oral cavity. Under the suspicion of malignancy, an incisional biopsy was performed.

Therefore, he underwent complete staging work up including dynamic contrast-enhanced computed tomography multidetector (CT) of the neck & chest, which showed a well-defined solid mass in the left part of the tongue (Figg. 1-2). There was no radiological evidence of cervical metastasis, but only homolateral lymph nodes that were about 10 mm at the maximum dimension. There were no pulmonary lesions and no lymphadenopathy was seen in either hila. There were no pleural and pericardial effusions, but there were signs of vascular stasis in the dorsal segments of the lungs. The main airways were free.

In the present case, the presurgical staging of the tumour according to the TNM system proposed by the American Joint committee on Cancer (AJCC) was evaluated and was found to be stage I (T2N0M0).

After staging, the patient was hospitalszed and underwent left tonsillectomy.

He received general anaesthesia by administration of propofol in TCI (4 mcg/ml), continuous infusion of remifentanil (0.2-0.5 mcg/kg/min) and rocuronium (0.6 mg/kg in bolus). Neuromuscular function was monitored using Train of Four (TOF) nerve stimulation and acceleromyography (TOF watch SX®) at the adductor thumb muscle, starting after the induction of anaesthesia.

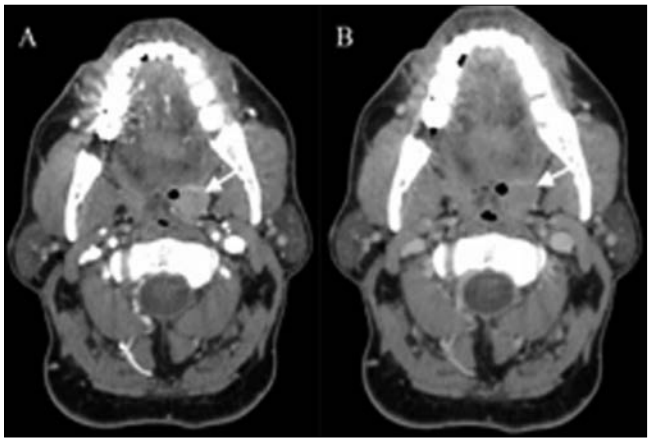

Fig. 1. Multidetector CT. Images A and B were acquired in different phases after contrast administration (arterial and venous phases respectively). A well-defined solid mass, oval in shape, is well depicted in the left tongue (white arrows).

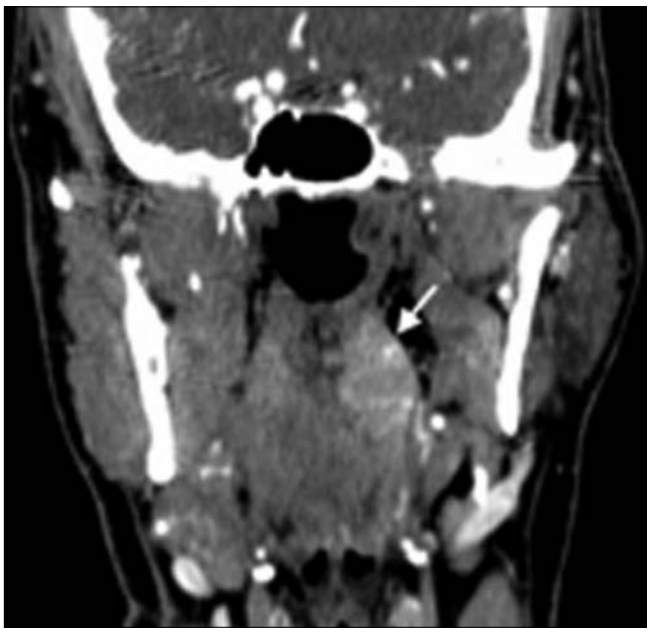

Fig. 2. Coronal reformatted MDCT image. Image clearly shows the lesion (white arrow), with moderate enhancement after contrast medium.

TOF and PTC (post tetanic count) were assessed to evaluate the depth of the neuromuscular block. Four minutes after the beginning of drug infusion, laringoscopy and tracheal intubation were performed using a videolaryngoscope (GlideScope®). The tonsil was removed along with part of the front pillar palatal adhering to it.

After completion of surgery, patient was extubated and admitted to recovery room for postoperative monitoring. Pain control was achieved by the intravenous administration of acetaminophen (15 mg/kg up to 1 g) and morphine (0.05 mg/kg).

The patient was vomiting blood in the immediate postoperative period. The intra-oral examination revealed bleed-

ing from the left tonsil and thus he was sent back to the operating room for surgical revision. A rapid sequence intubation, avoiding mask ventilation, was performed by means of propofol (2 mg/kg), fentanyl (2 mcg/kg) and rocuronium (1.2 mg/kg) in bolus. Anaesthesia was maintained with sevoflurane (2-2.5%). At the end of surgical haemostasis, neuromuscular block was still deep (TOF 0, PTC 3), so it was antagonised by the administration of sugammadex (4 mg/kg). A TOF ratio of 0.9 was reached in 160 sec. Thus the patient was extubated, monitored in recovery room for about 60 min and then moved to the ward. The patient was discharged, after two days, without any other post-operative complications.

At histopathological evaluation, the tonsil was about 3.6 x 2.5 x 1.3 cm in size and on gross examination presented an exuberant papillary outgrowth on the oropharynx face (Fig. 3). On the cut surface, the tumour was friable in its exophytic component. Histological features showed a proliferation of epithelial immature-basaloid cells around a fibrovascular axis, having the typical appearance of papillary growth pattern. The tumour cells showed high nuclear pleomorphisms with hyperchromasia, open and fine chromatin and numerous mitotic figures. Stromal invasion was evident with multiple nests of tumor cells and dense lymphoplasmacytic inflammation at the tumour-stromal interface (Figg. 4-5).

Two 10 μm tissue sections paraffin wax embedded from palatine tonsil were sent to the Clinical Virology Unit of the Central Laboratory of the University Hospital "Policlinico-Vittorio Emanuele", Catania, for the detection of HPV DNA. The sections, after the deparaffinisation steps, were processed using the Qiagen QIAmp DNA Mini kit (QIAGEN Gmbh, Hilden, Germany).

HPV DNA detection was accomplished by amplification of a target sequence within L1 ORF (HPV-HS Bio, AB Analitica s.r.l, Padua, Italy). HPV typing was performed with a reverse line blot hybridisation assay with specific probes for the most frequent HPV-genotypes (HPV-type, AB Analitica s.r.l., Padua, Italy). The genotype HPV 16 was detected. To evaluate the viral oncogenic activity, the HPV E6/E7 mRNA was performed by the NucliSENSE EasyQ HPV v1.1 (NASBA DIAGNOSTICS, bioMérieux bv, NL-5281 RM Boxtel). HPV 16 mRNA was also detected.

Based on clinical, radiographical, general and histopathological examination, a final diagnosis of palatal tonsil papillary squamous cell carcinoma was made with definite stage T2N0M0.

Acording to postoperative oncologic evaluation, no additional radiochemotherapy treatment was needed.

The clinical and radiological (MR ± CT) follow up, performed at 5 years excluded local and regional recurrences (Fig. 6).

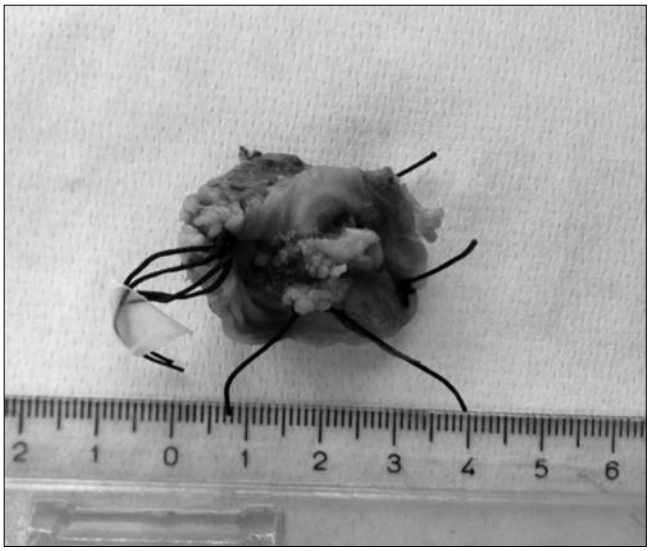

Fig. 3. At gross examination an exuberant papillary neoplastic outgrowth in the tonsil was evident.

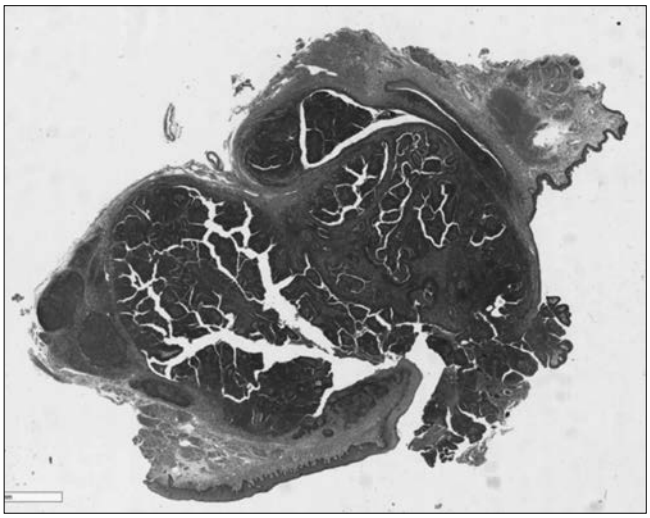

Fig. 4. At low magnification, a characteristic papillary finger-like pattern of growth was evident (H&E x 25).

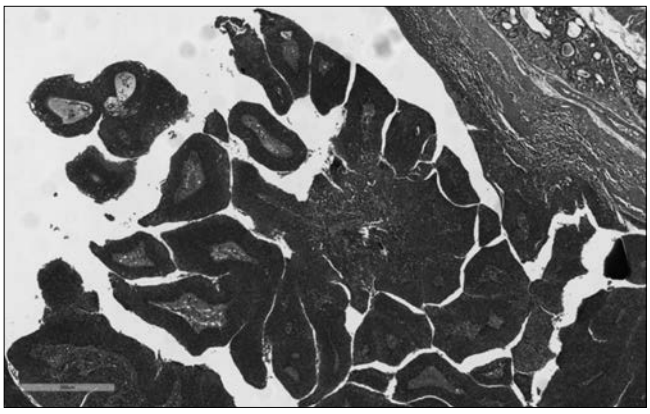

Fig. 5. At high magnification, papillary stalks in PSCC showed well visible fibro-vascular axis and markedly pleomorphic immature-basaloid neoplastic cells (H&E x 200).

Discussion

PSCC has been accepted as a clinical pathological distinct neoplasm [3 9]; in the second edition of the World Health Organization (WHO), published in 1991, the term PSCC was applied to "invasive squamous cell carcinomas which have an exophytic papillary component" [10]. The differential diagnosis includes squamous papilloma and verrucous carcinoma. Squamous papilloma can be considered a precursor lesion of PSCC, cellular pleomorphism and mitotic activity allow differential diagnosis. Verrucous carcinoma lacks cytologic features of malignancy, has a well-differentiated squamous epithelium with marked keratinisation and invades the stroma with a pushing, rather than infiltrating border. The small number of documented cases have shown a strong male predilection from 50 to 70 years of age. The confirmation of the rare involvement of the tonsil by Cobo et al. [8] in a review, report data on the localization of the tumour and document higher involvement of the larynx and alveolar ridge. The other sites affected were buccal mucosa, sinonasal tract, nasopharynx and oropharynx [8]. The major predisposing factors are represented by smoking and alcohol abuse, although there is no significant evidence in the literature. In our case, the medical history of the patient was not significant and he did not report any history of alcohol or tobacco abuse and he was not immunosuppressed.

HPV infection is involved in the pathogenesis of PSCC in a manner similar to that of other squamous cell carcinomas of the head and neck mucosa by the viral oncogenes E6 and E7 that initiate carcinogenesis [11]. In the literature, there are several articles analysing the relationship of HPV with PSCC [2]. Cobo et al [8]. reported one case of PSCC associated with HPV infection. Jo et al. [7], reviewed 31 PSCCs of the upper aerodigestive tract and reported an identifiable high-risk HPV by *in situ* hybridization in 68% of cases. The tumours related to HPV infection seem to have a better prognosis and for this reason, those authors propose reporting HPV status when these tumours are encountered [7].

In fact, even in the present case, HPV 16 was detected in palatal tonsil tissue. Moreover, the oncogenic activity of this virus was demonstrated by the detection of the E6/E7 HPV mRNA. A wider use of these molecular techniques, especially of mRNA tests, could be extremely useful in prevent the evolution of HPV-related lesions toward invasive carcinoma. This can be achieved by a close cooperation among the specialists involved. In relation to genotype, there is no homogeneity of results with respect to the techniques used for diagnosis. In spite of this, the 6/11 and 16/18 genotypes are mainly detected [2 12 13].

Suarez P.A. et al. [2], conducted a clinicopathologic and molecular study on PSCC of the upper aerodigestive tract, qualifying this tumour as an informative model for defining how viral oncogenes cooperate with other factors in genomic instability, carcinogenesis and tumour development.

PSCC may present as either *in situ* (non-invasive form) or invasive tumour. In the majority of reports, T2 lesions were most common. In our case, the exophytic neoplastic lesion was classified as the early invasive form with stage T2 without clinical radiological evidence of nodal involvement.

The treatment of choice is surgery to which possible neck dissection (generally selective neck dissection) is added, if necessary. Radiation therapy may follow surgery in cases of high-T or in cases where there are positive resection margins. The 5-year overall survival is satisfactory with complete resolution of the disease in over 80% of cases [8].

Conclusions

A recent review of the literature and the complete description of the clinical biological characteristics of this tumour, in case treated, enable clinicians to define this very rare cancer of the head and neck.

Acknowledgements

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