Case presentation

**VERRUOUS CARCINOMA ACKERMAN – ORAL FLORID PAPILLOMATOSIS. CASE PRESENTATION**

Virgil Pătrașcu¹, Alexandra Georgiana Bocîrnea¹, Raluca Niculina Ciurea²

¹Dermatology Department, University of Medicine and Pharmacy of Craiova
²Pathology Department, University of Medicine and Pharmacy of Craiova

Corresponding author:
Virgil Pătrașcu, MD, PhD,
University of Medicine and Pharmacy of Craiova,
Petru Rares Street, No 2-4, 200345, Craiova, Dolj county, Romania
Tel.: 004-074273676,
E-mail: vm.patrascu@gmail.com

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Abstract

Verrucous carcinoma is a well differentiated type of squamous cells carcinoma, which may interest both the skin and mucous membranes. It is characterized by local invasion with minimal dysplasia and has a reduced metastatic potential.

Clinical case. We present the case of an 80-year-old rural patient with verrucous carcinoma, with the objective to highlight the clinical-evolutionary, histopathological and therapeutic aspects of this disorder. The treatment was hemi-verbilumectomy, and the post-surgical development was favorable.

Discussions. Ackerman’s verrucous carcinoma is also known as oral florid papillomatosis, a term created by Rock and Fisher in 1960. Wechsler and Fisher have highlighted the aggressive but clinically benign local nature of the disease by using the term "oral florid papillomatosis". Oral verrucous carcinoma may extend to underlying tissue and regional lymph nodes. Therapy for oral verrucous carcinoma is a challenge, because recurrences and anaplastic transformation are frequent after radiotherapy. Surgical treatment is superior, but radiotherapy is generally considered to be a last resort.

Conclusion. Patients with verrucous carcinoma should be closely monitored, as they may develop second cancer, an aggressive epidermoid carcinoma, or anaplastic transformation of a pre-existing verrucous carcinoma.

Introduction

Verrucous carcinoma is a highly differentiated squamous cells carcinoma, which may interest both the skin and mucous membranes (1). It is characterized by local invasion with minimal dysplasia and has a reduced metastatic potential (2). It was first described by Ackerman, in 1948, in the oral mucosa (3).

Clinical case

An 80-year-old patient living in a rural area is hospitalized for an imprecisely defined, infiltrated, papillomatous, albuminous, 0.5-1.5 cm area located on the lower limb and lining of the lower lip (Figures 1 and 2). Tumor formation began with a year before hospitalization, increasing in size. The patient applied various topical medications but their names cannot be specified here.

Hereditary-collateral background: insignificant.
Personal pathological history: denied.
Working conditions: chronic sun exposure for 50 years (formerly tractor driver).
Behavior: was a heavy smoker (currently 3-4 cigarettes/day) and a chronic alcohol consumer.
Objective exam: phototype III; nutrition status - underweight (BMI=17.6); digestive system - edentulous patient.
Laboratory exploration: hematological parameters, glycemia, urea, creatinine, AST, ALT, protein electrophoresis, and urine summary were all within the normal range, except ESR=70 mm/h.

We practiced the excision of the tumors at the level of the lower lip half with 6 mm of healthy tissue by hemivermillonectomy, followed by suture in a plane (Figure 3). The piece was sent for histopathological examination. The histopathological result confirmed the diagnosis of verrucous carcinoma (Figure 4) with invasion in the submucosa, adjacent to the striatal muscle (Figure 5) and intraepidermal micro abscesses (Figure 6).

Recommendations: avoiding tobacco and alcohol use as well as very hot and spicy foods, photoprotection, periodic re-evaluation.

Discussions

Ackerman verrucous carcinoma is also known as oral florid papillomatosis, a term created by Rock and Fisher (4) in 1960. They observed several papilloma formations confluent in the oral cavity and larynx in three patients. In 1962, Wechsler and Fisher (5) highlighted the aggressive but clinically benign local nature of the disease by using the term “oral florid papillomatosis”. Oral verrucous carcinoma may extend to underlying tissue and regional lymph nodes.
Epidemiology
In the United States, Ackerman's verrucous carcinoma accounts for 2-12% of all oral carcinomas (6-9). In men over the age of 64, the incidence is 3.2 cases per 100,000 people/year (10).

It has male predominance, although in one study, about 60% of cases were reported among women (11). Ackerman documented 31 cases, of which 26 were men (9). In his study, Ackerman specified that the average age of the subjects was 67 years. In another study, most patients were aged between 40 and 50 (12).

Pathogenesis is not elucidated, but several factors have been mentioned:
- chronic inflammatory phenomena: osteomyelitis, ulcers, scars (burns, frostbite);
- repeated microtraumatism through inappropriate prostheses;
- HPV viral etiology (1);
- smoking is implicated in both epidermoid carcinoma (EC) and verrucous carcinoma (13); for those who chew tobacco, oral cancer occurs at the place where tobacco is placed (14).

In 1967, Barnett and Hyman (15) linked HPV to oral florid papillomatosis based on ultrastructural results. HPV types 2, 3, 6 and 11 are associated with verrucous carcinoma. In one study, HPV types 6 and 11 were detected in seven of 17 cases with oral verrucous carcinoma (16). In laryngeal verrucous carcinoma, HPV 16 and 18 were present in 13 out of 29 cases (17).

HPV can facilitate the development of verrucous carcinoma due to oncogene expression. Onco-protein E6, encoded by HPV types 16 and 18, promotes p53 degradation (19, 20).

Research has shown that the use of chewing tobacco and smoking tobacco is strongly correlated with oral florid papillomatosis, but not in all patients. It is unclear why some patients develop verrucous carcinomas and others classic EC.

Favorable factors may include lichen planus, leukoplakia, chronic lupus erythematosus, and chronic candidiasis.

Verrucous carcinoma comprises the following clinical entities:
1. oral florid papillomatosis;
2. epithelioma cuniculatum (plantar verrucous carcinoma);
3. papillomatosis cutis carcinoides;
4. giant condyloma acuminatum (Buschke-Löwenstein tumor) (1).

Clinical
Ackerman verrucous carcinoma occurs in the form of white, papillomatous lesions on the oral mucosa with a size of 0.5-1 cm (12). Tumor can begin in the mucosa or semi-soft lip. Of the 31 Ackerman-
man patients described, 18 had verrucous carcino-
oma in the oral mucosa, eight on the lower gum, 
two on the hard palate, and one on the upper gum, 
tongue and tonsils.

It most commonly develops in the jugular mucosa 
and can extend to the jaw or to the cheek. It may 
also develop in the gums, floor, and more rarely 
at the level of the tall palate, tongue and commit-
tees (1). The tongue can reveal obvious alterations, 
mainly in the form of grueling masses (21).

It can be accompanied by local infection and re-
gional inflammatory adenopathy that can be con-
fused with lymph node metastases. Concomitant 
infection can create the impression that the tumor 
is infiltrated. Verrucous carcinoma metastasizes 
very rarely remotely.

Differential diagnosis

- EC;
- Heck disease;
- oral hemangiomas;
- oral mucosal infections;
- leukoplakia;
- Acanthosis nigricans.

Investigations

Histopathological results suggest well-differenti-
ated EC (22) and similar to conventional EC. The 
findings include prominent microvilli, small tono-
filaments and underdeveloped desmosomes.

Oral verrucous carcinoma presents patterns of 
exophytic and endophytic growth (23). Marked 
hyperkeratosis occurs, sometimes with paraker-
tosis. The granular layer has tumor cells that can 
be vacuolized, similar to coil cells from acuminate 
condylomatosis.

Verrucous carcinoma is characterized by a well 
differentiated epithelium supported by an edema-
tous stroma with chronic inflammatory cells of lym-
phohistiocytar origin. These tumor masses extend 
into the dermis and deep structures, forming si-
nuses and cysts filled with keratin (24).

In the oral verrucous carcinomas, rare areas of 
focal destruction of the basal membrane are ob-
served. Atypical mitosis, cell necrosis and multi-
nucleated keratinocytes are rarely obvious. We can 
see the centripetal keratinization of the individual 
keratinocyte islets. The cytological characteristics 
of individual cells are relatively benign, with mini-
mal dysplasia. Individual cells may be large, with 
pronounced and large nucleous. Intracytoplasmic 
glycogen is poorly represented in verrucous carcino-
ma compared to keratoacanthoma and pseudo-
epitheliomatous hyperplasia.

Some oral verrucous carcinomas may be associ-
ated with small outbreaks of EC (16, 25, 26) or re-
gional lymphatic metastases (27, 28). In one study 
(26), it was observed that 21 out of 104 oral ver-
rucous carcinomas had poorly differentiated EC 
outbreaks. Such dysplasia outbreaks are associ-
ated with a double recurrence rate and a 10% inci-
dence of lymphatic metastasis (27).

If clusters of poorly differentiated cells are pre-
sent, the tumor is a classical EC with a high ma-
lignant potential and a metastatic tendency. Verru-
cous carcinomas with small outbreaks of EC may 
be more aggressive.

Blood and lymph vessels were not found in tu-
mor cells. This finding is probably correlated with 
the absence of metastases in patients with muco-
sal verrucous carcinoma.

In oral verrucous carcinoma, genotyping for HPV 
may be useful (29).

Magnetic resonance imaging (MRI) can be used 
to determine the extent of the tumor and whether 
bone or other underlying structures are involved.

Computed tomography (CT) can be used to 
demonstrate the exact location and size of the 
tumor, for preoperative staging and surgical plan-
ing. Dual energy CT can be used to assess tumor 
margins (30).

Prognosis

Verrucous carcinoma is a locally destructive tu-
mor that spreads to adjacent structures. Metasta-
ses in regional lymph nodes occur occasionally 
(5%), and remote metastases are very rare.

Most verrucous carcinomas originate in the oral 
cavity (55.9%) and larynx (35.2%), and the survival 
rate relative to five years is 77.9%. For localized 
verrucous carcinoma, the survival rate after surgery 
is 88.9%, compared with 57.6% after irradiation.

A retrospective study in 302 patients with oral 
verrucous carcinoma (31) showed that early-stage 
tumors accounted for 39.7% and those in late-stage 
for 60.4%. In 68% of patients, the tumors recurred.

Radiotherapy has been implicated in the ana-
plastic transformation of verrucous carcinomas, 
although anaplastic transformation may also re-
present the natural progression of verrucous car-
cinoma (28).

Treatment

Therapy for oral wart carcinoma is a challenge, 
because recurrences and anaplastic transforma-
tion are frequent after radiotherapy (32). The most 
commonly used treatment in the United States is 
surgical excision (69.7%), followed by surgery 
combined with irradiation (11%) and irradiation 
alone (10.3%) (12). Irradiation can be used in ad-
vanced cases.

Surgical treatment has superior results, whereas 
radiotherapy is generally considered to be a last 
resort. In case of oral verrucous carcinomas, it has 
been reported that irradiation may lead to meta-
stasis; however, there are specialists who are con-
fidently using this treatment (33-35). In one study, 
none of the 16 patients with verrucous carcinoma
had anaplastic transformation characteristics after radiotherapy (36). There are authors who believe that radiotherapy is the right choice for all types of verrucous carcinomas, with results comparable to surgery (3, 34, 35).

However, in another study, 17 cases were described. In seven cases with oral verrucous carcinoma and in one case with nasal cervical carcinoma, the initial treatment was radiotherapy. Despite regression of tumors, three patients experienced rapid anaplastic transformation (observed in the histopathological examination) with aggressive behavior, with onset at two, five and eight months post-treatment.

In studies conducted by Perez et al. (27) and Fonts et al. (37), the excellent immediate response to irradiation was followed by anaplastic transformation, announced by rapid tumor growth. Patients with similar results were also described in further studies (38-42). A case with oral verrucous carcinoma treated with a 6-MeV linear accelerator has developed undifferentiated EC (37).

Proton radiotherapy can induce complete regression in oral verrucous carcinoma (40).

Photodynamic therapy, which involves application of 20% 5-aminolevulinic acid, followed by fractional irradiation for three minutes with red light, may be an effective treatment for oral verrucous carcinoma (43). Photodynamic therapy with systemic photosensitising may be effective in some cases (44). It can be used once a month for several months and can be a good option for elderly patients.

Intravenous bleomycin (45) and oral or intravenous methotrexate (46, 47) can also be used. Mohs surgery and diathermocoagulation are other methods of treatment (48).

Conclusion

Patients with verrucous carcinoma should be closely monitored as they may develop second cancer, aggressive EC, or anaplastic transformation of preexisting verrucous carcinoma occurs.


Bibliography