CASE REPORT

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Invasive keratinizing squamous cell carcinoma of the left external auricular canal and the middle ear – case report

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Abstract

The rather low incidence of auricular neoplasms irrespective of localization is likely to cause confusion of diagnosis with the more frequent benign ear pathology. Because of this, the elapsed time until confirmation of the diagnosis facilitates the evolution of the disease to the detriment of the patient's health. The diagnosis of an ear neoplasm can hide under the ordinary appearance of external otitis, chronic otorrhea or episodes of various types of ear pain. Evolution of such a malignant pathology is quite rapid and highly aggressive locoregional complications are the subject of discussions regarding the interpretation of the results of paraclinical tests and the medical-surgical treatment approach that must take into account the histological structure, the size of the tumor, and the invasion of neighboring tissue.

Keywords: outer ear, middle ear, squamous cell carcinoma.

Introduction

The anatomical complexity of these two segments of the ear requires a competent specialist's approach in order to establish an early and definitive diagnosis [1].

The ear canal and the middle ear are rare sites of malignancies, among which squamous cell carcinoma is the most commonly occurring cancer type [2, 3]. This form of cancer is an aggressive disease, extremely difficult to treat and is listed as having a serious prognosis – dependent on the stage of disease and the primary treatment [3, 4]. Its evolution may mimic a benign affection of the ear; many patients present with non-specific signs of chronic infection and inflammation, which is why detection and diagnosis of this malignant type of cancer creates such difficulties. Additionally, the infections that precede the development of the tumor lead to delay of diagnosis [5, 6].

In this report, we present a case of advanced squamous cell carcinoma of the left external auditory meatus and the middle ear, in a patient whose cancer was initially diagnosed and treated as external furuncular otitis. The paraclinical tests – computed tomography (CT) and magnetic resonance imaging (MRI) – play an important role in the staging, treatment planning and follow-up of the patients with malignant external auditory canal (EAC) tumor [7].

Cases of auricular neoplasm are very rare. Most of the time, due to unspecified signs on onset and a great variety of clinical aspects, the illness is diagnosed late, due to the misleading evolution that generate diagnostic confusions, as in this case.

The present case, hospitalized in our Clinic, has a rich past of consultations and treatments carried out in various outpatient services, as a result, the lack of complex means of investigation, the confusion of diagnosis and the time elapsed until the admission caused the disease to evolve rapidly and exceed the limits of the ear zone. The time elapsed from the onset of the disease to the positive clinical diagnosis is at the expense of the patient.

We consider that it is necessary to present as many cases as possible, so that, in time, we can obtain homogeneous groups with sufficient statistical power, adequate tumor staging system and optimal therapeutic protocols.

Case presentation

In our paper, will detail the case of Z.V., a 41-year-old male patient, initially diagnosed with otitis of the left external ear, caused by a furuncle. The treatment at that time was focused on the above-mentioned diagnosis and consisted of antibiotic, analgesic, and anti-inflammatory drugs. Also, curettage was performed on the two small swollen areas of auricular tissue but with no results.

Recurrence of symptoms and worsening patient outcomes after eight months of failure treatments were the reasons for which the patient was sent to the Ear, Nose and Throat (ENT) Clinic for further investigations. The patient followed a short-term treatment with Amitriptyline for a depressive state, but without signs of myocardial damage.

Upon admission to the ENT Clinic of the Emergency County Hospital, Constanţa, Romania, on 8.05.2017, with Observation Sheet No. 443, the patient was fully inves-

tigated (laboratory, pulmonary X-ray, CT, MRI, cardiac exam, tumor biopsy).

The clinical examination of the patient revealed: unilateral abundant mucopurulent otorrhea (with negative results in laboratory examinations), the presence of two slightly swollen formations, at the level of the antitragus and at the level of the left ear concha, painful spontaneously and, at palpation, discrete erythema at concha level, due to mucopurulent otorrhea, left parotid gland swelling in upper 1/3, left minor facial paresis, and EAC destruction with the disappearance of anatomical features.

The endoscopic examination highlighted, once more, the destructive aspect of the external auditory conduct with the disappearance of the cutaneous parts, and the erosion of the anterior wall of the external auditory conduct, all embedded in a slightly white-yellow granulomatous mass, which is difficult to evacuate (Figures 1 and 2).

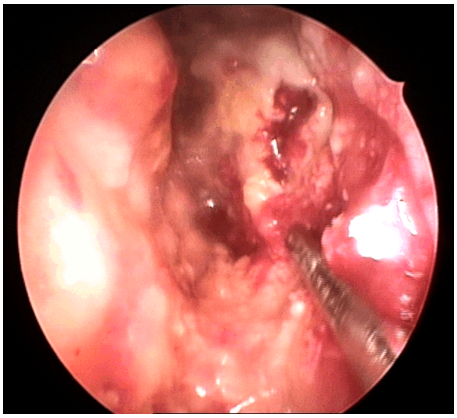

Figure 1 – ***Endoscopy: affected integrity of the left external acoustic canal.***

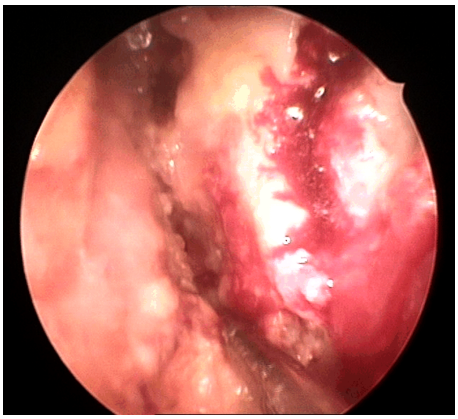

Figure 2 – ***Endoscopy: skin erosion and erosion of the anterior external auditory canal (EAC) wall.***

Regarding the general status of the patient, we mention that he suffered from type II diabetes mellitus and high blood pressure (160/90 mmHg). The blood tests showed the following changes: middle leukocytosis with monocytosis, and lymphopenia.

A basal pulmonary condensation was noticed and the left lung at pulmonary X-ray.

CT with contrast substance highlighted a tissue mass with air inclusions and a non-homogeneous capture with dimensions of 38/52/42 mm present in the left EAC, with an apparent extension in the tympanic cavity; this infiltrates the periauricular subcutaneous tissue and the superior 1/2 of the ipsilateral parotid gland. The mass associates bone erosions of the anterior external auditory meatus wall, the anterior mastoid wall and the temporal zygomatic process, and intraparotid necrotic adenopathy with dimensions of 10/14 mm and 14/16 mm, lymphoganglionar masses with transverse diameters between 6–9 mm situated submandibular and bilateral, at the level of the jugular carotid (Figure 3). MRI with contrast substance highlighted temporal, zygomatic and sphenoid bone osteolysis, which also concerned the left temporomandibular joint (approx. 7 mm thick) and associated meningeal hypertrophy in the left lower anterior temporal pole (Figure 4).

The results of the examinations confirmed – up to the completion of the histopathological exam – the suspicion of auricular neoplasm. Upon microscopic inspection, biopsy fragments (of various sizes from 0.1/0.1 cm to 0.4/0.4/0.3 cm, which measure overall 2/1/0.2 cm, grayish-white in color and with elastic consistency) were drawn from the EAC.

Morphopathological characteristics highlighted: nine fragments of tissue biopsied from the external acoustic meatus of the left ear, from which eight fragments were histopathologically characterized by the presence of moderately differentiated squamous cell carcinoma, neighboring tissue invasion with areas of ulceration and underlying granulation tissue; there are areas of necrosis, focal hemorrhage and a moderate inflammatory infiltrate (lymphocytes, plasma cells, histiocytes, neutrophils) with a diffuse distribution; possible vascular invasion; perineural invasion undetectable.

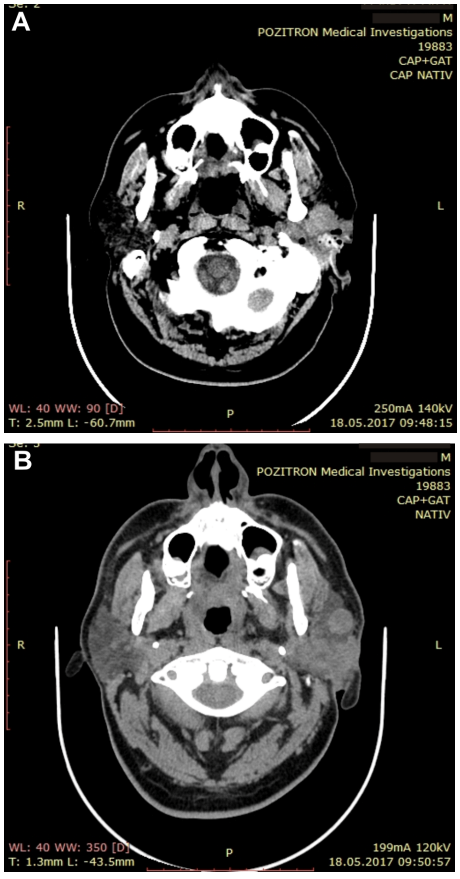

Figure 3 – ***Computed tomography: local and left parotid tumor invasion.***

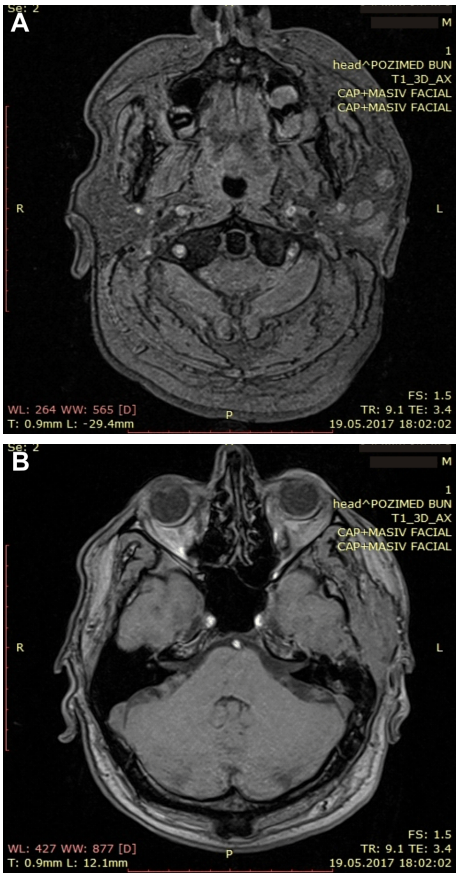

Figure 4 – ***Magnetic resonance imaging: parotid invasion and hypertrophy of the meninges on the left side.***

One of these fragments shows ceruminous glands without atypia. One fragment of tissue is represented by cartilage with a normal histological structure and no tumor invasion. The surgical excision borders cannot be assessed due to the fragmentation of the biopsy piece.

The histopathological examination showed an invasive, moderately differentiated G2 keratinizing squamous cell carcinoma (Figures 5 and 6).

Hematoxylin–Eosin (HE) staining was applied to 4 μm thick sections of formalin-fixed, paraffin-embedded tissue samples of the tumor. The immunohistochemical (IHC) analysis was performed with ready-to-use antibodies from Biocare (USA). Before immunostaining the paraffin sections, a few more steps were required: deparaffinization, rehydration and antigen retrieval. Then, the tissue sections were incubated with the following antibodies: Ki67 (clone SP2); p63 (clone 4A4); CD34 (clone QBEnd10). 3,3'-Diaminobenzidine (DAB) was used as chromogen with brown staining of the concerned antigen. The sections were finally counterstained with Mayer's Hematoxylin. Each immunostaining was evaluated from the perspective of distribution pattern, percentage of positive cells and intensity of reaction.

IHC results of this study revealed an overexpression of the p63 biomarker, with intense nuclear reaction and diffuse pattern in more than 50% of the tumor cells (Figure 7). Ki67 immunostaining also showed an intense nuclear reaction in more than 25% of the malignant cells, especially in the invasive tumor front (Figure 8). CD34 biomarker is expressed in the endothelium and marks the blood vessel, proving the neoplastic invasion (Figure 9).

IHC examination confirmed the vascular tumor invasion. The Oncology Commission of our Hospital staged this tumor as T4N2CMx – Stage IVA.

Discussion

Squamous cell carcinoma of the external acoustic meatus is the most common neoplasm in the EAC region, a rare tumor with a reported incidence of one to six cases per million population per year [3]. It accounts for less than 0.2% of all tumors of the head and neck area [2, 3]. Squamous cell carcinoma of the EAC is often associated with chronic otitis media [3, 8, 9].

Staging is still under discussion for these forms of carcinoma, the rarity of this disease explains why there is no staging system for this type of neoplasm [6]. Arriaga *et al.* [10], in 1990, suggested a staging system which has since entered the literature as the Pittsburgh Staging System. In 2000, this System underwent a minor revision by Moody *et al.* [11].

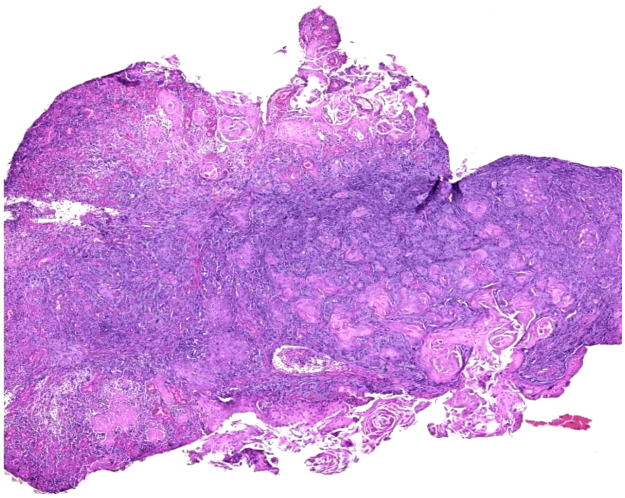

Figure 5 – ***Moderately differentiated, invasive, keratinizing squamous cell carcinoma consists of malignant epithelial cells proliferation, disposed in islands and cords (HE staining, ×40).***

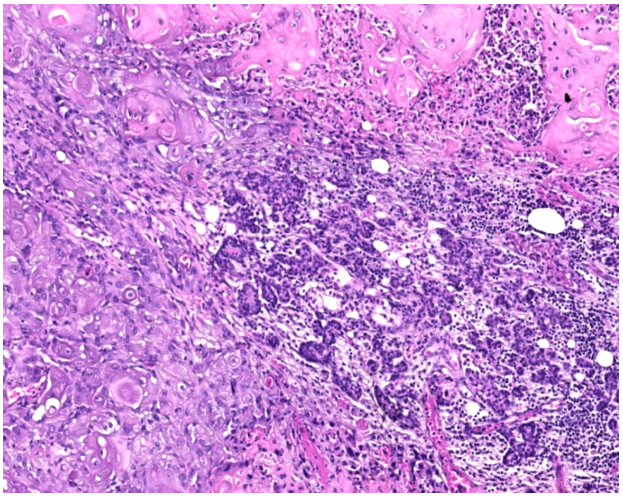

Figure 6 – ***Keratinizing squamous cell carcinoma with different sized keratin pearls present in the tumoral islands; without invasion of ceruminous glandular structures of the external ear canal (HE staining, ×100).***

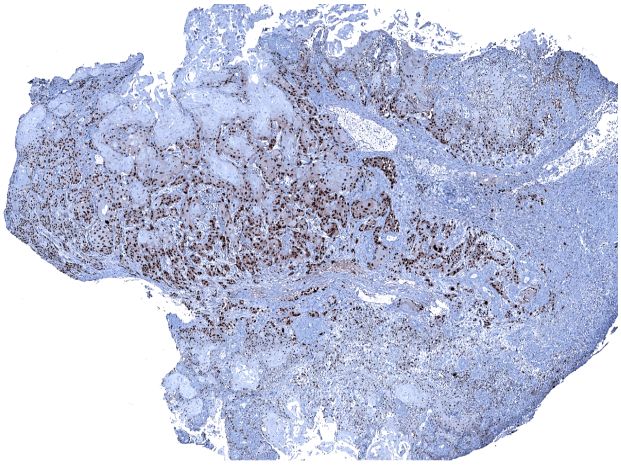

Figure 7 – ***p63 immunostaining with intense nuclear and diffuse reaction (Anti-p63 antibody immunostaining, ×40).***

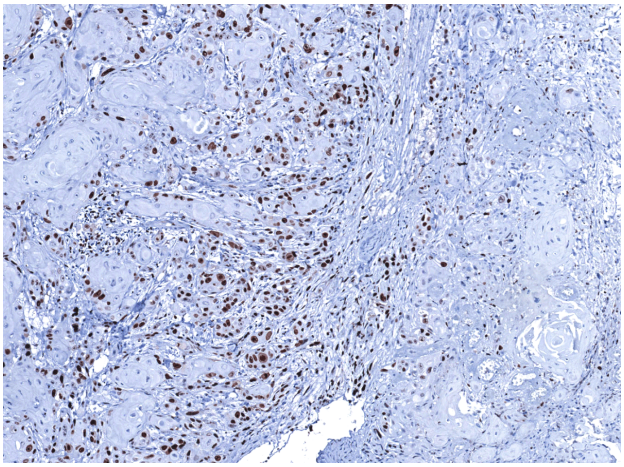

Figure 8 – ***Intense nuclear immunostaining of Ki67 antibody (Anti-Ki67 antibody immunostaining, ×100).***

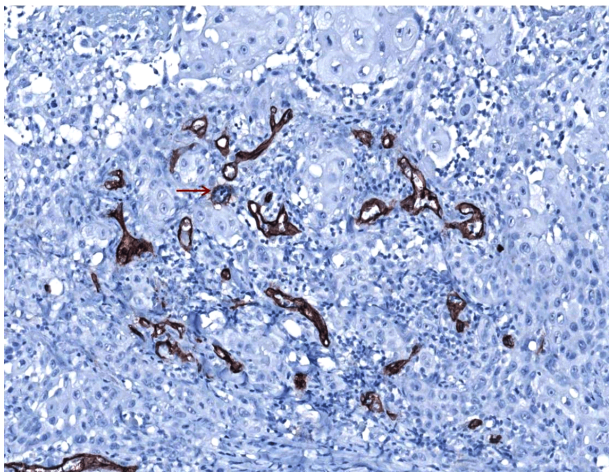

Figure 9 – ***Intravascular tumor invasion (red arrow, →) highlighted by CD34 immunostaining (Anti-CD34 antibody immunostaining, ×100).***

According to the authors' suggestions, this case can be classified as a T3 stage – the tumor reaching the middle ear (Bassereau & Laccourreye) [10] or T3 – tumor extending to adjacent structures: dura mater, parotid gland, temporomandibular joint (Stell). According to the Pittsburgh Staging System, we can consider the tumor a Pittsburgh stage T4 (tumor involvement of the petrous apex, cochlea, carotid and jugular foramen, dura mater, temporomandibular joint or the styloid process, as well as the presence of facial paresis) [11, 12].

The paraclinical exams – CT with contrast substance and MRI – help increase the accuracy of the diagnosis and reveal the locoregional complications of the existing condition [5–7]. For the high blood pressure values, found during the cardiovascular examination, the patient received treatment. If we had opted for the surgical decision, other medical investigations would have been necessary to find out if any myocardial damage exists [13].

The histopathological exam was decisive, confirming the diagnosis of keratinizing squamous cell carcinoma.

Regarding the immunohistochemical results, the p63 biomarker is a nuclear protein encoded by the *p63*-gene, a member of *p53*-gene family, and has an important role in the normal development of an individual [14]. In tumor pathology, many authors have demonstrated the utility of this biomarker in highlighting the squamous cell carcinoma [14, 15]. Moreover, it was shown that the p63 antibody can be considered as a prognostic factor, because its overexpression is associated with a more aggressive and invasive evolution of squamous cell carcinoma [15]. In our study, the intense reaction of p63 immunostaining proves the squamous origin of the tumor and might explain the severe clinical evolution. Ki67 antibody is an important marker of tumor-cell proliferation rate and is correlated with the invasive potential of the squamous cell carcinoma [16]. In the present case, an intense nuclear immunostaining of Ki67 was observed at the invasive tumor front, which was proved to be related to the histological grading [17].

CD34 immunostaining is useful to identify the vascular structure and to appreciate the tumor angiogenesis, which is associated with disease progression [18]. Intravascular tumor invasion, defined as the presence of malignant cells inside the vessel lumen, represents an early phase of metastasis and speaks for a poor prognosis [19].

As diagnostic guidelines in this case, we must consider the absence of any favorable local and clinical subjective evolution of the patient (persistent pain under antibiotic treatment, accompanied by hearing loss and, very important, the appearance of a left facial paresis, which may reflect an aggravation of the patient's condition). This case falls in the age group of people less than 50 years old; the patient denies past ear diseases such as chronic otorrhea, eczema of the EAC or prolonged sun exposure.

In this stage, local resection of the external auricular canal does not seem to be sufficient [12, 20]. The recommended treatment is a subtotal petrography (block resection of the external auditory tube, tympanic membrane, osseous chain, mastoid cells and internal ear) associated with parotidectomy and dissection of lymph nodes (two and five), following the examination in the mixed oral–neurosurgeon–oncology team [9, 21–24].

Postoperative radiotherapy is advised as soon as possible after the lesion has healed [25, 26] approx. six weeks after surgery [27].

The prognosis is reserved in such cases due to the extensive character of the tumor, the neck node metastasis, the facial nerve paralysis, the spontaneous pain, the middle ear involvement, the cervical or periarticular lymphadenopathy and the associated chronic otitis media [2, 6, 9, 28, 29], as seen in the Fahr's syndrome [30].

Conclusions

Statistically, early-stage cancer is associated with a higher treatment success and survival rate, compared to late-stage cancer. The biopsy and imaging exams (CT, MRI) play a major role in establishing the diagnosis and therapeutic conduct. The recommended therapeutic conduct in this case was surgical intervention to increase survival chances, but unfortunately, our patient opted for palliative radiotherapy for head and neck cancer. In terms of malignant ear disorders, the neoplasm of the external ear canal grows freely in the absence of more complex investigations, which sometimes are made too late.

Conflict of interests

The authors declare that they have no conflict of interests.

Acknowledgments

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