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Adenoid Cystic Carcinoma of the Parotid: About 4 Clinical Cases

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Abstract **Case Report**

Adenoid cystic carcinoma of the parotid gland is a rare, slow-growing malignancy characterized by extensive local infiltration, including perineural invasion and a propensity for local recurrence, as well as late distant metastases. Clinically, it is often expressed as swelling of the parotid region with or without facial paralysis. The diagnosis is histopathological. The standard of care is surgery, with radiotherapy and chemotherapy as options. We conducted a retrospective study of four cases who were treated for ACC of the parotid at the Department of Oncology-Radiotherapy of the Mohammed VI University Hospital of Marrakech between 2019 and 2024. Our patients benefited from partial surgery followed by radiotherapy (Patients 1 and 3), exclusive radiotherapy (Patient 2) and total surgery followed by chemotherapy (Patient 4) with encouraging responses. Maintaining the time limit between therapies is a major challenge in developing countries because, faced with technical, logistical, social and above all financial difficulties, our patients who benefited from post-operative radiotherapy did not respect this deadline. Currently, our patients are under surveillance. As recurrences and metastases occur late, this monitoring must last several years (more than 10 years).

Keywords: Adenoid Cystic Carcinoma, Parotid, Radiotherapy, Surgery, Delay.

INTRODUCTION

First described by Robin and Laboulbene in 1852[1, 2], adenoid cystic carcinoma (ACC) is a rare malignancy. It forms approximately 1% of all malignant tumors of the oral and maxillofacial region and 21.9% of all malignant tumors of the salivary glands [3, 4]. In the parotid gland, ACC is relatively rare, accounting for only 2–3% of all tumors [5]. Although ACC has a wide age distribution, the peak incidence occurs mainly in women, between the 5th and 6th decades of life [6].

ACC has three histopathological components: tubular, cribriform and solid. The solid component is the most aggressive [7]. Parotid ACC is clinically misleading due to its slow growth, which belies its relentless extensive subclinical invasion into adjacent structures. It is highly aggressive, with a remarkable capacity for recurrence, metastasis and high mortality. Hematogenous spread is more common than lymphatic spread, with common sites of metastases being the lung, bone, and viscera [8, 9]. Treatment of parotid ACC is primarily surgical although in some cases radiotherapy and chemotherapy are options. ACC remains an extremely difficult disease to treat due to a strong predisposition to recurrence and metastasis if a patient lives long enough, and this occurs even when radical excision has been performed [10].

We report here four cases of ACC of the right parotid gland followed in the Department of Oncology-Radiotherapy of the Mohammed VI University Hospital of Marrakech.

CASE PRESENTATION

We conducted a retrospective study of four cases treated for ACC of the parotid in our training between 2019 and 2024.

Patient 1:

A 74-year-old patient with asthma and cardiopathy, consulted us at the beginning of February 2019 for the management of a ACC of the left parotid. The onset of symptomatology would date back to 2014 with the appearance of a left parotid nodule which increased in size without associated signs. Initially, she consulted an ENT specialist who performed a superficial left parotidectomy on her in December 2018. The anatomopathological study of the surgical specimen revealed a nodule measuring 3 cm in long axis, the morphological appearance of which argues in favor of an

adenoid cystic carcinoma infiltrating the chorion with sheathing perineural, without vascular emboli with healthy boundaries between 1 mm and 3 mm associated with non-specific reactive adenitis.

Upon admission to our Department, the clinical examination revealed no abnormality, no mass, no lymphadenopathy and the post-operative cervico-facial CT also revealed no abnormality, no sign of recurrence. local. Subsequently, she benefited from adjuvant external radiotherapy at a dose of 54 Gy, between July and September 2019. During this treatment, she developed oropharyngeal radiomucositis after the 15th radiotherapy session. Under surveillance, the last cervico-thoracic CT in June 2024 did not reveal any suspicious-looking lesions.

Patient 2:

In October 2020, a 50-year-old patient, with no particular pathological history, consulted us for the management of a ACC of the left parotid.

The history of his illness dates back to 2019 with the onset of painful swelling in the left parotid region associated with left facial paralysis. During the clinical examination on admission, we observed swelling in the left parotid region fixed to the deep and superficial planes, without palpable lymphadenopathy with a discreet left facial paralysis.

Facial CT in September 2020 revealed significant left parotidomegaly encompassing the vessels. The parotid MRI of the same September 2020 revealed a tumor of the left parotid measuring 39 mm in long axis, infiltrating the subcutaneous fat and the left masseter muscle with lymphadenopathies bilateral jugulocarotid joints. The pathological study of the parotid biopsy from October 2020 revealed a ACC infiltrating the parotid parenchyma with sheathing. perineural, with vascular emboli. The thoraco-abdominal CT in October 2020 showed no secondary localization.

The process was deemed unresectable from the outset by maxillofacial surgery. The decision was to start concomitant radio-chemotherapy but given the patient's general condition, exclusive radiotherapy (70Gy) was decided, end of treatment March 2021.

Placed under surveillance, the MRIs of April and October 2021, those of March and October 2022 and those of February and December 2023 did not reveal any suspicious lesions.

Patient 3:

May 2023, a 71-year-old patient, diabetic and hypertensive on treatment, consulted us for treatment of an ACC of the right parotid.

Initially, he consulted the Maxillofacial Surgery Department of the Mohammed VI University Hospital in Marrakech for a painless swelling in the right parotid region gradually increasing in volume, without inflammatory signs nearby, nor facial paralysis, nor impact on the condition. general, evolving since February 2023.

The February 2023 ultrasound revealed a lesional formation in the right superficial parotid lobe, measuring 24 mm in long axis. Facial MRI in March 2023 revealed a tumor-like lesional process in the superficial lobe of the right parotid gland, measuring 23 mm in long axis, infiltrating the nearby cheek soft tissues and the right pre-stylial space, with a small adenomegaly ipsilateral parotid.

Parotid cytology in March 2023 highlighted atypia of undetermined significance (AUS) (Category III – Milan system).

Operated in April 2023 with a right superficial parotidectomy, the anatomopathological study of the surgical specimen revealed an ACC, measuring 3 cm in long axis, with the presence of vascular emboli without sheathing. perineural and the closest surgical limit was 1 mm.

Then he was transferred to us. On his admission to our department, he was a stable conscious patient, with a scar next to the clean right parotid region without a mass nearby. He performed a post-operative facial MRI revealing a right parotid residue of infectious origin associated with diffuse infiltration of the parotid parenchyma, the jugal soft tissues, the right pre-stylus space and the ipsilateral pterygoid muscles and a thoraco-abdomino-pelvic CT scan. -pelvic not showing any secondary location.

The multidisciplinary consultation meeting decided on external RTH at a dose of 66 Gy in 33 fractions of 2 Gy; started in August 2023, it ended in October 2023. Placed under surveillance since then, there have been no signs of recurrence during various surveillance assessments, the last one dates from March 2024.

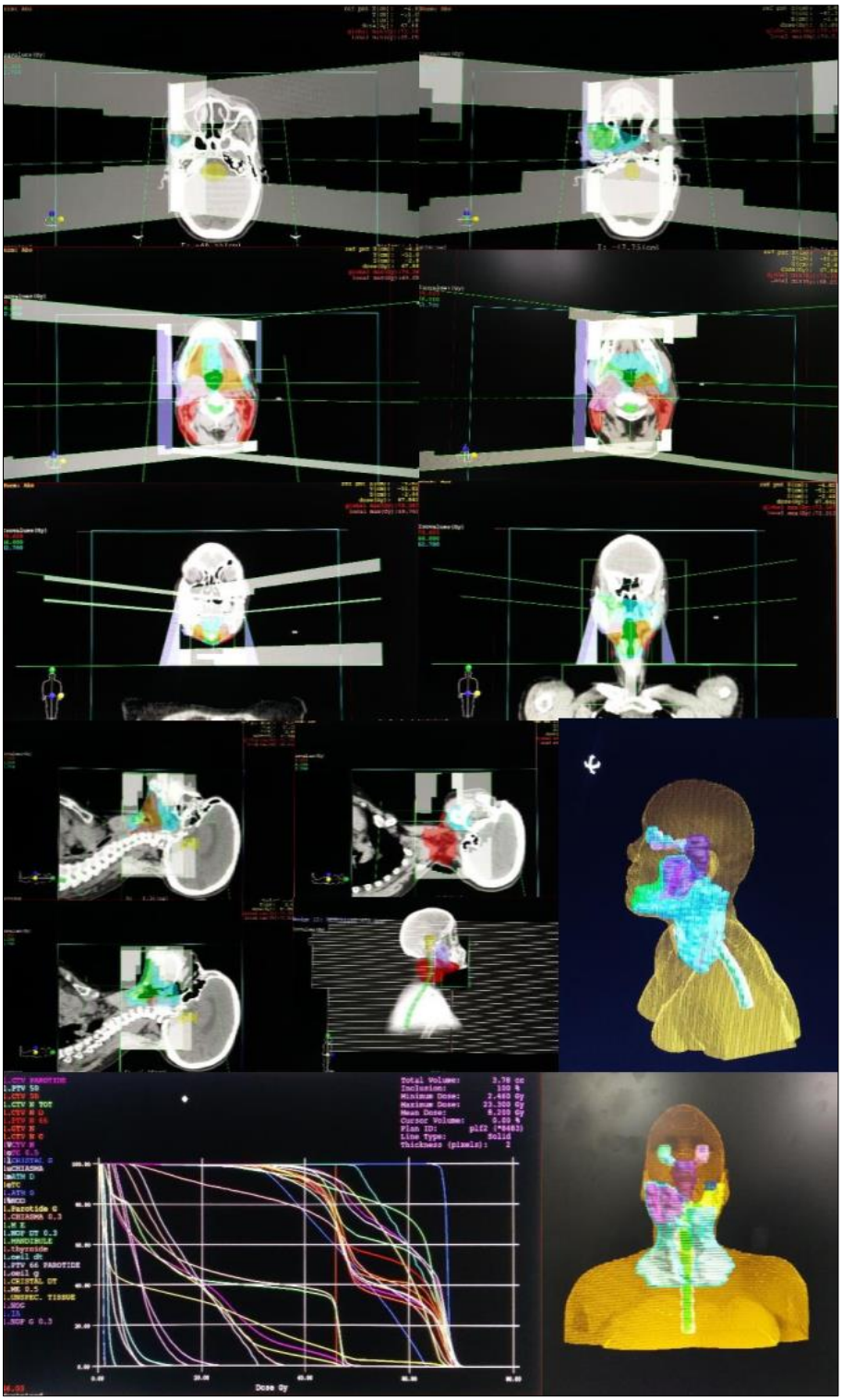

Figure 1. Dosimetry and Ballistics of Radiotherapy for Patient 3

Patient 4:

At the beginning of January 2024, a 50-year-old hypertensive patient presented with recent-onset swelling of the right parotid region. On admission, the patient presented with a firm, deep-lying swelling of the parotid region measuring 30 mm long without cutaneous or intraoral signs and facial paralysis.

A parotid MRI in February 2024 revealed a right intra-parotid nodular lesion at the expense of the superficial lobe of 24.5 mm, associated with a small nearby nodule of 15.3 mm long axis with a suspicious appearance and the right intra-parotid lymph nodes and sub - angulo -maxilla and sub-centimetric bilateral jugulocarotid, without sign of extra-parotid infiltration.

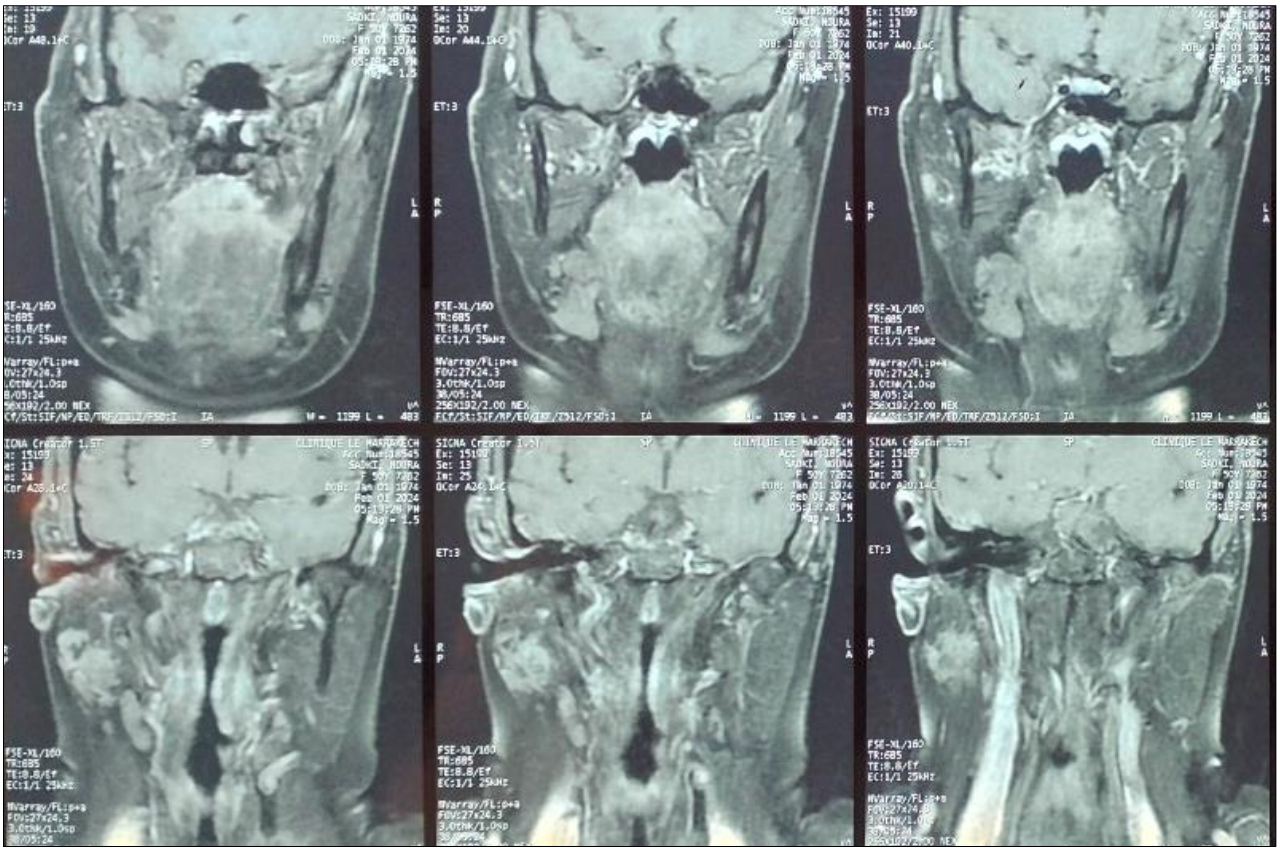

Figure 2: Parotid MRI of Patient 4

The cytological study after cytoponction in the same February 2024 revealed inflammatory cytology without analyzable atypical cells; followed by a biopsy, the histopathological study of which revealed a ACC focally transformed into a cribriform appearance and centered by foci of necrosis, infiltrating the parotid parenchyma with sheathing. perineural, without vascular emboli or metastases to contiguous lymph nodes. The immunohistochemical study showed a morphological appearance and an immunohistochemical profile in favor of an infiltrating and partially transformed ACC.

In February 2024, the patient underwent a right total parotidectomy with sacrifice of the cervical branch of the facial nerve infiltrated by the tumor associated with lymph node dissection of lymph node areas IIa, IIb and III.

Anatomopathological analysis of the surgical specimen confirmed the initial findings, i.e., ACC infiltrating the parotid parenchyma, with cribriform masses, brought back with sheathing perineural, without vascular emboli, nor metastases at the lymph nodes and with extension to the skin tissue brought back.

Then, in March 2024, she underwent a post-operative imaging evaluation coupled with an extension assessment, consisting of a facio-cervico-thoraco-abdominal CT, reporting at the level of the cervico-facial level of surgical evidence at the level of the right parotidectomy site with millimetric jugulo -carotid and bilateral sub - angulo -maxillary lymph nodes and at the level of the thoracic level, the presence of pre and latero -tracheal lymphadenopathy, pre -carinal and the inter-aortic -pulmonary window measuring for the largest 19.7 mm long axis.

Completed by a PET-CT with ^{18} F-FDG, in the same month of March 2024 which revealed, at the cervico-thoracic level, a magma of mediastinal lymphadenopathies, measuring for the largest, 20 mm long axis, hypermetabolic interesting the right pre and latero -tracheal, aortic -pulmonary, subcarinal and left hilar window groups; and at the abdominopelvic level, localized hepatic hypermetabolism at segment VI.

The disease being metastatic, the patient received chemotherapy based on vinorelbine plus cisplatin (3 courses – Last course: May 2024), she developed non-febrile neutropenia after the second course; evaluation imaging made from a cervico-thoraco-abdomino-pelvic CT from May 2024, compared to that from March 2024, and a cervico-facial MRI from May 2024 shows regression of the disease. Given this good evaluation, the patient benefited from 3 other courses of vinorelbine plus cisplatin, end of treatment July 2024. Currently, she is under surveillance.

Table 1: Summary table of 4 cases presented

	Patient 1	**Patient 2**	**Patient 3**	**Patient 4**
Age	74 years old	50 years old	71 years old	50 years old
Sex	Female	Male	Male	Female
Parotid	Left	Left	Right	Right
Reason for consultation	Swelling	Swelling	Swelling	Swelling
Time to diagnosis	4 years	1 year	Less 1 month	Less 1 month
TNM	$T_2 N_0 M_0$	$T_{4a} N_{2c} M_0$	$T_2 N_0 M_0$	$T_{4a} N_{2c} M_1$
Surgery	Yes	No	Yes	Yes
	Partial parotidectomy		Partial parotidectomy	Total parotidectomy
Radiotherapy	Adjuvant	Exclusive	Adjuvant	No
	54 Gy	70 Gy	66 Gy	
Chemotherapy	No	No	No	Yes
				Vinorelbine + CDDP
Targeted therapies	No	No	No	No
Immunotherapy	No	No	No	No

The average age of our patients is 61.25 years with a sex ratio of 1:1. All our patients consulted for swelling in the parotid region. The diagnosis was made by medical imaging and histopathological analyses. Tumors deemed resectable were treated with primary surgery followed by adjuvant radiotherapy (Patients 1 and 3); for the unresectable tumor, the therapeutic strategy focused on exclusive radiotherapy (Patient 2) and the metastatic disease received chemotherapy preceded by radical surgery of the primary tumor (Patient 4).

Despite its aggressive nature, ACC of the parotid gland has so far responded well to surgery, radiotherapy and chemotherapy. All patients are under surveillance and the average time of this surveillance is 24.5 months.

DISCUSSION

Accounting for only 2-3% of parotid tumors [5-11], ACC has a peak incidence mainly in women [12], and between the 5th and 6th decade of life [6]. The latter corroborates with our study whose average age of patients is 61.25 years.

Fine needle aspiration cytology can be used for diagnostic purposes; however, diagnosis is notoriously difficult and is often compromised by false negative assessments [13]. This was confirmed by Patient 4, although it guided the diagnosis in Patient 3. The histopathological and radiological diagnosis guides the therapeutic strategy, in addition if it involves a possible sacrifice of the facial nerve [14].

Histologically, ACC can be divided into 3 components: cribriform, tubular and solid. Most cancers have a combination of these components. The solid component has the poorest prognosis. These 3 components define 3 grades of ACC: grade I consisting of cribriform and tubular components without solid component, grade II consisting of less than 30% of the solid component and grade III of more than 30% of solid component [15, 16]. Only Patient 4 benefited from this detail; his disease could be classified as grade I because he only had the cribriform component.

Although parotid ACC usually grows slowly, local recurrence and distant metastases often occur, leading to a poorer long-term prognosis [17, 18]. In general, these metastases occur late, several years after the diagnosis of the primary tumor [17-20], and could remain asymptomatic for a prolonged period [21]. The occurrence of mediastinal lymphadenopathy is often synchronous or metachronous [22], Patient 4 presented synchronous lymphadenopathy.

The standard treatment for ACC of the parotid is surgery [23], total (case of Patient 4) or partial (case of Patients 1 and 3) parotidectomy. Radiotherapy is indicated in advanced stages deemed unresectable and in patients with surgical contraindications or refusing surgery, either alone or concomitantly with chemotherapy. Patient 2 received exclusive radiotherapy (70 Gy). It is also indicated postoperatively because ACC is a tumor with a high risk of recurrence [14-24]. Although no improvement in survival is reported, the use of adjuvant radiotherapy improves locoregional control and disease-free survival [8-25], Patients 1 and 3 benefited from this adjuvant radiotherapy at respective doses of 54 Gy and 66 Gy.

The doses were prescribed according to the recommendations: the dose is > 60-66 Gy for postoperative radiotherapy and 70 Gy for exclusive radiotherapy [23]. The delays between surgery and radiotherapy for our two patients did not respect the recommendations of learned societies of six weeks or less [26], they were 26 weeks for Patient 1 and 15 weeks for Patient 3 meeting this deadline is a major challenge for our developing countries because we are experiencing technical, logistical, social and financial difficulties.

Some chemotherapeutic responses have been reported in ACC [27]. Patient 4 benefited from surgical

treatment of the primary tumor, a total parotidectomy, for sterilization and loco-regional control, followed by chemotherapy to control the general disease thus improving overall survival and recurrence-free survival.

The main factors associated with patient survival are the clinical and histological stage as well as the type of surgery (conservative or radical) [7-28].

Metastases or recurrences being very late require monitoring for more than 10 years in order to diagnose them a little earlier. This monitoring is carried out by clinical examination and imaging: a cervico-facial MRI for loco-regional recurrences and a thoraco-abdominal CT for distant metastases. Despite a prolonged course, 10-year survival is less than 50% for all grades [29, 30], ACC causes mortality of 75 to 80% over a 30-year period and the majority between 5 and 10 years later initial treatment [30]. All of our patients are currently under surveillance.

CONCLUSION

ACC is a rare malignant epithelial tumor of the parotid gland. Slow growing, it has a remarkable propensity for local dissemination, especially perineural, and for recurrence. The histopathological study is a better diagnostic approach than cytology after cytology which exposes the practitioner to false negatives. Imaging (MRI and CT) constitutes a standard in the current management of this tumor for both diagnostic and therapeutic procedures and subsequent monitoring.

Surgery is the therapeutic standard; however, radiotherapy can be used postoperatively or alone or in conjunction with chemotherapy in unresectable tumors and chemotherapy in metastatic or recurrent situations. Immunotherapy and targeted therapies remain promising areas of research.

Since metastases can appear very slowly and years after diagnosis, early management is essential to improve overall survival and recurrence-free survival and long-term monitoring is imperative.

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