Rare disease

Adenoid cystic carcinoma of head and neck: apropos of a case

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Summary

Adenoid cystic carcinoma (ACC) is a rare malignant neoplasm, arising from glandular tissues, found mainly in the head and neck. Generally, it presents insidiously but can behave aggressively making its course unpredictable. Surgery and adjuvant radiotherapy continue to be the cornerstone for its treatment. ACC remains extremely difficult to treat. The authors report a case of a 37-year-old woman with bloody rhinorrhea for 6 months. She was diagnosed with a left nasal cavity lesion that was biopsied, and the anatomopathological result showed ACC. The patient was submitted to a left extended maxillectomy, microsurgical reconstruction and radiotherapy.

BACKGROUND

Adenoid cystic carcinoma (ACC) is a rare form of adenocarcinoma, which is a broad term describing any cancer arising from glandular tissues, mainly found in the head and neck, accounting for 1–2% of all the malignancies in this location.¹ It most commonly occurs in the salivary glands (major and minor), but it can appear elsewhere in the body.¹ Regardless of where it starts, characteristically it shows a very slow growth pattern, high local recurrence rate and distant metastases mainly to the lung and bone.² This tumour tends to spread along nerves, which is related to high recurrence rates at nerve stumps at the cranial base.³ Lymph node metastases are present in only about 5–10% of cases.⁴ Local recurrences, years after surgery, are the rule.

Women are slightly more affected than men (female-to-male ratio is about 3:2), mostly between 30 and 70 years of age and there are no risk factors proven to be involved in this type of cancer.

The initial symptoms of ACC depend on tumour location. Early lesions of the salivary glands may appear as painless, usually slow-growing masses, underneath the normal lining of the mouth, throat, sinuses or skin of the face. Other symptoms may include difficulty swallowing, hoarseness and paralysis of a facial nerve (the most commonly involved are facial and trigeminal).

Five-year survival rates are optimistically high (approximately 89%), but 10–20-year survival rates are 40%.^{2 5}

Three histological types are described in the literature: tubular, cribriform and solid (worst prognosis, with a 10-year survival rate of about 34%).^{1 6 7} According to Szanto *et al*,⁸ ACC is graded into three behavioural groups: grade I—tumours with cribriform or tubular growth; grade II—tumours with less than 30% solid growth; grade III—tumours with 30% or more solid growth. When the cribriform pattern is present, a higher local recurrence rate must be expected. The solid pattern is associated, more often, with distant metastases.²

Surgery is the best treatment for ACC, provided it can be done safely and is likely to have a good outcome. Wide

resection margins (minimum of 2 mm) are mandatory, as ACC presents an incomplete capsule, infiltrative nature and perineural involvement with spread along the nerve. Perineural invasion is a poor prognostic sign for both local recurrence and distant metastases.⁶

The authors choose to report this case because ACC is a rare unknown disease by many health professionals, has a biological behaviour poorly understood and its treatment is still a big challenge for any surgeon.

CASE PRESENTATION

A female Caucasian patient, 37 years of age, with no personal medical history or family history of carcinoma, presented herself to the Gaia Plastic, Reconstructive and Maxillofacial Unit with a clinical history of left bloody rhinorrhea and ipsilateral nasal obstruction for 6 months,

Figure 1 CT scan: tumour occupying the left maxillary sinus.

without any other complaint (namely weight lost, anorexia, asthenia, etc). She had already sought otorhinolaryngology service, and was diagnosed with a left nasal lesion studied with a CT scan (figures 1–3) with 3D picture reconstruction (figure 4) and a fine-needle aspiration biopsy (FNAB). Maxillofacial CT scan showed a tumour occupying the left maxillary sinus, extending to the floor of the orbit, pterigoid fossa and invading the lacrimal sac and nasal septum. The FNAB performed to the left maxillary sinus revealed an ACC. At this time, the patient's complaints were still the bloody rhinorrhea and nasal obstruction. Bone scintigraphy and thoracic CT scan were negative.

She was submitted to an extended left maxillectomy (figures 5–8).

The postoperative period progressed uneventfully with a good primary healing (figure 9).

The histopathological result was ACC, mainly the cribriform type, with solid growth pattern areas (grade II) and perineural invasion (figures 10 and 11).

Free tumour margin was accomplished, the smallest being of 2.2 mm.

INVESTIGATIONS

Our patient was first observed by an otorhinolaryngologist who diagnosed her to have a left nasal lesion. Then a maxillofacial CT scan was performed with 3D picture reconstruction as well as an FNAB.

The CT scan confirmed the diagnosis of the maxillary lesion (already detected in physical examination) and assessed the disease extent and the projection of surgical treatment.

FNAB gave the diagnosis of ACC so a surgical treatment was proposed to the patient.

To exclude metastases, the patient was also submitted to a bone scintigraphy and a thoracic CT scan that were both negative.

Histopathological findings confirmed the initial suspicion of ACC.

Figure 2 CT scan: tumour occupying the left maxillary sinus.

Figure 3 CT scan: tumour extending to the floor of the orbit, pterigoid fossa, lacrimal sac and nasal septum.

DIFFERENTIAL DIAGNOSIS

The diagnosis delay has to do with the fact that bloody rhinorrhea can be attributed to a chronic sinusitis, which is self-limited and does not worry the patient.

It is important to perform the differential diagnosis between nasossinusual chronic infection and nasossinusual tumours (such as inverted Schneiderian papiloma, lymphoma, adenocarcinoma, etc),⁹ which was accomplished by the otorhinolaryngology team. Nasal polyps are benign lesions that can be manifested by bloody rhinorrhea as well. They result from chronic inflammation due to asthma, recurring infection, allergies, drug sensitivity or certain immune disorders, that were not present in our patient.

Figure 4 CT scan with three-dimensional picture reconstruction.

Figure 5 Extended left maxillectomy (orbital floor bone, nasal septum and cartilage included) and ipsilateral functional neck dissection.

All of these lesions and differential diagnoses must be excluded with anamnesis, physical examination, imagiological exams and FNAB.

TREATMENT

The patient was submitted to an extended left maxillectomy, including the orbital floor bone, nasal septum and cartilage (figures 5 and 6). The left infraorbital nerve was cut as far posteriorly in the orbit. An ipsilateral functional neck dissection (figure 5) was also performed and no metastases were found. Reconstruction was accomplished by a free right muscle *rectus abdominis* flap (Figures 7 and 8) and ipsilateral iliac bone graft, both through a Pfannenstiel incision.

This was a curative intent surgery (R0 resection with free tumour smallest margin of 2.2 mm).

The treatment was completed with adjuvant radiotherapy (60 Gy) delivered to the tumour field, because of the perineural invasion detected on the histopathological exam.

Figure 6 Maxillectomy.

Figure 7 Free right muscle rectus abdominis flap.

OUTCOME AND FOLLOW-UP

Multidisciplinary oncological group decided for adjuvant radiotherapy.

Two-year follow-up without evidence of disease recurrence.

In our institution, the follow-up consists, in the first year, of a clinical exam every 3 months, maxillofacial CT scan and chest film every 6 months. After the fifth year of follow-up both are performed once a year.

Bone scintigraphy is performed only if there are any symptoms that suggest bone metastases.

DISCUSSION

ACC diagnosis is always late because, generally, patients are asymptomatic and the tumour growth is gradual and sub-mucosal (hiding early diagnosis), consequently the time elapsed from the first clinical manifestation through the diagnosis is long, as it happened with our patient (6 months).¹

Clinical and radiological examination always underestimates the real extent of the tumour,⁶ so resection extension depends primarily on this information (tumour size) but finally on what the surgeon finds in the operating theatre.¹

MRI or CT scan are the mainstay for ACC diagnosis. The first one is useful for detecting perineural invasion

Figure 8 Free right muscle rectus abdominis flap.

Figure 9 Primary healing (2 months after surgery).

and the second one creates a 3D picture helping the surgeon to project the surgical procedure. FNAB can direct the diagnosis but in most cases a definite diagnosis can only be achieved after removal of the lesion.⁹

Characteristically, ACC is known for having long periods of indolence followed by growth spurts and long-term follow-up (15–20 years) is required as this tumour recurs late in its course.⁶

Standard treatment so far consists of complete surgical resection followed by adjuvant radiotherapy in case of risk factors (close margins, perineural invasion, extensive primary tumour (T3, T4) or high-grade histology). The choice of therapy is affected by site, stage, grade and tumour behaviour. Most authors consider curative intent surgery and adjuvant radiotherapy, the cornerstone of ACC treatment.¹⁰ Surgery is considered the most successful if the free tumour margin is at least of 2 mm (as it happened with our patient). Postoperative radiotherapy seems to have significant impact on the recurrence rate.¹⁰ To achieve local control, radiation doses of 60 Gy or more are recommended.¹¹ ACC cells have low mitotic indices so chemotherapy has little role in this disease, taking place almost only when distant metastases are present.

Figure 10 Adenoid cystic carcinoma arising from minor salivary gland (4×10).

Figure 11 Adenoid cystic carcinoma perineural spread (20×10).

However, the optimal therapy has not been established (population-based studies examining ACC are scarce).⁵

Histologically these tumours are grade in three different groups, with different aggressivity and behaviour. Our patient's tumour was classified as grade II, so we are about to expect local recurrence (because of cribriform pattern) and moderate aggressiveness (less than 30% of solid pattern).

Research is being done around molecular markers that may influence treatment and prognosis. It is already known that patients with ACC p53 positivity have worse prognoses than others, being resistant to therapy.² Other markers studied are c-kit (CD117), c-erbB2 and intercellular adhesion molecule 1. C-kit, a tyrosine—kinase receptor, promotes cellular growth in normal or neoplastic tissues. It recently has been found that it has expression in about 80% of ACC cases.¹ Imatinib mesylate, an inhibitor of c-kit, is being considered and already used in ACC treatment with promising results.¹² Diana Bell et al tested imatinib mesylate in two initially unresectable ACC, which resulted in significant tumour regression.⁷

To conclude, ACC is a rare and extremely unpredictable neoplasm regarding its evolution and behaviour. It tends to recur locally and produces distant metastases, mainly to lung and bone, however not leading to a short-term death.¹

Some changes in prognosis and the natural course of the disease are being done, thanks to new therapies directed to new molecular markers found to be present in these tumours, such as c-kit.

Learning points

- ▶ Adenoid cystic carcinoma (ACC) is a rare malignant unpredictable neoplasm of glandular tissues.
- ▶ It tends to spread along nerves or through the bloodstream.
- ▶ ACC metastasises to lung and bone.
- ▶ Surgery with wide resection margins is the gold standard for ACC treatment.
- ▶ Long-term follow-up is needed.

Competing interests None.

Patient consent Obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Graça SAR, Sequeira H, Coelho G, Costa H. Adenoid cystic carcinoma of head and neck: apropos of a case. *BMJ Case Reports* 2012;10.1136/bcr-02-2012-5914, Published XXX

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