

Novel Approach to an Uncommon Case: Acinic Cell Carcinoma of the Salivary Glands Treated with Lenvatinib

COLLADA SÁNCHEZ, VL.¹, ÁLVAREZ CRIADO J. ¹, CASTELO FERNÁNDEZ B.², HERRERO AMBROSIO A.¹

1 Servicio Farmacia Hospitalaria. Hospital Universitario La Paz

2 Servicio Oncología. Hospital Universitario La Paz

Fecha de recepción: 26/01/2025 Fecha de aceptación: 03/03/2025

DOI: : <http://dx.doi.org/10.4321/S1699-714X20250005000012>

ABSTRACT

Acinic cell carcinoma (ACC) of the salivary glands is a rare neoplasm, representing approximately 6-8% of salivary gland carcinomas. This case report discusses the treatment and outcomes of a 65-year-old male with recurrent metastatic ACC. Initially treated with surgery and radiotherapy, the disease recurred in the lungs and pleura after six years, prompting a switch to systemic therapies. The first-line carboplatin-paclitaxel regimen was selected for its favorable safety profile in a frail patient. Upon progression, lenvatinib, a receptor tyrosine kinase inhibitor targeting VEGF and c-kit pathways, was introduced with notable symptom control and a 12-month progression-free period. Despite a subsequent relapse, lenvatinib improved the patient's quality of life and provided valuable insights into its application for ACC treatment. This report highlights the challenges of managing rare tumors, emphasizing the lack of consensus on therapeutic standards due to limited evidence. It underscores the potential role of lenvatinib in targeting specific mutations associated with ACC and its contribution to personalized oncology care. This real-world case illustrates the feasibility of lenvatinib as a therapeutic option in refractory ACC, providing both clinical benefit and a contribution to the literature for future case management.

RESUMEN

El carcinoma de células acinosas (ACC) de las glándulas salivales es una neoplasia poco frecuente, que representa aproximadamente el 6-8% de los carcinomas de glándulas salivales. Este caso describe el tratamiento y los resultados de un varón de 65 años con ACC metastásico recurrente. Tratada inicialmente con cirugía y radioterapia, la enfermedad recidivó en los pulmones y la pleura al cabo de seis años, lo que motivó el cambio a terapias sistémicas. El régimen de carboplatino-paclitaxel de primera línea se seleccionó por su perfil de seguridad favorable en un paciente frágil. Tras la progresión, se introdujo lenvatinib, un inhibidor de los receptores tirosina cinasa dirigido a las vías del VEGF y c-kit, con un notable control de los síntomas y un periodo libre de progresión de 12 meses. A pesar de una recaída posterior, lenvatinib mejoró la calidad de vida de la paciente y proporcionó información valiosa sobre su aplicación para el tratamiento de la ACC. Este informe pone de manifiesto los retos que plantea el tratamiento de los tumores poco frecuentes, haciendo hincapié en la falta de consenso sobre las normas terapéuticas debido a la escasez de pruebas. Subraya el papel potencial de lenvatinib en el tratamiento de mutaciones específicas asociadas al AAC y su contribución a la atención oncológica personalizada.

Este caso del mundo real ilustra la viabilidad de lenvatinib como opción terapéutica en el ACC refractario, proporcionando tanto un beneficio clínico como una contribución a la literatura para el manejo de casos futuros.

Keywords: lenvatinib, Salivary Glands, rare-tumor.

INTRODUCTION

Acinar cell carcinoma (ACC) of the salivary glands is primarily located in the parotid glands. Although it is considered an extremely rare tumor, accounting for only 0.6% of all carcinomas, it represents approximately 6-8% of all salivary gland carcinomas.¹ ACC is most prevalent in women, with an average age of diagnosis around 50 years.²

The signs and symptoms of ACC are nonspecific and vary based on tumor size and anatomical location. However, the most frequent symptoms include paresthesia, pain in the affected area, and headache.³

Surgical excision is the primary treatment for low-grade tumors with favorable pathological features; however, the treatment paradigm for high-grade malignancies remains less well-defined, with most studies recommending surgery followed by adjuvant radiotherapy.^{4,5}

For decades, ACC was considered a low-grade tumor with a favorable prognosis; however, its propensity for recurrence and metastasis has led to its current classification as a neoplasm with an uncertain course.⁶

The average recurrence rate is estimated to be around 35%, with the most frequent metastases being to the cervical lymph nodes and lungs.⁷

CASE REPORT

A 65-year-old male patient was diagnosed with ACC in March 2015 following recurrent episodes of facial paralysis and associated pain. At diagnosis, the disease was localized, and a radical treatment with curative intent was chosen, involving radical parotidectomy and petrosectomy, followed by 30 sessions of radiotherapy.

The patient remained asymptomatic for six years; however, in January 2021, he presented to the emergency department with asthenia and progressive dyspnea. A chest X-ray revealed a massive pleural effusion, and biopsy confirmed metastasis from the previously diagnosed acinar carcinoma, one of the most frequently reported metastatic sites in the literature.

In this scenario, first-line treatment options included the combination of cyclophosphamide, adriamycin, and cisplatin (CAP) or carboplatin-paclitaxel, with the latter being chosen due to its lower toxicity profile for a frail patient.

MAGNAMENT AND OUTCOMES

In September 2021, the patient experienced pleural disease progression, and treatment with lenvatinib was considered. After evaluation by the special uses committee, lenvatinib was approved, and the patient began therapy with 24 mg daily, with a weekend rest. Tolerance to the drug was acceptable, with grade 1 mucositis and diarrhea managed through dietary adjustments.

In September 2022, the patient experienced pleural and pericardial relapse. Next-generation sequencing (NGS) was requested to identify potential therapeutic targets. However, immunohistochemical analysis of DNA repair proteins revealed preserved expression of MLH1, PMS2, MSH2, and MSH6, excluding the patient as a candidate for immunotherapy. Given that the primary objective was symptom control (e.g., fatigue and pain), treatment with doxorubicin was initiated.

Considering that the main objective of the patient was to control the symptoms derived from the disease (such as fatigue or pain), treatment with doxorubicin was decided.

As of September 1, 2024, the patient has been under doxorubicin treatment for 22 months, maintaining an acceptable general condition, with nausea and vomiting as the only side effects.

DISCUSSION

Although ACC is still considered a neoplasm with a generally favorable prognosis, it is a limiting pathology with a high recurrence rate, and no consensus exists regarding standard treatment regimens, especially after initial radiotherapy. Various chemotherapeutic regimens have been proposed as adjuvant therapies, though none have been tested in randomized clinical trials, partially due to the rarity of the neoplasm.¹

In this case, the decision to treat with lenvatinib was based on evidence from current literature, which reports vascular endothelial growth factor (VEGF) mutations in up to 76% of ACC patients and c-kit receptor mutations in 90% of cases.⁹

Lenvatinib is a receptor tyrosine kinase (RTK) inhibitor that selectively targets VEGF receptors and other RTKs involved in oncogenic and proangiogenic pathways, such as c-kit. A review of the literature identified only one published phase II clinical trial, which did not gain regulatory approval, investigating lenvatinib for ACC treatment. This study reported a

time-to-event of 8 months, although the sample size was limited (n=35).¹⁰

For our patient, the time-to-event was 12 months.

This case represents one of the few real-world accounts of ACC treatment with lenvatinib. Through this treatment, the patient achieved a new therapeutic line that significantly contributed to an optimal quality of life. Importantly, this case not only benefited the patient but also contributes valuable data to the available scientific literature, benefiting similar cases worldwide.

BIBLIOGRAFÍA

1. Al-Zaher N, Obeid A, Al-Salam S, Al-Kayyali BS. Acinic cell carcinoma of the salivary glands: a literature review. *Hematol Oncol Stem Cell Ther*. 2009;2(1):259-64. doi: 10.1016/s1658-3876(09)50035-0. PMID: 20063555.
2. Juhlin CC, Asa SL, Jatta K, Naserhojati Rodsari H, Shabo I, Haglund F, Delahunt B, Samaratunga H, Egevad L, Höög A, Zedenius J. Perithyroidal Salivary Gland Acinic Cell Carcinoma: Morphological and Molecular Attributes of a Unique Lesion. *Head Neck Pathol*. 2021 Jun;15(2):628-637. doi: 10.1007/s12105-020-01187-3. Epub 2020 Jun 9. PMID: 32519264; PMCID: PMC8134583.
3. Cantù G. Adenoid cystic carcinoma. An indolent but aggressive tumour. Part A: from aetiopathogenesis to diagnosis. *Acta Otorhinolaryngol Ital*. 2021 Jun;41(3):206-214. doi: 10.14639/0392-100X-N1379. PMID: 34264913; PMCID: PMC8283400.
4. Sheng D, Zhang Y, Xue T, Zhou XY, Li XQ. Identification of LMO2 as a new marker for acinic cell carcinoma of salivary gland. *Diagn Pathol*. 2022 Jan 30;17(1):15. doi: 10.1186/s13000-022-01192-w. PMID: 35094691; PMCID: PMC8802521.
5. Ali SA, Kovatch KJ, Yousif J, Gupta S, Rosko AJ, Spector ME. Predictors of distant metastasis in acinic cell carcinoma of the parotid gland. *World J Clin Oncol*. 2020 Jan 24;11(1):11-19. doi: 10.5306/wjco.v11.i1.11. PMID: 31976306; PMCID: PMC6935691.
6. Vander Poorten V, Triantafyllou A, Thompson LD, Bishop J, Hauben E, Hunt J, Skalova A, Stenman G, Takes RP, Gnepp DR, Hellquist H, Wenig B, Bell D, Rinaldo A, Ferlito A. Salivary acinic cell carcinoma: reappraisal and update. *Eur Arch Otorhinolaryngol*. 2016 Nov;273(11):3511-3531. doi: 10.1007/s00405-015-3855-7. Epub 2015 Dec 19. PMID: 26685679.
7. Grasl S, Janik S, Grasl MC, Pammer J, Formanek M, Weinreb I, Perez-Ordóñez B, Hope A, Hosni A, de Almeida JR, Irish J, Gilbert R, Goldstein DP, Erovic BM. Nodal Metastases in Acinic Cell Carcinoma of the Parotid Gland. *J Clin Med*. 2019 Aug 27;8(9):1315. doi: 10.3390/jcm8091315. PMID: 31461946; PMCID: PMC6780641.
8. Cavaliere M, De Luca P, Scarpa A, Savignano L, Cassandro C, Cassandro E, Iemma M. Acinic cell carcinoma of the parotid gland: from pathogenesis to management: a literature review. *Eur Arch Otorhinolaryngol*. 2020 Oct;277(10):2673-2679. doi: 10.1007/s00405-020-05998-6. Epub 2020 May 4. PMID: 32367151.
9. Mueller SK, Haderlein M, Lettmaier S, Agaimy A, Haller F, Hecht M, Fietkau R, Iro H, Mantsopoulos K. Targeted Therapy, Chemotherapy, Immunotherapy and Novel Treatment Options for Different Subtypes of Salivary Gland Cancer. *J Clin Med*. 2022 Jan 29;11(3):720. doi: 10.3390/jcm11030720. PMID: 35160172; PMCID: PMC8836387.
10. Tchekmedyian V, Sherman EJ, Dunn L, Tran C, Baxi S, Katabi N, Antonescu CR, Ostrovnaya I, Haque SS, Pfister DG, Ho AL. Phase II Study of Lenvatinib in Patients With Progressive, Recurrent or Metastatic Adenoid Cystic Carcinoma. *J Clin Oncol*. 2019 Jun 20;37(18):1529-1537. doi: 10.1200/JCO.18.01859. Epub 2019 Apr 2. PMID: 30939095; PMCID: PMC6599407.