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Case Report

ADENOID CYSTIC CARCINOMA OF THE NASOPHARYNX: A RARE CASE AND REVIEW OF PARTICLE THERAPY APPROACHES

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ABSTRACT

Nasopharyngeal adenoid cystic carcinoma (NACC) is an exceptionally rare malignancy, representing <1% of nasopharyngeal tumors. Over the last decade, fewer than 200 cases have been reported worldwide, usually presenting at an advanced stage with perineural invasion and skull base involvement. The role of surgery is often limited, and particle therapy, including intensity-modulated proton therapy (IMPT) and carbon ion radiotherapy (CIRT), has emerged as a promising alternative. We report the case of a 35-year-old male with NACC presenting with nasal obstruction, epistaxis, and cranial nerve involvement. MRI revealed a 45×35×40 mm mass extending to the clivus, cavernous sinus, and parapharyngeal space. Histopathology confirmed adenoid cystic carcinoma (ACC) (cribriform and solid type), with immunohistochemistry positive for CD117 and CK7, focally positive for p63 and smooth muscle actin (SMA), and negative for p40 and Epstein-Barr virus (EBV) (*in situ* hybridization). The patient underwent IMPT to a total dose of 45 Gy (relative biological effectiveness [RBE]) in 15 fractions, as recommended by a multidisciplinary tumor board. Treatment was well tolerated, with grade 2 mucositis, grade 2 otitis media, and mild xerostomia. However, pulmonary metastases developed within 10 months, and systemic therapy with lenvatinib *plus* doxorubicin was initiated with limited efficacy. This case illustrates the challenges of managing NACC, emphasizing the role of particle therapy for local control (LC), the importance of multidisciplinary evaluation, and the need for vigilant follow-up given the high risk of distant metastases. Collaborative registries and clinical trials are warranted to optimize treatment strategies for this rare disease.

Introduction

Adenoid cystic carcinoma (ACC) of the nasopharynx is an exceptionally rare malignancy, accounting for <1% of all nasopharyngeal carcinomas and approximately 0.1-0.4% of head and neck tumors. (1,2) There is no clear sex predominance, and the mean age at diagnosis is 40-60 years, although younger cases have been reported in the literature. (3) Fewer than 200 cases have been documented over the past decade, mostly as isolated case reports or small series. (4-7)

Clinically, nasopharyngeal ACC (NACC) is typically diagnosed at an advanced stage due to its indolent but infiltrative growth pattern, with frequent skull base invasion and cranial nerve involvement at presentation. (8-10) Although regional lymph node metastases are uncommon, distant spread is frequent, and the lungs represent the most common metastatic site, often determining prognosis. (7,11-13)

Therapeutic options are challenging due to the nasopharynx's anatomical complexity and the high likelihood of perineural extension. (14) Surgery with postoperative radiotherapy is considered the treatment of choice when feasible; however, complete resection is often not possible. In such cases, definitive radiotherapy – especially with advanced modalities such as intensity-modulated proton therapy (IMPT) or carbon ion radiotherapy (CIRT) – has emerged as a promising alternative, showing favorable local control (LC) and tolerability compared with conventional photon-based approaches. (15-21)

We report the case of a young patient with NACC treated with proton therapy, followed by systemic therapy, and review the current literature on management strategies for this rare tumor.

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Case Report

A 35-year-old male, light smoker and occasional alcohol consumer, presented in May 2021 with right ear fullness unresponsive to antibiotics and steroids. By September 2021, he developed pain, trismus, and temporomandibular dysfunction. MRI revealed a 45×35×40 mm mass in the right nasopharynx, with skull base extension. Biopsy confirmed adenoid cystic carcinoma with solid and cribriform features. Immunohistochemistry was positive for CK7, CD117, SOX10, and heterogeneous for S100, with Ki-67 of 20%.

A few weeks later, the patient developed diplopia, headache, epistaxis, and facial nerve palsy. PET/CT showed intense uptake at the primary site. The case was discussed at a multidisciplinary tumor board, which recommended IMPT; the patient received 45 Gy to the nasopharynx and ipsilateral neck in 15 fractions of 3 Gy each, at a schedule of 5 fractions per week. Headache, nausea, grade 2 mucositis, hearing loss, xerostomia, and alopecia were reported as late effects.

Follow-up MRI (Figure 1), after 6 months, showed partial regression of the primary tumor, but 10 months after diagnosis, pulmonary metastases appeared in chest CT scan (Figure 2); chemotherapy with lenvatinib and doxorubicin (20mg/mq d1,8,15q28) was initiated with limited benefit. The disease progressed, and the patient died about one year after diagnosis.

Discussion

ACC of the nasopharynx is a rare entity that usually presents at an advanced stage, with perineural invasion and skull base extension. (22-24) Regional lymph node involvement is uncommon, whereas distant metastases occur more frequently, with the lungs representing the most common metastatic site, with a time to onset ranging from 1 to 5 years. (8,11,12)

Particle therapy has emerged as a promising treatment strategy. With IMPT, multi-institutional series have reported 2-year LC rates of approximately 92% and overall survival (OS) near 89%, with grade ≥3 acute toxicities in 14% and late toxicities in 6%, and no treatment-related deaths. (15) In the postoperative setting, excellent LC with minimal high-grade toxicity has been documented. (17) CIRT, often delivered as a boost after IMRT, has achieved 2-year LC rates around 83% and 5-year LC rates of 49%, with OS of 87% at 2 years and 69% at 5 years. (17) Larger head and neck ACC cohorts have demonstrated superior outcomes with IMRT *plus* CIRT boost compared with IMRT alone, (18,25-27) while postoperative series report a median OS of 93 months. (19) These data suggest that IMPT provides excellent short-term control with favorable tolerability, whereas CIRT may offer superior long-term tumor control, particularly in advanced or unresectable cases. (27-29)

Recent reviews have identified fewer than 200 cases of NACC reported worldwide, mostly as single case reports or small series. (1,2,4-7) In these cohorts, most patients presented with advanced disease and cranial nerve involvement, consistent with our case. (10,30) However, our patient was relatively young and experienced rapid progression despite multimodal treatment, underscoring the aggressive potential of this tumor even when arising in the nasopharynx.

The role of the multidisciplinary tumor board is particularly relevant for rare tumors such as NACC, for which no standardized treatment guidelines exist. (31-35) In this case, tumor board discussion allowed a tailored therapeutic decision, leading to proton therapy as the primary approach. This reflects the increasing recognition of particle therapy as an important tool in head and neck ACC, especially when conventional surgery or IMRT are not feasible. (26,36,37)

Long-term follow-up is essential, as distant metastases – particularly to the lungs – remain the major cause of treatment failure. (8,11,12) Our case confirmed this pattern, with early development of pulmonary metastases following initial locoregional control. Emerging systemic therapies, including tyrosine kinase inhibitors such as lenvatinib, and investigational immunotherapy approaches, may provide additional options, although evidence remains limited and further studies are required. (8)

Given the rarity of NACC, collaborative efforts and multicenter registries are needed to improve understanding of its natural history and to optimize the integration of advanced local and systemic therapies. Reported cases from the past decade are summarized in Table 1.

Conclusions

NACC is an exceptionally rare malignancy, often diagnosed at an advanced stage with skull base extension and cranial nerve involvement. When feasible, surgery followed by postoperative radiotherapy remains the standard of care. In unresectable cases, advanced particle therapies such as IMPT and CIRT offer encouraging local control with acceptable toxicity profiles, representing valuable alternatives to conventional approaches.

Our case highlights the importance of multidisciplinary tumor board discussion in guiding management, the need for vigilant long-term follow-up to detect distant spread – particularly to the lungs – and the role of innovative radiotherapy modalities in improving outcomes. Despite advances in local therapy, systemic progression remains the major challenge, underlining the necessity for further clinical research and the development of collaborative registries to optimize treatment strategies for this rare and aggressive disease.

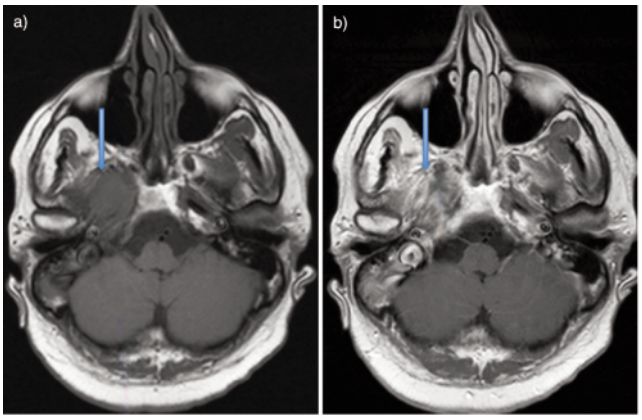

Figure 1. a) Axial T1 non-contrast and **b**) T1 post-contrast MRI images show an enhancing lesion in the right nasopharyngeal lateral recess invading the levator veli palatini muscle.

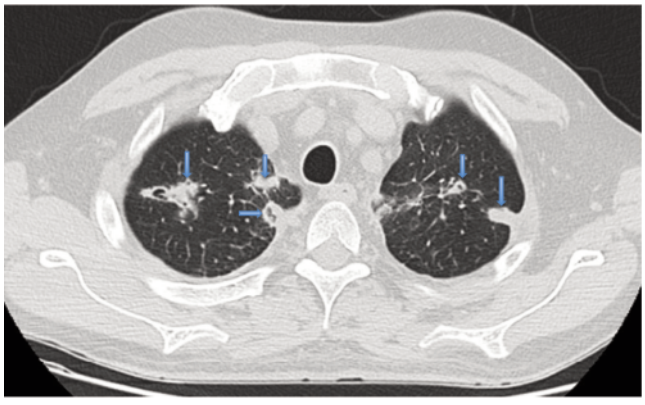

Figure 2. Axial CT image shows multiple solid nodular and rounded lesions of variable size. Some of the nodules show cavitation.

Table 1. Reported cases of NACC in the last decade.

Author, year	Patients (n), gender	Age (years)	Stage of disease/TNM	Surgery	Radiotherapy	Chemotherapy	Survival/ recurrence of disease
Afani *et al*.,[2] 2016	1 M	45	T4N0M0	No	Yes	Cisplatin, 5-FU, cetuximab	7-year OS
Boon *et al*.,[29] 2016	1 M	45	T4N2cM0	No	Yes	Docetaxel, cisplatin, 5-FU	Remission at 10 months
Phan *et al*.,[21] 2017	1 F	71	T4N0M0	No	IMRT	Cisplatin	Recurrence of disease after 2 years
Tatari *et al*.,[31] 2018	1 F	55	NR	Yes	Yes	No	No disease recurrence at 1 year
Ng *et al*.,[5] 2019	2 M	21 and 30	NR	Yes	Yes	No	No recurrence after quarterly check-ups
Gentile *et al*.,[9] 2019	1 F	33	T4bN0M0	Yes	IMRT	Cetuximab, 5-FU, cisplatin	Lung metastases after 1 year, local disease recurrence at 3 years
Akbaba *et al*.,[17] 2019	16 M 43 F	50 (mean)	NR	Yes	IMRT+CIRT	Cyclophosphamide, doxorubicin, cisplatin in 10 pts with lung metastases	5-year OS 69%, DPFS 51%
Arora *et al*.,[6] 2021	3 F	28, 67, and 60	NR	Yes	Yes	No	No recurrence after 4 years, 15 months and 8 months
Hu *et al*.,[20] 2022	4 M 18 F	42 (mean)	Stage I: 1 pt Stage III: 2 pts Stage IV: 19 pts	8 pts	CIRT+PBRT	No	30-months OS 100%, DPFS 85%
Pahwa *et al*.,[23] 2022	1 F	67	Stage IV	Yes	Yes	No	Absence of recurrence at 6 months
Alsubaie *et al*.,[7] 2023	1 M	56	T4N1M1	No	Yes	Cisplatin, doxorubicin, cyclophosphamide	Local tumor control after 1 year
Wu *et al*.,[11] 2024	22 M 28 F	47 (mean)	Stage I-II: 13 pts Stage III-IV: 37 pts	34 pts	IMRT	14 pts	5-year OS 84%, DPFS 67.5%
Chen *et al*.,[8] 2024	5 M 7 F	40 (mean)	Stage III: 3 pts Stage IV: 9 pts	Yes	Yes	Paclitaxel-cisplatin (only in metastatic patients)	After 2 years: 4 pts in remission, 5 alive with locoregional disease control, 3 deceased, metastases in 3 pts (two of whom died)
Hu *et al*.,[12] 2024	7 M 19 F	45 (mean)	Stage I: 1 pt Stage II: 1 pt Stage III:3 pts Stage IV: 21 pts	11 pts	PBRT+CIRT or IMPT+CIRT	No	4-year OS 92%, 5-year OS 54.8%, 10 patients with distant metastases (7 to the lung)

TNM, tumor-node-metastasis; FU, fluorouracil; OS, overall survival; IMRT, intensity-modulated radiotherapy; NR, not reported; DPFS, disease-progression-free survival; CIRT, carbon ion radiotherapy; PBRT, proton beam radiotherapy; IMPT, intensity-modulated proton therapy.

Conflict of interest: the authors have no conflict of interest to declare.

Ethics approval and consent to participate: not required.

Consent for publication: informed consent for the publication of the clinical information and any accompanying images included in this manuscript was obtained from the patient's relatives**.**

Availability of data and materials: all data underlying the findings are fully available.

References

1. Wu S, Liu J, Quan R, Han L. A rare case of nasopharyngeal adenoid cystic carcinoma treated with cetuximab-based induction therapy followed by concurrent chemoradiotherapy. Oral Oncol 2019;89:161-3.
2. Afani L, Errihani H, Benchafai I, Lalami Y. [Nasopharyngeal adenoid cystic carcinoma, a rare but highly challenging disease with unmet therapeutic needs: A case-report and review of the literature]. Cancer Radiother 2016;20:400-4.
3. Sninate S, Allioui S, Tbouda M, et al. Nasopharyngeal adenoid cystic carcinoma presenting with exophthalmos: A case report. Radiol Case Rep 2021;16:956-60.
4. Lin D, Gray S, McCarty J, et al. Adenoid Cystic Carcinoma of the Nasopharynx with Skull Base Involvement: Retrospective National Cohort Analysis of Treatment Paradigms, Outcomes, and Provider Density. J Neurol Surg B Skull Base 2022;83:99-104.
5. Ng BHK, Tang IP. Adenoid Cystic Carcinoma of the Nasopharynx: A Case Series. Indian J Otolaryngol Head Neck Surg 2019;71:731-3.
6. Arora V, Yadav V, Mandal G, et al. Adenoid cystic carcinoma of the nasopharynx—a rare entity: our institutional experience and therapeutic approach. Indian J Surg Oncol 2021;12:428-31.
7. Alsubaie NM, Alhussien A, Alghulikah A, et al. A rare nasopharyngeal adenoid cystic carcinoma: case report and literature review. Am J Case Rep 2023;24:e938858.
8. Chen Y, Shi Y, Yu H. Adenoid cystic carcinoma of the nasopharynx: a retrospective study of 12 cases. Ear Nose Throat J 2024.
9. Gentile MS, Yip D, Liebsch NJ, et al. Definitive proton beam therapy for adenoid cystic carcinoma of the nasopharynx involving the base of skull. Oral Oncol 2017;65:38-44.
10. Gadkaree SK, Parikh AS, Rodarte AI, et al. Adenoid Cystic Carcinoma of the Skull Base: Response to Radiation Therapy and Outcomes in a

Retrospective Case Series. J Neurol Surg B Skull Base 2020;81:505-10.
11. Wu WB, Cai WL, Zou YH, et al. Outcomes of patients in nasopharyngeal adenoid cystic carcinoma in the IMRT era: a single-center experience. BMC Cancer 2024;24:576.
12. Hu W, Hu J, Huang Q, et al. Long-term outcomes after particle radiation therapy in patients with nasopharyngeal adenoid cystic carcinoma. BMC Cancer 2024;24:742.
13. Amit M, Binenbaum Y, Sharma K, et al. Adenoid cystic carcinoma of the nasal cavity and paranasal sinuses: a meta-analysis. J Neurol Surg B Skull Base 2013;74:118-25.
14. Liang YF, Kong B, Xiang WY, et al. Nasopharyngeal adenoid cystic carcinoma: a case report and review of the literature. Int J Clin Exp Pathol 2014;7:4516-8.
15. Pelak MJ, Walser M, Bachtiary B, et al. Clinical outcomes of head and neck adenoid cystic carcinoma patients treated with pencil beam-scanning proton therapy. Oral Oncol 2020;107:104752.
16. Holliday E, Bhattasali O, Kies MS, et al. Postoperative Intensity-Modulated Proton Therapy for Head and Neck Adenoid Cystic Carcinoma. Int J Part Ther 2016;2:533-43.
17. Akbaba S, Ahmed D, Lang K, et al. Results of a combination treatment with intensity modulated radiotherapy and active raster□scanning carbon ion boost for adenoid cystic carcinoma of the minor salivary glands of the nasopharynx. Oral Oncol 2019;91:39-46.
18. Jensen AD, Nikoghosyan AV, Poulakis M, et al. Combined intensity-modulated radiotherapy plus raster-scanned carbon ion boost for advanced adenoid cystic carcinoma of the head and neck results in superior locoregional control and overall survival. Cancer 2015;121:3001-9.
19. Adeberg S, Windisch P, Ehret F, et al. Intensity Modulated Radiotherapy (IMRT) With Carbon Ion Boost in the Multimodal Treatment of Salivary Duct Carcinoma. Front Oncol 2019;9:1420.
20. Hu J, Hu W, Gao J, et al. The role of carbon-ion radiotherapy in the treatment of adenoid cystic carcinoma of the nasopharynx. Ann Transl Med 2022;10:1198.
21. Phan J, Ng S, Pollard C, et al. A Rare Case of Unresectable Adenoid Cystic Carcinoma of the Nasopharynx Treated with Intensity Modulated Proton Therapy. Cureus 2017;9:e1688.
22. Dong J, Tian L, Li S, et al. Differences in extension patterns between adenoid cystic carcinoma of the nasopharynx and nasopharyngeal carcinoma on MRI. Int J Clin Exp Pathol 2015;8:15960-8.
23. Pahwa S, Sharma A, Kamboj M, et al. Nasopharyngeal adenoid cystic carcinoma with intracranial spread: A rare presentation. Indian J Pathol Microbiol 2022;65:200-2.
24. Samant S, van den Brekel MW, Kies MS, et al. Concurrent chemoradiation for adenoid cystic carcinoma of the head and neck. Head Neck 2012;34:1263-8.
25. Pazdro-Zastawny K, Krajewska J, Zastawny M, Dorobisz K. Carbon Ion Radiotherapy in the Head and Neck Cancers Treatment and its Potential Role in Personalized Treatment Approach- A Review of the Current Knowledge. Curr Oncol Rep 2025;27:657-68.
26. Silverman DA, Carlson TP, Khuntia D, et al. Role for postoperative radiation therapy in adenoid cystic carcinoma of the head and neck. Laryngoscope 2004;114:1194-9.
27. Huber PE, Debus J, Latz D, et al. Radiotherapy for advanced adenoid cystic carcinoma: neutrons, photons or mixed beam? Radiother Oncol 2001;59:161-7.
28. Elkholti Y, Cosmidis A, Ardiet JM, et al. Adenoid cystic carcinoma of the nasopharynx: a case report and a discussion about prognostic factors and the role of local treatments. Tumori 2013;99:e55-60.
29. Boon IS, Warfield AT, K Ahmed S, et al. Dedifferentiated adenoid cystic carcinoma of the nasopharynx: a rare entity of head and neck cancer. BMJ Case Rep 2016;2016:bcr2016215889.
30. Pommier P, Liebsch NJ, Deschler DG, et al. Proton beam radiation therapy for skull base adenoid cystic carcinoma. Arch Otolaryngol Head Neck Surg 2006;132:1242-9.
31. Tatari M, Anajar S, Hassnaoui J, et al. Nasopharyngeal adenoid cystic carcinoma, suggestion of therapeutic innovations: A case report and review of literature. Ann Med Surg 2018;30:32-5.
32. Ryckman JM, Kusi Appiah A, Simone CB 2nd, Verma V. Treatment approaches for nasopharyngeal adenoid cystic carcinoma. Acta Oncol 2018;57:995-1001.
33. Cao CN, Luo JW, Xu GZ, et al. Management of Nasopharyngeal Adenoid Cystic Carcinoma. J Oral Maxillofac Surg 2013;71:e203-9.
34. Kuno H, Fujii S. A case of adenoid cystic carcinoma arising from the nasopharynx. Jpn J Clin Oncol 2013;43:942.
35. Bradley PJ. Adenoid cystic carcinoma of the head and neck: a review. Curr Opin Otolaryngol Head Neck Surg 2004;12:127-32.
36. Jensen AD, Krauss J, Weichert W, et al. RadioImmunotherapy for adenoid cystic carcinoma: a single-institution series of combined treatment with cetuximab. Radiat Oncol 2010;5:102.
37. Kokemueller H, Eckardt A, Brachvogel P, Hausamen JE. Adenoid cystic carcinoma of the head and neck—a 20 years experience. Int J Oral Maxillofac Surg 2004;33:25-31.