
ORIGINAL ARTICLE

Radiotherapy for Polymorphous Low-grade Adenocarcinoma of the Head and Neck

D Begosh-Mayne, A Holtzman, RJ Amdur, P Dziegielewski, WM Mendenhall

Department of Radiation Oncology, College of Medicine, University of Florida, Florida, United States

ABSTRACT

Objective: To review the clinical course and outcome of patients who underwent radiotherapy (RT) for polymorphous low-grade adenocarcinoma (PLGA) of the head and neck.

Methods: Medical records of patients who underwent RT for PLGA of the head and neck at our institution between June 1993 and March 2013 were reviewed.

Results: Two men and two women aged 43 to 76 years who underwent primary ($n = 1$) or postoperative ($n = 3$) RT for PLGA of the oropharynx ($n = 2$) or oral cavity ($n = 2$) were reviewed. Three patients underwent resection and postoperative RT, and one patient with a hard palate tumour involving the pterygoid plate underwent RT alone. Intensity-modulated RT ($n = 2$) or 3-dimensional RT ($n = 2$) was performed with dose ranging from 60 to 79.2 Gy in 30 fractions once daily ($n = 1$) to 60-66 fractions twice daily ($n = 3$). Patients were followed up for 13 months to 9.5 years. Disease-free local control was achieved in those three patients with both surgery and postoperative RT. The patient treated with RT alone had recurrence and subsequently died of disease progression. No patient developed severe acute or late treatment-related toxicity.

Conclusion: Postoperative RT may improve local control of PLGA in patients with close or positive margins after surgery.

Key Words: Adenocarcinoma; Head and neck neoplasms; Radiotherapy

中文摘要

頭頸多形性低分級腺癌放射治療

D Begosh-Mayne, A Holtzman, RJ Amdur, P Dziegielewski, WM Mendenhall

目的：回顧頭頸多形性低分級腺癌（PLGA）患者接受放射治療的臨床病程和結果。

方法：回顧分析1993年6月至2013年3月期間在本院接受PLGA放射治療患者的病歷記錄。

結果：回顧分析兩男兩女年齡43至76歲接受根治性（ $n = 1$ ）或術後（ $n = 3$ ）放療治療口咽（ $n = 2$ ）或口腔（ $n = 2$ ）PLGA的患者。三名患者接受切除手術及術後放射治療，另一名患有翼狀板硬膠

Correspondence: Dr WM Mendenhall, 2000 SW Archer Road, PO Box 100385, Gainesville, Florida, United States.
Email: mendum@sbands.ufl.edu

Submitted: 29 Mar 2016; Accepted: 19 Aug 2016.

Disclosure of Conflicts of Interest: The authors have no conflicts of interest to disclose.

Funding/Support: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

腫瘤的患者僅接受放療治療。調強放療 (n = 2) 或三維放療 (n = 2) 以30份每日一次 (n = 1) 至 60-66份每日兩次 (n = 3) 進行；總劑量為60至79.2 Gy。患者隨訪期為13個月至9.5年。3名接受手術和術後放療的患者實現了無病局部控制。僅接受放療治療的患者3個月後出現復發，最終因病情惡化死亡。沒有患者發生嚴重急性或晚期治療相關中毒。

結論：術後放療可改善陽性或近切緣PLGA的局部控制。

INTRODUCTION

Polymorphous low-grade adenocarcinoma (PLGA) is a rare, slow-growing, malignant epithelial tumour of the salivary gland that typically occurs in the oral cavity, particularly the hard palate. It is distinguished from other adenocarcinomas of salivary gland origin.^{1,2} Its tumour cells are characterised by infiltrative borders with highly variable growth patterns that include tubular, solid, cribriform, trabecular, fascicular, and papillary-cystic formations. This multicomponent histology makes PLGA difficult to distinguish from pleomorphic adenomas and adenoid cystic carcinomas.^{3,4}

Standard of care is wide local excision. PLGA has a low risk of regional node or distant metastases so elective neck dissection is usually not performed.^{5,6} Adjuvant radiotherapy (RT) is indicated in patients with positive margins or high-risk features such as nerve invasion. Primary RT is preferred in inoperable patients because of tumour size or medical co-morbidities.⁷ PLGA usually presents as an indolent asymptomatic growth with low malignant potential; RT doses range from 66 Gy for microscopic disease to 70 Gy for gross residual disease.⁸ We reviewed the clinical course and outcome of patients who underwent RT for PLGA of the head and neck.

METHODS

This study was approved by the institutional review board of our hospital and conducted in compliance with Declaration of Helsinki. We retrospectively reviewed medical records of patients who underwent RT for PLGA of the head and neck at our institution between June 1993 and March 2013.

RESULTS

Two men and two women aged 43 to 76 years who underwent primary (n = 1) or postoperative (n = 3) RT for PLGA of the oropharynx (soft palate; n = 2) or oral cavity (hard palate; n = 2) were reviewed (Table). No patient had regional lymph node involvement or distant metastasis at the time of diagnosis.

Three patients underwent resection: one had close margins, one had microscopically positive margins, and the other had negative margins but perineural invasion. One patient with a hard palate tumour involving the pterygoid plate underwent RT alone (79.2 Gy, 66 fractions twice daily) because the lesion was thought to be not completely resectable due to its size and location. Intensity-modulated RT (n = 2) or 3-dimensional RT (n = 2) was performed with dose ranging from 60 to 79.2 Gy in 30 fractions once daily (n = 1) to 60-66 fractions twice daily (n = 3).

Patients were followed up every 2 to 3 months for the first 2 years, every 4 months for the third year, every 6 months for the fourth and fifth years, and yearly thereafter. Chest radiography was taken annually. Computed tomography was taken when physical examination showed suspicious findings. Local control was defined as no evidence of disease at the primary site.

Patients were followed up for 13 months to 9.5 years; none was lost to follow-up. Disease-free local control was achieved in the three patients treated with both surgery and postoperative RT. The patient treated with RT alone had recurrence at level 2 lymph nodes at 3 months, and then at the nasal lacrimal duct extending into the medial canthus and the right orbit at 6 months, and then at the 11th rib at 11 months. The patient received supportive care and subsequently died of disease progression. No patient developed severe acute or late treatment-related toxicity.

DISCUSSION

Wide local excision is the preferred treatment for PLGA.⁶ Patients with negative or even close margins and no adverse features should be followed up regularly as local recurrence may take years to develop.⁵ Lymph node metastasis is unlikely and thus elective neck dissection is unnecessary.

In a retrospective study of 460 patients, margin-free

Table. Patient characteristics and outcome.

Sex / age, y	Tumour site	Surgery	Resection margin	Radiotherapy	Outcome
M / 76	Soft palate	Wide local excision	Close, 1 mm	72.4 Gy, 60 fractions twice daily	No evidence of disease after 4.5 years
F / 72	Soft palate	Wide local excision	Positive	70 Gy, 60 fractions twice daily	No evidence of disease after 2 years
F / 43	Hard palate	Maxillectomy	Negative	60 Gy, 30 fractions once daily	No evidence of disease after 9.5 years
M / 59	Hard palate	None	–	79.2 Gy, 66 fractions twice daily	Dead with disease after 1.1 years

surgery correlated with a 10-year overall survival rate of 98%.⁷ The overall survival rate was higher in patients with surgery followed by postoperative RT (94%) and surgery alone (92%), compared with RT alone (75%).⁷ Although negative margins following resection is the best prognostic factor, a non-morbid surgery is not always feasible because of the location and extent of the tumour.^{7,9,10}

The role of RT in treatment of PLGA remains unclear.^{7,11} Patients with positive margins, high-risk features, or inoperable tumours are usually referred for RT.⁷ In a study of 40 patients with PLGA followed up for a minimum of 10 years, those who underwent surgery with positive or unknown margins followed by postoperative RT had fewer recurrences, with a local control rate of 100% after 10 years.⁴ In a study of 164 patients with PLGA, 15 of 17 patients treated with postoperative RT had no evidence of disease.¹¹ Those treated with RT alone had an increased rate of recurrence but a comparable survival rate compared with those treated with surgery alone.¹¹ Nonetheless, there may have been selection bias favouring the surgery-alone group. Two patients declined surgery, and it is unclear why other patients underwent RT alone.¹¹

In our patient treated with RT alone (79.2 Gy in 66 fractions twice daily), hyperfractionation was used as it has been used for squamous cell carcinomas of the head and neck.^{12,13} The short disease-free interval and both regional and distant recurrences suggest that the tumour was a biologically more aggressive malignancy despite histologically consistent with a PLGA.

CONCLUSION

Postoperative RT may improve local control of PLGA in patients with close or positive margins after surgery.

REFERENCES

1. Freedman PD, Lumerman H. Lobular carcinoma of intraoral minor salivary gland origin. Report of twelve cases. *Oral Surg Oral Med Oral Pathol.* 1983;56:157-66. [cross ref](#)
2. Evans HL, Batsakis JG. Polymorphous low-grade adenocarcinoma of minor salivary glands. A study of 14 cases of a distinctive neoplasm. *Cancer.* 1984;53:935-42. [cross ref](#)
3. de Araujo VC, Passador-Santos F, Turssi C, Soares AB, de Araujo NS. Polymorphous low-grade adenocarcinoma: an analysis of epidemiological studies and hints for pathologists. *Diagn Pathol.* 2013;8:6. [cross ref](#)
4. Evans HL, Luna MA. Polymorphous low-grade adenocarcinoma: a study of 40 cases with long-term follow up and an evaluation of the importance of papillary areas. *Am J Surg Pathol.* 2000;24:1319-28. [cross ref](#)
5. Pogodzinski MS, Sabri AN, Lewis JE, Olsen KD. Retrospective study and review of polymorphous low-grade adenocarcinoma. *Laryngoscope.* 2006;116:2145-9. [cross ref](#)
6. Paleri V, Robinson M, Bradley P. Polymorphous low-grade adenocarcinoma of the head and neck. *Curr Opin Otolaryngol Head Neck Surg.* 2008;16:163-9. [cross ref](#)
7. Patel TD, Vazquez A, Marchiano E, Park RC, Baredes S, Eloy JA. Polymorphous low-grade adenocarcinoma of the head and neck: a population-based study of 460 cases. *Laryngoscope.* 2015;125:1644-9. [cross ref](#)
8. Verma V, Mendenhall WM, Werning JW. Polymorphous low-grade adenocarcinoma of the head and neck. *Am J Clin Oncol.* 2014;37:624-6. [cross ref](#)
9. Abu El-Naaj I, Leiser Y, Wolff A, Peled M. Polymorphous low grade adenocarcinoma: case series and review of surgical management. *J Oral Maxillofac Surg.* 2011;69:1967-72. [cross ref](#)
10. Seethala RR, Johnson JT, Barnes EL, Myers EN. Polymorphous low-grade adenocarcinoma: the University of Pittsburgh experience. *Arch Otolaryngol Head Neck Surg.* 2010;136:385-92. [cross ref](#)
11. Castle JT, Thompson LD, Frommelt RA, Wenig BM, Kessler HP. Polymorphous low grade adenocarcinoma: a clinicopathologic study of 164 cases. *Cancer.* 1999;86:207-19. [cross ref](#)
12. Mendenhall WM, Riggs CE, Vaysberg M, Amdur RJ, Werning JW. Altered fractionation and adjuvant chemotherapy for head and neck squamous cell carcinoma. *Head Neck.* 2010;32:939-45. [cross ref](#)
13. Beitler JJ, Zhang Q, Fu KK, Trotti A, Spencer SA, Jones CU, et al. Final results of local-regional control and late toxicity of RTOG 9003: a randomized trial of altered fractionation radiation for locally advanced head and neck cancer. *Int J Radiat Oncol Biol Phys.* 2014;89:13-20. [cross ref](#)