

Case Report

Our experience with topical 5 fluoro uracil in sinonasal neoplasia

Shaoni Dhole Sanyal*, Debashish Biswas, Ranjan Raychowdhury

Department of ENT Head and Neck Surgery, Vivekananda Institute of Medical Sciences, Kolkata, India

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***Correspondence:**

Dr. Shaoni Dhole Sanyal,

E-mail: shaoni.sanyal@gmail.com

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ABSTRACT

Sino-nasal neoplasms account for 3% of all head and neck cancers. Adenocarcinoma of the paranasal sinuses accounts for 9% of all sino-nasal malignancies and is the most common malignancy of the ethmoid sinus. Other neoplasms which involve the ethmoidal sinuses include inverted papilloma and squamous cell carcinoma. Traditionally, the treatment of choice for an adenocarcinoma of the ethmoidal sinuses involved craniofacial resection. This procedure is related with high rates of mortality and morbidity. Knegt et al reported greater success, both in terms of clinical outcome and survival data, with a less aggressive surgical approach coupled with repeated topical 5 fluorouracil (5FU) applications as a chemotherapeutic agent. Over the last 10 years we have treated selected cases of sinonasal neoplasia with a protocol similar to Knegt. Two (adenocarcinoma and inverted papilloma) of our four cases remain well and are on follow-up. The other two (undifferentiated carcinoma) were lost to follow-up. The rarity of sino-nasal neoplasms make them an unlikely subject for a randomised control trial. With that in mind surgical debridement and topical 5 fluorouracil seems to offer an acceptable treatment for adenocarcinoma of the sinonasal tract in properly selected cases. It may also have a role in Squamous cell carcinoma of ethmoidal or maxillary sinus and in preventing recurrence of inverted papilloma.

Keywords: Fluorouracil, Paranasal sinus, Adenocarcinoma, Inverted papilloma, Squamous cell carcinoma

INTRODUCTION

Sinonasal neoplasms account for 3% of all head and neck cancers. Adenocarcinoma of the paranasal sinuses accounts for 9% of all sinonasal malignancies and is the most common malignancy of the ethmoid sinus.¹ The craniofacial approach, first described by Smith et al was adopted in the 1980s for the clearance of anterior skull base malignancy.² However, survival rates for ethmoid adenocarcinoma have not improved significantly.³

Knegt et al reported greater success, both in terms of clinical outcome and survival data, with a less aggressive surgical approach coupled with repeated topical 5 fluorouracil (5FU) applications as a chemotherapeutic agent.^{4,5}

Inverted papilloma (IP) is a relatively uncommon benign epithelial tumour of the nasal cavity and sinus that is locally aggressive, tends to recur (12%-20%), and is associated with squamous cell carcinoma (SCC) (3%-7%).⁵ It is treated primarily by surgery with a reported recurrence rate of 17-50%.⁶ Recently topical 5-FU has been used as an adjunct to reduce recurrence.⁶

CASE REPORT

Following tumour excision, 0.5% 5 FU cream is instilled in the cavity which is then packed with cream-soaked ribbon gauze brought out nasally. The pack is replaced every two weeks endoscopically. At 12 weeks any suspicious tissue is sent for histopathological examination.

Case 1

A 58-year-old female patient presented with a one-year history of left nasal obstruction and occasional epistaxis, associated with mild headache and left-sided orbital pain for 3 months. There were no other co-morbidities.

Clinically a firm reddish mass was seen in the left nasal cavity, extending into nasopharynx on posterior rhinoscopy. There were no palpable neck nodes. On diagnostic nasal endoscopy the mass was non tender, did not bleed and extended from the middle meatus.

A contrast enhanced CT scan revealed a heterogenous opacification involving the left nasal cavity, left maxillary sinus, anterior and posterior ethmoids. There was no erosion of lamina papyracea or skull base. (Figure 1).

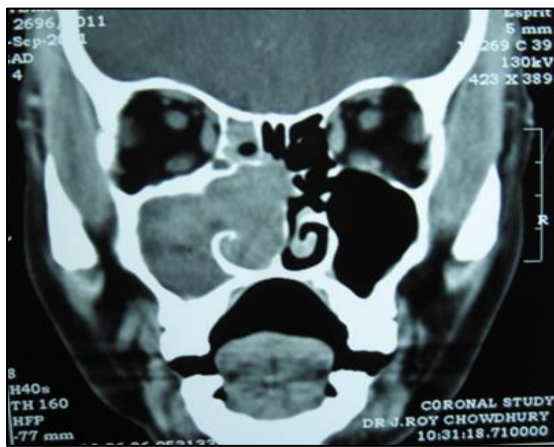


Figure 1: Contrast enhanced coronal and axial scans showing extent of the neoplasm.

A biopsy established the histopathological diagnosis of grade II intestinal-type adenocarcinoma. It was staged T3N0M0.

The patient underwent left medial maxillectomy by a lateral rhinotomy approach with topical 5FU as per our protocol. (Figure 2, 3, 4)

At 12 weeks there was a well epithelialized cavity with no evidence of recurrence on mucosal biopsy. The patient remains on follow up after 8 years.

Case 2

A 65 years old male patient presented with an established diagnosis of undifferentiated cancer of the left ethmoidal air sinus (T3N0M0). The patient refused consent for orbital exenteration, so underwent endoscopic assisted revision medial maxillectomy. The disease could not be cleared from the left periorbital; a 5 FU pack was placed in situ. The pack was changed three times over six weeks until commencement of radiotherapy. The patient developed nasopharyngeal recurrence 8 months later; he

was referred to oncology and subsequently lost to follow-up.



Figure 2: Lateral rhinotomy performed.



Figure 3: Tumour excised.

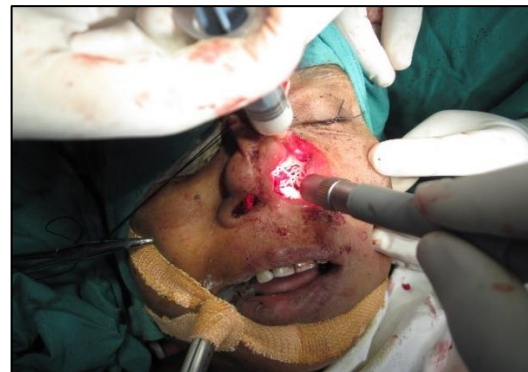


Figure 4: Application of 5-FU.

Case 3

A 65 years male patient presented with right sided nasal obstruction, intermittent epistaxis and occasional retro-orbital pain for 2 months. Biopsy suggested undifferentiated SCC of right maxillary sinus (T3N0M0). An endoscopic medial maxillectomy was performed along with topical 5FU packing as per protocol. At 10 weeks, mucosal biopsy showed recurrence and the patient was referred for chemo-radiotherapy.

Case 4

A 38 years old female patient with a large right sided nasal mass underwent debulking biopsy which diagnosed Inverting papilloma. She was lost to follow up. After 2 years, she returned with a large recurrence and underwent right medial maxillectomy by lateral rhinotomy approach. The disease recurred twice more over the next 4 years. At her third recurrence endoscopic excision was performed with topical 5 FU as per our protocol. She has been disease free for the last five years.

DISCUSSION

Traditionally adenocarcinoma of the sinuses has been treated by surgical clearance followed by external beam radiotherapy or chemoradiotherapy. The surgical approaches include anterior craniofacial resection or extended/total maxillectomy which have significant complications and post-operative morbidity.

Lund et al reported 42 patients treated by craniofacial resection with 5 and 10-year survival of 43% and 38% respectively.⁷

Shah et al reported a 5 and 10-year survival of 57% and 29% respectively.⁸

In a retrospective multicenter French study, 418 patients with ethmoid adenocarcinoma underwent surgical resection followed by radiotherapy with a 5-year survival rate of 64%.¹

Topical 5-FU was used by Knecht et al in 1985, in a series of patients with squamous cell (61%) and undifferentiated carcinoma (37%).⁴ In 2001, they reported the use of topical 5-FU in 62 patients with T3/T4 adenocarcinoma of ethmoids after surgical debulking by medial maxillectomy and sphenoidectomy. Recurrence (8 patients) was treated with repeated application of 5-FU and radiotherapy. Disease free survival in the 2nd, 5th and 10th post-operative years were 96%, 87% and 74% respectively.⁵

Almeida and Capper identified two treatment cohorts: one from 1986 to mid-1996 (n=18), the other from mid-1996 to 2006 (n = 13). The first group received primary radiotherapy and subsequent craniofacial resection as necessary. The second group underwent tumour exenteration with topical 5FU application. Of the 14 patients who were treated primarily using radiotherapy, seven died of the disease and seven died of other causes, being disease-free up to the time of death. Of the 11 patients treated with surgical debulking and topical 5FU, one died of the disease and four died of other causes, being disease-free up to the time of death. The remaining six patients remained alive and well.⁹

Adriaensen et al published their retrospective study of 121 cases of inverted papilloma (72 revision and 49 primary).

5-fluorouracil was applied postoperatively in 18 (5 primary and 13 revision) cases when it was difficult to be sure that all diseased mucoperichondrium or mucoperiosteum had been completely removed. The recurrence rate was 4.1% for primary cases, 18.1% for revision cases and 5.6% after topical 5 FU use. One patient had transient periorbital swelling. None had any major complications.⁶

Singh et al in 2018 reported application of topical 5-FU by frontal trephination for complete coverage of the frontal region of the anterior skull base in a 37-year-old man with T2N0M0 ethmoid adenocarcinoma. The procedure was well tolerated in an outpatient setting and the patient was disease free 3 years postoperatively.¹⁰

In our series, we had patients with adenocarcinoma, squamous cell cancer and undifferentiated cancer of the paranasal sinuses and one patient with recurrent inverting papilloma. The patient suffering from adenocarcinoma was treated with 5 FU as its effectiveness had already been established. Both patients with squamous cell cancer and undifferentiated cancer were unable to arrange early RT, hence 5 FU packs were used in an attempt to control local disease. The patient with recurrent inverted papilloma was treated with topical application of 5 FU after we heard of Adriaensen's results.

CONCLUSION

The rarity of sino-nasal neoplasms make them an unlikely subject for a randomised control trial. With that in mind surgical debridement and topical 5 fluorouracil seems to offer an acceptable treatment for adenocarcinoma of the sinonasal tract in properly selected cases. It may also have a role in Squamous cell carcinoma of ethmoidal or maxillary sinus and in preventing recurrence of inverted papilloma.

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