

Novel Use of Autologous Fat Stem Cell Injections in Skull Base Osteoradionecrosis

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Abstract

Osteoradionecrosis (ORN) is a challenging complication after radiation therapy (RT) to the nasopharynx and skull base. Adipose-derived stem cells (ADSCs) have recently been suggested to improve wound healing due to radiation necrosis.

Methods:

We report two cases of ORN of the nasopharyngeal region treated with ADSC injections to the surrounding wound. The first patient had a clival chordoma managed with endoscopic surgical resection and post-operative stereotactic body radiation. The second patient had salvage reirradiation for recurrent nasopharyngeal carcinoma.

Results:

Both patients underwent endoscopically assisted injections, but the thin surrounding tissue limited the injection. Successful implantation and tissue regrowth occurring over months around the injection sites were identified. The patient with nasopharynx cancer underwent a second injection after the encouraging results of the first injection.

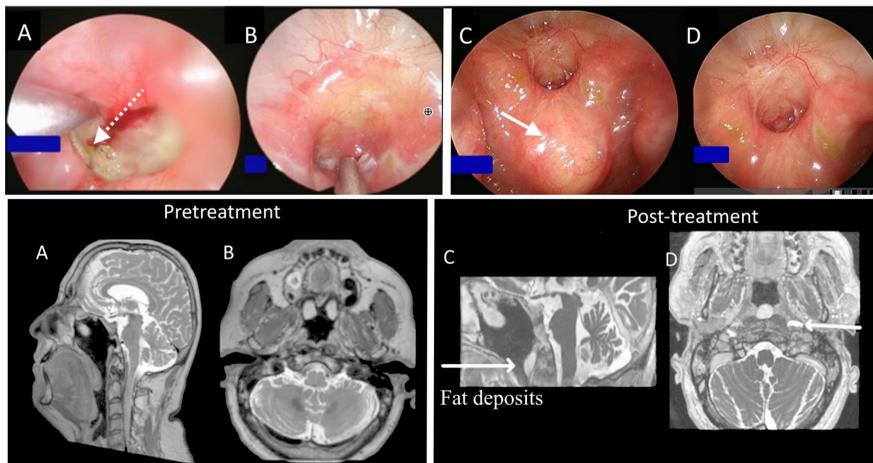
Conclusion:

This is the first case report to our knowledge of ADSCs injections in the tissue bed of the nasopharyngeal skull base for management of ORN. Wound healing was observed, but more experience is necessary to understand the long-term benefits of ADSCs injections.

Methods and Materials

Two patients with progressive skull base ORN refractory to conventional management underwent endoscopic evaluation and debridement followed by autologous fat harvest via liposuction. Harvested fat was processed and transferred into small syringes for endoscopic delivery. ADSCs were injected into surrounding irradiated soft tissue under endoscopic guidance, with attention to minimizing spillage and avoiding critical structures. Outcomes were assessed by serial endoscopy, imaging, culture and pathology results when obtained, and clinical symptom monitoring over follow up.

Patient 1: Pre and Post Treatment



Patient 1: Endoscopy reveals exposed bone eroding into clivus (A) oriented in inferior clivus (B). C demonstrates the injected fat pad (arrow) and mucosalization of the defect in clivus (D). **MRI** imaging shows fat injection anterior to the odontoid and lateral into prevertebral space (arrows).

Results

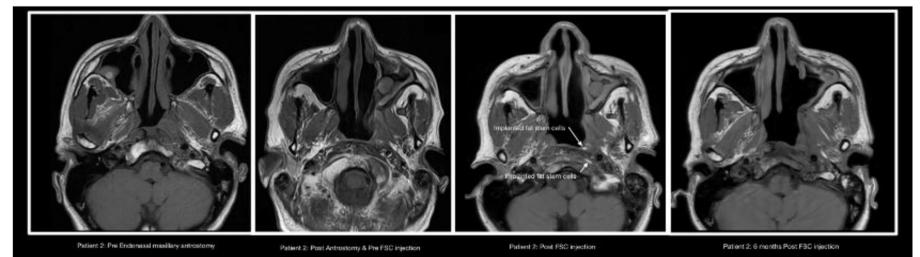
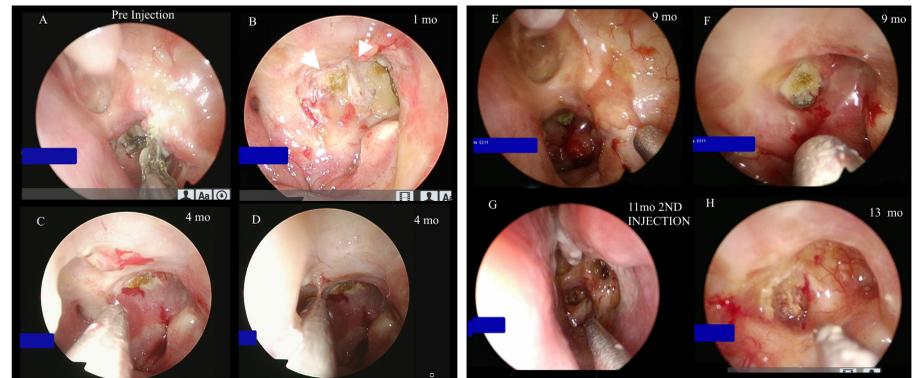
Case 1 (Clival chordoma): A 60-year-old male underwent endonasal resection with flap reconstruction followed by stereotactic body radiation therapy (40 Gy in 5 fractions). Five years later he developed progressive clival ORN with exposed bone and diplopia despite antibiotics and medical therapy. After surgical debridement, ADSCs were injected endoscopically into prevertebral musculature and adjacent tissue, and an inferior turbinate flap was used for coverage. At follow up, ADSC injection sites appeared viable with granulation tissue and a marked reduction in exposed bone from an initial 1 cm defect to approximately 2 mm at six months, with subsequent debridement revealing underlying mucosalized tissue.

Case 2 (Recurrent nasopharyngeal carcinoma): A 54-year-old male old male was treated with two rounds of chemo radiation (IMRT, Proton therapy) for EBV+ nasopharyngeal carcinoma. 1 year after reirradiation he developed progressive osteoradionecrosis treated with multiple course of antibiotics (oral and intravenous), PENTOCLO, and hyperbaric oxygen over the next year. He developed seizures from temporal lobe necrosis. He was treated medically and then with surgical debridement of the temporal lobe. Nasopharyngeal symptoms of ORN continued over the next 2.5 years treated with surgical debridement with local flap, a second round of hyperbaric oxygen, and multiple courses of antibiotics managed by infectious disease consultant. At about 4 years after reirradiation and 4 months after the second course of HBO, due to recurrent progression around the region of foramen lacerum he was considered for a free flap and offered ADSC injection. Over the course of the following year after injection, the wound demonstrated evidence of improved healing. A demarcation of the bone around the clivus, and he was taken for a repeat debridement and second ADSC injection was given after 13 months and the wound has nearly completely mucosalized 2 months later after while still on antibiotics.

Introduction

ORN is a late complication of radiation therapy characterized by chronic, non healing necrosis of irradiated bone and surrounding soft tissue. Skull base ORN is especially difficult to treat due to limited vascularized tissue, complex anatomy, and proximity to critical neurovascular structures. Current approaches include antibiotics and irrigations, medical therapy such as pentoxifylline and tocopherol with or without clodronate, hyperbaric oxygen, repeated debridement, and reconstructive surgery, yet progression may persist and morbidity can be high. Regenerative therapies such as ADSCs may promote angiogenesis and tissue repair and represent a potential adjunct for refractory skull base ORN

Patient 2: Endoscopy Progression



Patient 2 Pre Treatment A-D: A) initial defect after hyperbaric oxygen. B) the ulcer recurred and progressed; this is 1 month after first injection showing ulceration into parapharyngeal space lining the petrous course of the carotid with chronic fibrinous ulceration, muscular necrosis and exposed bone near lacerum. C) is 4 mo after injection with new mucosa on the choanae, but fibrosis along petrous bone and lacerum. D) shows the choanae, a chronic source of ulceration and bleeding is now completely mucosalized. **Post Treatment E-H:** E) shows the pterygoid region and choana mucosalized. F) shows new granulation tissue in the parapharyngeal ulcer and mixture of mucosa and granulation in the nasopharynx, but persistent demarcated bone in the clivus. G) 1 month after second injection granulation is replaced by mucosa in all regions. H) shows the debrided bone in the clivus is now predominately mucosalized along with the entire defect into the parapharyngeal space. **Second Panel, MRI** Shows the presence of new fatty deposits after injection.

Discussion

These cases demonstrate feasibility of endoscopic ADSC delivery for skull base ORN and suggest potential for improved mucosal healing and stabilization of progressive disease. Both patients showed evidence of ADSC survival and local tissue regeneration over time. Delivery was constrained by limited supporting tissue in the irradiated skull base, particularly near the carotid artery and deeper bony defects. Skull base ORN can arise not only after nasopharyngeal carcinoma treatment but also after radiation for chordoma, emphasizing the need for strategies applicable across skull base tumor types. While existing data on oncologic safety of fat grafting is reassuring, further work is needed to clarify optimal technique, patient selection, and durability of benefit in the skull base

Conclusions

Autologous ADSC therapy is a potential novel adjunct for skull base ORN when conventional options are limited. In two refractory cases, ADSC injection was feasible and associated with improved mucosal healing and reduced exposed bone, though complete resolution was not yet achieved and technical constraints limited delivery to the deepest areas. Larger studies with standardized protocols and longer follow up are needed to define long term outcomes and optimal integration into multidisciplinary ORN management

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