Nasopharyngeal Carcinoma: Case Presentation and Literature Review of Treatment Innovation with Immunotherapy

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Abstract:
Nasopharyngeal carcinoma (NPC), a rare head and neck malignancy arises from the epithelial lining of nasopharyngeal mucosa. The confluence of various risk factors: latent Epstein-Barr Virus (EBV) infection, genetic susceptibility, smoking, alcohol consumption and high nitrosamine) diet is thought to contribute to NPC pathogenesis. Radiation therapy serves as the mainstay of treatment for early-stage while concurrent chemotherapy and radiation are the basis of treatment for locoregional advanced disease with overall 80% 5-year survival rate. Recurrent or metastatic disease pose treatment challenges as re-irradiation, repeat cycles of chemotherapy and surgery follow with high likelihood of treatment toxicity or postoperative morbidities. Typically reserved for nonresectable recurrent or metastatic disease, immunotherapy serves as novel treatment for NPC. NPC tumor microenvironment predominated by a dense infiltrate of immune cells hosts an ideal target for immunotherapy. Several clinical trials have investigated the efficacy of anti-PD-1 antibodies such as pembrolizumab, nivolumab, and camrelizumab with promising results. Treatment of recurrent and metastatic NPC remains a challenge; however, the advent of immunotherapy has provided additional options and potential for preventative and therapeutic measures.

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Nasopharyngeal Carcinoma: Case Presentation and Literature Review of Treatment Innovation with Immunotherapy

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Case Presentation
A 60-year-old female presented with T2N0M0 non-keratinizing Epstein Barr Virus (EBV) negative squamous cell carcinoma of the left nasopharynx (NPC). She underwent 6 weeks of chemoradiation with cisplatin. Post treatment PET/CT illustrated cervical lymphadenopathy and persistent disease in the nasopharynx (Image 1). Biopsy of cervical nodal uptake confirmed persistent disease. Thus, left neck dissection was performed. She was then referred to our center for endoscopic endonasal resection and craniotomy with carotid resection/bypass. Surgical margins were negative. However, 7-month post-treatment PET/CT illustrated residual disease, which was confirmed on biopsy (Image 2). She started pembrolizumab and experienced interval improvement over the course of 8 months. She then completed 4 cycles of gemcitabine/cisplatin. Due to persistent disease, she continued pembrolizumab and started capecitabine as well. Given disease progression, lenvatinib was added in lieu of capecitabine. She remains on pembrolizumab and lenvatinib three years since initial diagnosis with stable disease.

Literature Review
Radiation therapy serves as the mainstay of treatment for NPC in early-stage disease while concurrent chemoradiation is the basis for locoregional advanced disease with 80% 5-year survival rate.¹⁻⁶ Approximately 15% of patients experience recurrent or metastatic
disease. Locoregional recurrence may prompt surgical intervention. Recurrence or metastasis pose treatment challenges as re-irradiation, repeat chemotherapy and surgery are associated with treatment toxicity and morbidity.

Immunotherapy is reserved for nonresectable recurrent or metastatic disease. Current strategies include immune checkpoint inhibitors, EBV-directed vaccination, and adoptive T-cell therapy.

The immunosuppressive NPC tumor microenvironment boasts an overexpression of inhibitory immune checkpoints, an ideal target for immune checkpoint inhibitors (ICIs). Clinical trials have investigated the efficacy of anti-PD-1 antibodies such as pembrolizumab, nivolumab, and camrelizumab with promising results. KEYNOTE-028 trial investigated the efficacy of pembrolizumab in unresectable recurrences -revealing a 26% objective response rate (ORR) and 33% 1-year progression free survival (PFS). However, the KEYNOTE-122, phase III trial illustrated that pembrolizumab did not improve PFS or ORR compared to chemotherapy. A phase II trial assessing nivolumab response in recurrent or metastatic NPC noted a 20% ORR with 59% 1-year overall survival (OS). Two single-arm phase I trials evaluated camrelizumab as 1) monotherapy in recurrence or metastasis with a 34% ORR and 27% 1-year PFS and 2) combined with gemcitabine/cisplatin (GP) in patients with recurrence or metastasis disease yielding a 91% ORR and 61% PFS. JUPITER-02 trial assessed the efficacy of toripalimab combined with GP versus placebo and GP, revealing 49.4% of patients in the combination arm experienced PFS, compared to 27.9% in the control arm. A meta-analysis of ICIs noted 27% ORR and 61% OS.
EBV-directed vaccination offers preventative and therapeutic strategies against infection with EBV, a key contributor to the pathogenesis of NPC. Previous clinical trials investigated peptide and viral vaccines by targeting EBV glycoproteins: gH/gL and gB, membrane proteins critical for epithelial cell infection, and virus like proteins target antigens such as LMP1 or LMP2, key drivers in malignant transformation of EBV infected cells. A phase I trial noted partial clinical response in advanced-EBV associated NPC.

Ultimately, treatment of recurrent or metastatic NPC remains complex and requires a multifaceted approach. The advent of immunotherapy, primarily anti-PD1 antibodies, as novel treatment for recurrent or metastatic NPC has provided an additional treatment option. Although clinical trials have illustrated promising results, long term follow up studies are necessary.

References


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Image 1: MRI imaging throughout treatment course: pre-surgical, post-surgical, 3 months post-surgery, and 6 months post-surgery.

A. Pre-Surgical MRI  
B. Post operative MRI  
C. 3 months post operative MRI  
D. 6 months post operative MRI illustrating recurrence in the left nasopharynx

Image 2: PET/CT scan imaging illustrating recurrence post-surgery and immunotherapy treatment response.

A. PET/CT illustrating recurrence post-surgery  
B. 6 months PET/CT illustrating complete response to Pembrolizumab