Proton therapy for sinonasal cancer

Session: Head and Neck  
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Background

- Sinonasal cancers are rare, affecting less than 1 in 100,000 people.
- In addition, cancers that arise in the sinonasal regions can be a variety of histologies, including squamous cell carcinoma, esthesioneuroblastoma, adenoid cystic carcinoma, melanoma, and others (1).
- The rarity, heterogeneity and anatomic complexity of the disease has made it difficult to make generalized treatment recommendations. Nonetheless, surgery is the primary treatment modality.
- However, many of these tumors occur near sensitive anatomic structures (e.g. central nervous system, eye and visual pathways) rendering surgery challenging.
- Thus, patients often undergo either postoperative or definitive radiation therapy to control the complications of local disease extension.
- Advances in photon (or x-ray) based radiation therapy have allowed physicians to deliver higher doses of radiation therapy while sparing important normal tissues.
- Proton beam therapy, a form of charged particle therapy, is another way to deliver radiation while sparing normal tissues (2).
- The advantage of proton beam therapy is that it does not deposit radiation dose beyond a certain depth in the body, which allows for complete sparing of normal tissues.
- In a systematic review and meta-analysis published in 2014, researchers found that charged particle therapy (e.g. proton therapy and carbon ion therapy) may allow for better disease control than photon (or x-ray) therapy. (3).

Study Objectives and Methods

- Researchers at the University of Florida Health Proton Therapy Institute reviewed their experience treating patients with sinonasal cancers with proton beam therapy.
- The goal of the study was to estimate the clinical outcomes and toxicities of proton therapy for these malignancies.

Patient Characteristics

- The study examined 84 adults with sinonasal cancers treated with proton therapy.
- The majority of patients were treated with proton therapy as adjuvant therapy after surgery (87%), but some were treated with proton therapy as definitive therapy (13%).
- Histologies of these cancers included olfactory neuroblastoma (23%), squamous cell carcinoma (22%) and adenoid cystic carcinoma (17%), but did not include melanoma, sarcoma or lymphoma.
- Majority of tumors arose from the nasal cavity and ethmoid sinuses.
- Ninety-four percent (94%) of patients had locally advanced disease (T3-T4), and over half had high-grade pathology (grade 3).
- Even though 87% of patients had surgery, 26% of patients had gross disease at the time of proton therapy.
Treatment Details

- For patients that underwent surgery, the majority were endoscopic resections.
- In addition, 88% of surgical patients had a gross total resection of their disease, but only 17% were documented as margin negative on pathology.
- Patients were treated to a median dose of 73.8 Gy using 1.2 Gy treatments twice daily.
- The majority of patients (75%) also received chemotherapy.

Results

- Median follow-up was 2.4 years
- 3-yr survival was 68% in this populations
- After 3 years, 83% of patients had local control of their disease (no recurrence in area treated with proton therapy).
- The local control was even higher (90%) in patients that had complete surgical resection of their tumor.
- Twelve of 84 patients had local disease recurrence, and six of these occurred at the edge of the radiation field.
- However, a significant proportion of patients had disease recurrence outside of the locally treated region (3-year disease free survival was 63%), including leptominengeval spread.
- In addition, grade 3 or higher toxicities were observed in 24% of patients.
- Toxicities included a 2% rate of grade 3 vision loss, 5% rate of radiation necrosis of the brain, and 4% rate of treatment-related death.
- The most important predictor for survival was the presence or absence of visible disease at the time of radiation. Patients who had all their visible disease removed by surgery had better survival.

Authors’ conclusions

- The authors conclude that the use of twice daily (hyperfractionated) proton therapy with or without concurrent chemotherapy, mostly in patients who have undergone surgery, is a feasible approach for sinonasal cancer, with local control rates above 80%.

Clinical implications

- In the absence of larger prospective studies, which are difficult to do for rare, heterogeneous diseases like sinonasal cancer, the study provides important data on outcomes and toxicity.
- While the study demonstrates the potential of proton therapy, the rare but serious toxicities highlight the ongoing challenge of treating locally advanced lesions that are adjacent to critical structures.
- In addition, the rate of recurrences at the edge of the radiation treatment field remains an issue, as does the rate of disease spread outside the radiation field.