Successful Treatment of Recurrent Metastatic Nasopharyngeal Carcinoma With Oxaliplatin and Doxorubicin

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Summary: Nasopharyngeal carcinoma (NPC) is a rare tumor in children and often presents as advanced-stage disease. NPC in children is treated with neoadjuvant chemotherapy and radiotherapy. The prognosis for children who relapse after treatment is extremely poor. This report describes the successful treatment and long-term disease-free survival of a 16-year-old male patient with a history of stage IVA NPC, who recurred with pulmonary and hepatic metastases. The patient was treated with a novel combination of oxaliplatin and doxorubicin without irradiation.

Key Words: nasopharyngeal carcinoma, relapse, metastases, oxaliplatin, doxorubicin

Nasopharyngeal carcinoma (NPC) is a rare tumor in children associated with Epstein-Barr virus (EBV) infection. NPC accounts for approximately 1% of pediatric cancers. Most patients with childhood NPC have undifferentiated histology (WHO type III) and present with locoregionally advanced disease. Pediatric and adolescent patients are treated based on adult regimens. Radiotherapy is the principal mode of treatment. The addition of chemotherapy has been shown to improve survival in patients with locally advanced NPC. Combined modality therapy with chemotherapy and radiation is currently the standard of care in pediatric patients diagnosed with NPC. Approximately 20% to 50% of patients with NPC will have recurrent or metastatic disease. For patients who relapse with distant metastases the prognosis is poor, with reported median survival times ranging from 5 to 11 months.

Herein, we report successful treatment of an adolescent with recurrent metastatic NPC using oxaliplatin and doxorubicin without radiotherapy (RT).

CASE REPORT

A 16-year-old African American male patient presented with a 3-month history of jaw pain, nasal congestion, epistaxis, weight loss, and decreased hearing in his right ear. Physical examination revealed trismus and bilateral cervical lymphadenopathy. Magnetic resonance imaging of the head and neck revealed a large 5 × 5 cm mass in the right pterygoplatine fossa, extending into the nasopharynx, right orbit, and middle cranial fossa. A biopsy of the mass confirmed the diagnosis of undifferentiated NPC. Computed tomography scan of the chest, abdomen, and the pelvis, whole body technetium bone scan, and cerebrospinal fluid examination excluded the presence of metastatic disease. American Joint Committee on Cancer (AJCC) staging at diagnosis was T4N2M0 (stage IVA). EBV serology and EBV-encoded RNA staining of the tumor tissue were positive at diagnosis. He was treated with 5 cycles of neoadjuvant vinblastine, bleomycin, cisplatin, and methotrexate, followed by 70.2 Gy of RT to the prechemotherapy tumor volume and bilateral cervical lymph nodes. Magnetic resonance imaging of the neck at the end of the treatment revealed a small residual nonenhancing mass in the nasopharynx with no cervical lymphadenopathy.

Four months after the end of the treatment, the patient presented with bilateral wrist pain reminiscent of hypertrophic osteoarthropathy. Disease evaluation radiographic studies revealed a stable, residual nasopharyngeal mass, new bilateral lung nodules, and a solitary liver nodule. The patient received a total of 8 cycles of chemotherapy, which was the maximum allowed by the protocol. He tolerated this chemotherapy combination well, and uncomplicated grade 3 neutropenia and thrombocytopenia were the main side effects. Computed tomography scans at the end of the therapy revealed complete resolution of all metastatic lesions in the lung (Fig. 1C) and the liver (Fig. 1D). The patient remains in second continuous remission 6 years after the completion of therapy with grade 2 ototoxicity and minimal xerostomia related to his primary treatment. Radiation therapy was not used in the treatment of his disease recurrence.

DISCUSSION

Patients younger than 20 years of age account for approximately 2% to 3% of all NPC patients and the majority have undifferentiated histology. Despite improvements in chemotherapy and RT, 20% to 30% of patients with NPC will have recurrent disease. Most recurrences occur within 2 years of diagnosis, and the majority present with distant metastases. For patients who relapse with distant metastases, RT is usually not feasible because of organ toxicity threshold limits and treatment is attempted with chemotherapy alone. Patients who are not exposed to cisplatin at initial diagnosis are usually treated with cisplatin-based chemotherapy at relapse. Various combinations of chemotherapy have been tried in adults with recurrent NPC. Some responses were observed with reported median survival of 12 to 18 months and with a median time to progression of 5 to 10 months. There have been isolated reports of long-term remissions achieved in these patients by chemotherapy alone, mainly in patients not previously exposed to chemotherapy. Recently, pilot studies in adults with advanced
EBV-related NPC have shown that autologous EBV-specific cytotoxic T lymphocytes can produce objective responses and can control disease progression.16,17 Oxaliplatin is a platinum analog which does not have cross-resistance with cisplatin and carboplatin.18 Oxaliplatin lacks the nephrotoxicity and ototoxicity associated with cisplatin and is less myelosuppressive than carboplatin. The main dose limiting toxicity of oxaliplatin is peripheral neuropathy. Use of oxaliplatin has been studied in adults with newly diagnosed as well as recurrent NPC. Zhang et al19 conducted a phase III randomized trial in adults with advanced NPC, comparing concurrent chemoradiotherapy with weekly oxaliplatin (70 mg/m²) and RT, and RT alone. The 2-year overall survival (100% vs. 77%) and relapse-free survival (96% vs. 83%) were higher in the concurrent chemoradiotherapy arm compared with the RT arm. Another recent report described the combination of oxaliplatin and gemcitabine in 40 patients with recurrent undifferentiated or poorly differentiated NPC.20 The response rate was 56% with median survival and progression-free survival of 19.6 months and 9 months, respectively. Half of those patients had previous exposure to cisplatin or carboplatin. There is no data available about the effectiveness of oxaliplatin in children with NPC. Anthracycline has been used in combination with platinum agents in adult studies for NPC.10 Our report suggests that the combination of oxaliplatin and doxorubicin may be effective in recurrent NPC that has been previously treated with cisplatin. High rates of secondary malignant neoplasms, sensorineural hearing loss, and other morbidities have been reported in children who receive RT for NPC.21 In addition, cisplatin therapy contributes significantly to hearing loss. If tested and found effective in the phase 2 clinical trial setting, oxaliplatin could potentially be utilized in the treatment of newly diagnosed children and adolescents with NPC, where the omission of cisplatin may decrease morbidities associated with prolonged survival.

REFERENCES


