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Induction Chemotherapy Followed By Concurrent Chemoradiotherapy in a 14 Year Old Patient With Poorly Differentiated Nasopharyngeal Carcinoma: A Case Report on the use of the ARAR0331 Protocol

I. Introduction

A major consideration of radiotherapy in children is toxicity. Adults with nasopharyngeal carcinoma (NPCA) usually receive concurrent chemoradiotherapy with or without adjuvant chemotherapy as standard treatment; however, the rarity of pediatric NPCA patients makes the sequence and dosages of both modalities less clear-cut. Children are noted to be more sensitive to adverse effects of radiation, including the development of radiation-induced malignancies by a factor of 10-15. This provides a rationale for the possible role of dose de-escalation of radiation therapy to pediatric patients. Induction chemotherapy in pediatric NCPA patients has been used with good outcomes and its effect when combined with concurrent chemoradiotherapy has been evaluated in the ARAR0331 protocol published by the Children's Oncology Group. The results of which noted good 5 year overall survival at 88.2% and 5 year event-free survival at 85.5%.

II. Methodology

The objective was to discuss a case report of a 14 year old male patient with stage IV-A nasopharyngeal carcinoma in terms of tumor response, RTOG toxicity, and follow-up laboratories and ancillaries using the ARAR0331 Protocol.
The patient and his grandmother sought consulted at our institution with a chief complaint of a small, painful, palpable mass in his right neck, of one year duration, which was noted to have increased in size to around 5 x 5 cm around 5 months prior to consult. There was no associated fever or epistaxis. Endoscopy was done which revealed a polypoid nasopharyngeal mass extending into the right nasal cavity. Punch biopsy revealed squamous cell carcinoma, poorly differentiated. CT scan of the head and neck area revealed a lobulated mass at the right nasopharyngeal region, right masticator space, right pterygoid bone; same mass was extending to the right temporal lobe and sphenoid sinus; an enlarged level II lymph node on the right (2x3 cm) was noted. At this time, a working diagnosis of squamous cell carcinoma, poorly differentiated, nasopharynx, Stage IVA (T4N1M0) was made. Initially, patient was advised referral for intensity modulated radiation therapy (IMRT) due to concerns of late toxicity which would be decreased by the use of more conformal forms of radiation therapy; however, the patient's grandmother was concerned with potential costs of treatment and both the grandmother and patient made the decision to be treated at our institution. Both were duly appraised and were instructed about the potential toxicities of 2D conventional radiation therapy. Consent to treatment at our institution was given. A multidisciplinary meeting was convened which discussed the feasibility of using what was then a recently published protocol presented at the American Society of Clinical Oncology 2016 meeting: the ARAR0331 Protocol which involved induction chemotherapy followed by dose-adapted chemoradiotherapy. This protocol is illustrated (please see attached file).

III. Results

As the patient was classified as Stratum B. Patient was planned to undergo 3 cycles of 5-fluorouracil 1 g/m2/day with cisplatin 80 mg/m2 for the first 5 days of each cycle every 3 weeks. Patient was re-assessed post-treatment. Endoscopy revealed disappearance of previously noted mass. A repeat CT scan of the head and neck was also done revealing the disappearance of the mass at the right nasopharynx; disappearance of the previous superior extension; and a complete regression of the right cervical level II lymph node.
Patient was assessed to be a complete responder and underwent radiation therapy with a reduced dose of 61.2 Gy in 1.8 Gy per fraction for 34 fractions instead of the standard 70 Gy in 2.0 Gy per fraction for 35 fractions. Patient tolerated treatment for 7 weeks without complications. RTOG acute grade 1 toxicities to the skin, saliva, and mucous membranes were noted. On the third year of follow-up, patient only complained of slight dryness of mouth (RTOG Grade 1 late toxicity for salivary glands) Follow-up imaging up to 3 years post-treatment revealed absence of the mass and metastasis with most recent video nasopharyngoscopy showing no mass, lesion, or bulge at the nasopharyngeal area. Neurocognitive testing Mini-Mental Status Examination (MMSE) and Montreal Cognitive Assessement-Philippines (MOCA-P) revealed no cognitive impairment.

IV. Conclusions

The ARAR0331 protocol makes use of neoadjuvant chemotherapy using tri-weekly cisplatin and 5-FU followed by chemoradiotherapy with a response-adapted dose which, based on published results, gave excellent

5 year overall and event-free survival rates. This may help in potentially mitigating toxicities to pediatric patients both acute and late, including possibly reducing the risk of development of neurocognitive decline and secondary malignancies. The case reported has illustrated a complete response to induction chemotherapy with no note of locoregional recurrences, distant metastases, or severe late toxicities up to a 3 years of follow-up. To our knowledge, this was the first use of the ARAR0331 protocol for a case of pediatric NPCA in the country and this report helps illustrate the feasibility and effectiveness of said protocol in even the local, low-resource setting.

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