**INDUCTION CHEMOTHERAPY FOLLOWED BY CONCURRENT CHEMORADIOTHERAPY IN A 14 YEAR OLD PATIENT WITH POORLY DIFFERNTIATED NASOPHARYNGEAL CARCINOMA: JRRMMC EXPERIENCE OF THE ARAR0331 PROTOCOL**

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**BACKGROUND AND OBJECTIVE**

Adults with nasopharyngeal carcinoma (NPCA) usually receive concurrent chemoradiotherapy with or without adjuvant chemotherapy as standard treatment1; however, the rarity of pediatric NPCA patients makes the sequence and dosages of both modalities less clear-cut. Toxicity is a major concern and children are noted to be more sensitive to adverse effects of radiation. An option for de-escalation of dose based on induction chemotherapy response has been evaluated in the ARAR0331 protocol published by the Children’s Oncology Group2. 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.

**METHODS**

The patient and his grandmother sought consulted at our institution with a chief complaint of a small palpable mass in his right neck, of one year duration around 5x5 cm in size. Endoscopy was done which revealed a nasopharyngeal mass. Punch biopsy revealed squamous cell carcinoma, poorly differentiated. CT scan of the head and neck area revealed a right nasopharyngeal mass 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 toxicities; however, the patient’s grandmother was concerned with potential costs of treatment and they made the decision to be treated at our institution using 2D conventional radiation therapy. A multidisciplinary meeting was convened and a decision was made to have the patient undergo the ARAR0331 Protocol (see Figure 1).

  
*Figure 1.* ***An Illustration of the ARAR0331 protocol for Stratum B Complete/Partial Responders.***  *The ARAR0331 Protocol employs 3 cycles of induction cisplatin at 80 mg/m2 and 5-FU 1 g/m2/d as continuous infusion (CI) for 5 days; however, due to a slight delay in the initiation of radiotherapy, the decision to add 1 more cycle of induction chemotherapy was made. Patients received 3 cycles of concurrent cisplatin at 100 mg/m2.*

**RESULTS AND DISCUSSION**

*Table 1. Risk Stratification of ARAR0331 Protocol2*

|  |  |  |
| --- | --- | --- |
| **Stratum** | **Target Volume** | **Dose** |
| Stratum A | Nasopharynx and LN regions I-III, upper ½ IV-V | Stage I: 61.2 Gy Stage II: 66.6 Gy |
| Stratum B | Nasopharynx and LN regions I-V | CR/PR: 61.2 Gy. SD: 70.2 Gy |

As the patient was classified as Stratum B (see Table 1). Patient underwent protocol as seen in Figure 1. Patient was re-assessed post-treatment and imaging and endoscopy revealed complete regression of mass. As a complete responder, patient underwent radiation therapy with a reduced dose as seen in Table 1. Follow-up imaging and ancillaries are shown (see Tables 2 and 3).

*Table 2. RTOG Toxicity Grading during the six-week treatment and post-treatment*

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Week | | | | | | Post-Treatment | | | |
| RTOG toxicities | **1** | **2** | **3** | **4** | **5** | **6** | **1 mo** | **6 mos** | **1 yr** | **3 yrs** |
| Skin | **0** | **1** | **1** | **1** | **1** | **1** | **1** | **0** | **0** | **0** |
| Mucous Membrane | **0** | **0** | **0** | **0** | **1** | **1** | **0** | **0** | **0** | **0** |
| Eye | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** |
| Ear | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** | **0** |
| Saliva | **0** | **1** | **1** | **1** | **1** | **1** | **1** | **1** | **1** | **1** |
| Pharynx | **0** | **1** | **1** | **1** | **1** | **1** | **0** | **0** | **0** | **0** |
| Larynx | **0** | **0** | **0** | **0** | **1** | **1** | **0** | **0** | **0** | **0** |

*Table 3. Results of Laboratory and Ancillary Procedures (Post-treatment)*

|  |  |
| --- | --- |
|  | **Results** |
| Bone scan (December 2017) | No distinct scintigraphic evidence of bone metastasis |
| Chest X-ray (December 2017) | Normal chest findings |
| Whole Abdominal UTZ (December 2017) | Normal findings |
| Audiogram (January 2018) | Normal hearing threshold, bilateral |
| Dental Evaluation (January 2018) | Gums and teeth are in good condition. No signs of osteoradionecrosis |
| Blood Chemistry (January 2018) | Results Normal Values  Creatinine 75.91umol/L 62-123 umol/L  TSH 3.03 uIU/mL 0.25-4.0 uIU/mL  FT3 4.2 pg/mL 2.0-4.25 pg/ml  FT4 12.87 pg/mL. 7.0-18.0 pg/ml |
| CBC (December 2019) | Hemoglobin 16.1 g/dL 13.5-18.0  Hematocrit 47.0 %. 40-54 %  WBC 7.6 3.6-10.6  RBC 5.45 4.2-6.00  Platelet 278 150-450 |
| MMSE and MOCA-P Tests (January 31, 2018) | Score of 30 (normal/no cognitive impairment) |

**CONCLUSIONS**

The ARAR0331 protocol makes use of neoadjuvant chemotherapy followed by chemoradiotherapy with a response-adapted dose which, based on published results, noted good 5 year overall survival at 88.2% and 5 year event-free survival at 85.5%. This may help in potentially mitigating acute and late toxicities in pediatric patients. The case report illustrated a complete response to induction chemotherapy with no note of locoregional, distant failure, or severe late toxicities up to 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.

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**REFERENCES**

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