OUTCOME OF CHEMORADIATION IN THE MANAGEMENT OF A NIGERIAN CHILD WITH MAXILLARY NEUROBLASTOMA

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Abstract

Neuroblastoma is the most common of the extracranial solid tumours of childhood and infancy, we present the report of a patient diagnosed with Neuroblastoma of the Maxillary antrum at 3 years of age, who is clinically stable and disease free twelve years post treatment.

Keywords: Neuroblastoma, Maxillary antral carcinoma, Disease free

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Introduction

Neuroblastoma is the most common of extra cranial solid tumours of childhood and infancy. Wei JL, et al reported the first case of an isolated neuroblastoma of paranasal sinus among the caucasiand[1]. In a composite series, approximately 33% of all Neuroblastoma were found to arise from the adrenal medulla and 55% from all non pelvic abdominal sites. The pelvis accounted for 25%, thorax 13% and head and neck for 7%[2] . Neuroblastoma is the most

common tumours in early childhood with median age at diagnosis of 17 months, possessing diverse clinical unusual features[3,4]. It has been reported to have the highest spontaneous remission rate of any neoplasm in humans usually by maturation to ganglioneuroma [5,6]. Despite these peculiarities, it is most often a progressive, relentless disease spreading by lymphatics and blood stream.

The tumour is derived from sympathetic ganglia which originate from primitive neural crest cells and neuroblasts migrating from the mantle layer of the developing spinal cord[7]. Etiology of neuroblastoma is not known, but it may be considered a malignant manifestation of aberrant sympathetic nervous system development[8].

Stage, age at diagnosis, histology, tumor site, biologic markers are all important prognostic variables [9,10]. Multivariate analysis of groups of patients have demonstrated that stage of the cancer at diagnosis is the most improtant prognostic variable.[11]

Neuroblastoma of the maxillary antrum also known as Esthesioneuroblastoma (ENB) occurs with equal frequency in men and women and unlike most other neuroectodermal tumors, which manifest in childhood, Para-nasal sinus Neuroblastoma has a bimodal age distribution between 11-20 years and 51-60 years.[12,13]. The limited anatomic access of the paranasal sinuses makes early diagnosis difficult. Therefore most patients have advanced disease by the time of diagnosis. The most common presenting symptoms are epistaxis and nasal obstruction[14]. Some patients also present with complains of nasal mass or polyp. The tumour can spread submucosally in all directions, thereby involving the nasal sinuses, nasal cavity and surrounding structures. Patients with extensive tumour may have orbital symptoms such as proptosis and excessive lacrimation[15], while some may have obstruction of the lacrimal gland with periorbital edema.

Case Summary

The patient, a three year old boy presented in company of his mother to the department of radiotherapy, University College Hospital (UCH), Ibadan in January 1999 with a four month's history of frequent nasal discharge, three month history of fleshy growth from the right nostril and two month history of swelling in the right eye. The catarrh – like illness started initially as a watery discharge but soon became thick and copious. The growth in the nostril was initially small but his mother noticed it was progressively increasing in size. There was a history of occasional bleeding from the nostril. There was no history of trauma, or bleeding from other orifices. There was no family history of the disease. He was taken to an Ear, Nose and throat (ENT) surgeon at the University of Calabar Teaching Hospital, Calabar where an incisional biopsy was done. Two weeks after the incisional biopsy, the growth in the nostril was noted to have significantly increased in size with associated foul smelling purulent discharge. There was loss of the two (premolar) teeth from the right maxilla with an extension of the mass into the oral cavity, with a fungating mass in the right canine fossa. It was also noticed that he had developed a swelling in the right eye with progressive protusion of the right eye ball. He presented again at the teaching hospital, Calabar where a debulking surgery of right maxillectomy was performed and he was referred to radiotherapy for further treatment.

Examination at Radiotherapy department, Ibadan, revealed a young boy who was mildly pale, afebrile, anicteric, acyanosed, well hydrated with no pedal edema. He had palpable bilateral submandibular lymphadenopathy measuring 1x1 cm, mobile, non-tender with mild facial asymmetry. There was hypopigmentation of the skin over the right eyelid and edema involving the lower eyelid and maxillary region. There was also a residual disease in the right maxillary region.

Investigations done included an x-ray of the skull which revealed erosion of the floor of the right orbit. The chest x-ray and abdominopelvic ultrasound scan done were essentially normal. The values of the full blood count, electrolytes, urea and creatinine done were within normal ranges. The patient's mother could not afford a computed tomographic (CT) scan.

The histological diagnosis of the biopsy taken was reported as showing extensive necrotic tissue with a diffuse sheet of small round cells with attempt at rosette formation. Mitotic figures were few. An assessment of maxillary Neuroblastoma was made. Using international staging system his disease was stage 3 (AJCC Staging) in view of bilateral lymph nodes involvement and residual disesase after surgery.

Treatment

Patient was planned for and received external beam radiotherapy to the (R) maxilla region to include the floor of the orbit. Right anterior face and right lateral face wedged fields at 45^{o} with lead-shielding of the contralateral eye was planned. The patient received 40Gy in 20 daily fractions at 2Gy/fraction over 4 weeks. There were no immediate side effects of radiotherapy seen in the region treated except for hyper-pigmentation of the skin in the region which improved with time.

He also received 6 courses of cytotoxic chemotherapy, a combination of IV Cyclophosphamide 250mg, IV Methotrexate 25mg and IV Vincristine 0.5mg. This combination was given every 21 days.

He completed chemoradiation therapy by the 8^{th} August, 1999 and reported for post-treatment follow up six weeks after. There was complaint of mild nasal discharge which was intermittent. However there was no mass in the nasal, oral and orbital regions. He was then given follow-up appointments every 3 months for the first 2 years after treatment and then every 6 months for the next 2 years. He was regular and consistent with his follow-up visits for those periods with no complaints and assessments showed good disease control.

He was subsequently given yearly follow-up appointments which he kept. A slight depression of the right maxilla was noted after 5 years of completion of radiotherapy which was suspected to be a side effect of radiation. Patient has been clinically stable without any symptom or complaint. Chest x-ray and abdomino-pelvic ultrasound scan done were normal. An assessment of good disease control was made, with no clinical evidence of local recurrence or distant metastasis.

Patient was on regular 2 yearly follow-up visits and his last visit was in January 2012 which represents over twelve years of completion of treatment.

Discussion

The maxillary sinuses are the largest of the paranasal sinuses. They are pyramid-shaped cavities located in the maxillae. The lateral walls of the nasal cavity form the base and the roofs correspond to the orbital floors, which contain the infraorbital canals. The floors of the maxillary sinuses are composed of the alveolar processes. The apices extend toward and frequently into the zygomatic bones. Secretions drain by mucociliary action into the middle meatus via the hiatus semilunaris through an aperture near the roof of the maxillary sinus. Ohngren's line is a theoretic plane dividing each maxillary sinus into the suprastructure and infrastructure; it is defined by connecting the medial canthus with the angle of the mandible.

Malignant conditions of the nasal cavities or paranasal sinuses are lethal, and particularly unpleasant by its obvious nature to both the patient and the family. These tumours constitute less than one per cent of all malignancies and three per cent of head and neck tumours.[16]

The commonest malignancy in the maxillary sinus is squamous cell carcinoma, followed by undifferentiated carcinoma, and adenoid cystic carcinoma and adenocarcinoma.[16] Le *et al*. described 60 per cent of maxillary sinus malignancies to be squamous cell carcinoma, while adenocarcinoma comprised only four per cent of all malignancies in the maxillary sinus.[16]

Neuroblastoma in the para-nasal area which was first described in 1924 by Berger and Luc,[17] has a histological pattern similar to that of sympathetic ganglia, retina, and adrenal medulla[17] and thereafter became recognized as a distinct pathological entity, probably, as a result of immunohistochemistry and by means of electron microscopy techniques. [18] They have helped to differentiate Neuroblastoma from similar undifferentiated nasal cavity tumors and maxillary antral tumors. [18] Additional histologies include malignancies of salivary gland origin, of which adenoid cystic carcinomas predominate, adenocarcinomas and mucoepidermoid carcinomas. Rarer tumors include undifferentiated carcinoma, angiosarcomas, rhabdomyosarcomas, lymphomas, melanomas, and meningiomas.

Palpable submandibular lymphadenopathy was observed in the patient which was suggestive of a local spread. Study done by Bimbi G et al showed 8.3% of patients with maxillary sinus malignancies presenting with positive nodes.[19]

Regardless of the staging system used, metastasis from Neuroblastoma portends a poor prognosis. This patient already had involvement of the orbit, therefore was of poor prognosis at the time of commencement of treatment. The 5-year survival rate of patients with cervical metastasis has been reported to be 0%, whereas the survival of those without positive distant metastasis was greater than 60%.[20] The incidence of local or distant metastatic disease from primary Neuroblastoma has been reported at ranges between 10 to 40% in different study populations.[21] Computed tomography (CT) has been shown to be extremely useful in staging and treatment planning of this tumor [22]. However, magnetic resonance (MR) imaging has shown tremendous promise in surpassing CT for the mapping of neoplasms of the nasal cavity and paranasal sinuses [23]. Computed tomography allows detailed assessment of associated bony erosion or destruction, particularly of the cribriform plate. Contemporary MRI can delineate the precise margins of skull base tumors because of its multiplanar display

and superb tissue contrast. This patient's parents however could not afford to have a CT scan evaluation of the disease at presentation and still could not afford to do any during follow up.

Combined modality of surgery and external beam radiotherapy has been found to be the treatment of choice, particularly for advanced tumors, whereas surgery alone may be sufficient for small, well localized tumors. Neoadjuvant chemotherapy may offer improved local control and previous works have shown promising results.[24].

Chemoradiation has been the favoured approach to tumors with adverse prognostic features[8]; this was the treatment approach in this patient, considering the aggressive nature of his disease. There has been improvement in survival rates in patients with neuroblastoma, but is mainly among patients with more benign form of the disease than in patients with high risk neuroblastoma [25]. In a retrospective study of a ten year experience of maxillary antral carcinomas among Asian population, Sanjiv Sharma et al showed that 98.24% of carcinoma of the maxillary antrum presented with T3 and T4 lesions, with a three year disease free survival of 39.58% with radiation therapy alone and 51. 91% with combined modality treatment.[26]

Dulguerov and colleagues reported a 5-year survival rate of 45%.[27] Others have reported a survival rate as high as 70% with a local recurrence rate of 30%. [27] Prognosis depends on the stage and grade of the disease.

Conclusion

A long disease-free survival following chemo-radiotherapy was achieved in an African child with Neuroblastoma of the maxillary antrum. This patient has been clinically free of disease for12years of follow-up after treatment. This demonstrated a very good response to treatment

offered despite the advanced stage at presentation and thus reinforces the fact that early and adequate treatment can be curative in childhood cancer, even in a poor resource setting . However, further follow up is required as recurrence has been reported 20 years after treatment.

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