28/06/2018

**Name:**  Chereez Nel

**Date of Birth:** 16/01/2015

**Diagnosis:** Undifferentiated soft tissue sarcoma

**Date of Diagnosis:** 16/03/2018

**ICD10:**  C49.0

**PMB:** 952J

**Medical Aid:** Discovery

**Medical Aid Number:**  329854831

Chereez Nel is a 3 year old female who presented with 2 month history of right sided cheek pain and swelling. A CT scan of the head and neck confirmed a large contrast enhancing lesion in the right masticator space/infratemporal fossa. An MRI confirmed a 3.7 x 4.1x 4.1 cm well circumscribed lobulated mass in the right masticator space with restricted diffusion. There was a poor plane of separation between the mass and the medial pterygoid muscle, as well as invasion of the deep lobe of the parotid gland. The lesion extended superiorly into the right infra-temporal fossa with encroachment of Meckel’s cave on the right. It extended laterally displacing the right TM joint and mandibular ramus. A biopsy was performed by Dr A. Khan at Sunward Park Hospital o 16/03/2018. This showed a small round blue cell of childhood. Immunohistochemistry confirmed positive vimentin but was not diagnostic of a specific lineage of differentiation and was as such regarded as an undifferentiated high grade soft tissue sarcoma. Further molecular testing of the tumour was performed by MolGenDx in Basal. This confirmed an SLX4 mutation, FLCN and a RET mutation, all of which have no treatment implications and did not shed any further light on lineage.

Chereez was therefore treated in the very high-risk group of the EpSSG RMS 2005 protocol with IVADo. She is currently receiving week 13 of chemotherapy and has shown a remarkable clinical response. Undifferentiated sarcomas are high grade tumours and as with the other paediatric type soft tissue sarcomas, local control of the tumour is an essential part of therapy. Local control comprises both surgery and radiation.

Chereez’s case was presented at the Morningside Friday Head and Neck tumour board. It was felt that the tumour would not be able to be entirely removed because of the involvement of the skull base. Surgery would also be extensive, requiring splitting of the mandible, a fibula graft and a large flap and thus at this stage, it was suggested that the best option be to continue chemotherapy and reassess, and to explore radiation and potentially proton therapy.

Radiation therapy is an essential component of therapy. It does however, cause major side effects, and these effects are worse in young children who receive radiation to the head and neck region. These complications include: Facial growth retardation, neuroendocrine dysfunction, visual/orbital problems, dental abnormalities, hearing loss and hypothyroidism.

Currently intensity-modulated radiation is standard of care in the treatment of head and neck sarcomas.

Intensity-modulated radiation therapy (IMRT) is an advanced mode of high-precision radiotherapy that uses computer-controlled linear accelerators to deliver precise radiation doses to a malignant tumour or specific areas within the tumour. IMRT allows for the radiation dose to conform more precisely to the three-dimensional (3-D) shape of the tumour by modulating—or controlling—the intensity of the radiation beam in multiple small volumes. IMRT also allows higher radiation doses to be focused to regions within the tumour while minimizing the dose to surrounding normal critical structures. Typically, combinations of multiple intensity-modulated fields coming from different beam directions produce a custom tailored radiation dose that maximizes tumour dose while also minimizing the dose to adjacent normal tissues.

Because the ratio of normal tissue dose to tumour dose is reduced to a minimum with the IMRT approach, higher and more effective radiation doses can safely be delivered to tumours with fewer side effects compared with conventional radiotherapy techniques. IMRT also has the potential to reduce treatment toxicity, even when doses are not increased. Due to its complexity, IMRT does require slightly longer daily treatment times and additional planning and safety checks before the patient can start the treatment than conventional radiotherapy.

Proton therapy is a new form of radiation therapy, utilising protons rather than electrons. It has benefits over conventional radiation and over IMRT by delivering high doses to the tumour volume but at the same time by sparing more of the healthy surrounding tissues. This limits the side effects that especially young patients experience. Chereez is only 3 years old and thus the risk of side effects is very high. Unfortunately proton therapy is not available in South Africa, and is extremely expensive.

If proton therapy were to be considered, then Chereez would have to be transferred to the USA for treatment. Treatment would take at least 6 weeks and time would also be required to accurately plan the proton therapy. Centres offering proton therapy to International patients include Massachusetts General in Boston and Maryland in Baltimore. Costs are still estimates at this stage but are between $300 000 - $500 000. This excludes any accommodation, living expenses or chemotherapy that may need to be given concurrently with the radiation.

Chereez is a vibrant young child with a good chance of survival. Literature reports event free survival at approximately 50% for children with undifferentiated sarcoma who undergo multimodality therapy. Therapy however, must be done as safely as possible, with the aim of reducing long term side effects. The side effects that Chereez may experience from radiation to her right cheek are significant, and as such the option of proton therapy, although costly, is extremely attractive.

If you require any further information, please do not hesitate to contact me.

Kind regards

