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Radio Therapy Induced Secondary Malignancy: A Case Report and Review of Literature

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Abstract:- While radio-induced cancers are well known since the beginning of the 20th century, they did not represent a major concern for radiation oncologists for many decades. With better results of modern radiotherapy and prolonged follow-up of patients, secondary radio-induced cancers should now be systematically taken into account when irradiating patients. Here, we present a case of a radio-induced squamous cell carcinoma in a 12-year-old female.

Keywords:- *Secondary Malignancy, Myxofibrosarcoma, Squamous Cell Carcinoma.*

I. INTRODUCTION

Radiation therapy (RT) is a core pillar of oncological treatment, and an estimated 50% of all patients with cancer receive RT as a treatment modality (1) (2). Although RT is an effective means to treat the primary malignancy and to prevent disease recurrence, it is a "double-edged sword" that carries substantial morbidity due to the both acute and chronic adverse effects (3). A number of factors are associated in causing radiation induced malignancies (RTIMs) namely, age, genetic, type of treatment, dose and site of radiotherapy. (4)

The decision whether to use radiation to treat childhood cancer can be difficult for physicians and families. Evidence indicates that paediatric cancer survivors can develop cancer later on due to these treatments. (5) Here, radiotherapy in the form of intensity modulated RT (IMRT) in a case of myxofibrosarcoma later resulted in squamous cell carcinoma (SCC).

II. CASE REPORT

A known case of myxofibrosarcoma of left cheek area has now presented with a swelling over right side which has gradually progressed in size since last 6 months; along with the history of generalized weakness and weight loss.

On clinical examination, the patient was found to be lean and thin built with a metallic mesh placed on left cheek and a maxillary swelling on right side which was firm, non-tender, non-mobile and restricting the mouth opening. On oral cavity examination, the mass is seen protruding over the soft palate and hard palate with the shifting of right tonsillar fossa medially. Additionally, on left lower eyelid, cicatricial ectropion with lagophthalmos was seen. Rest of the systemic examination was within normal limits.

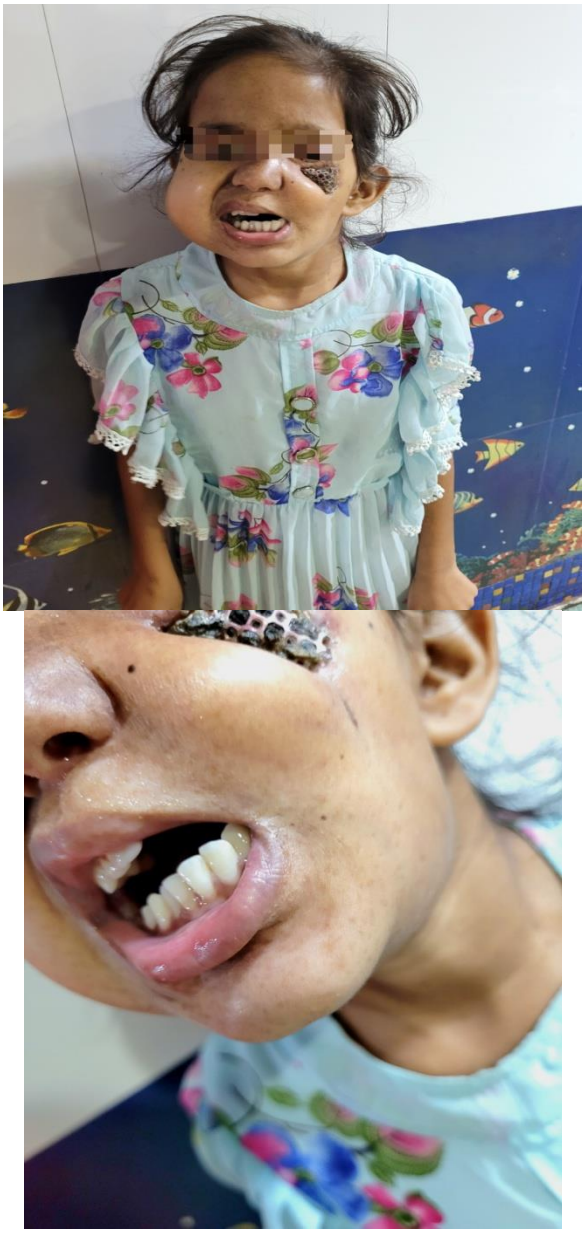

Fig. 1: Left sided maxillectomy and mesh repair; right side tumor swelling with restricted opening of mouth

III. REPORT FINDINGS AND REVIEW

The patient first reported 3 years back with a swelling on the left maxillary area for which a CECT and MRI PNS was ordered which revealed an expansile, well defined, heterogeneously enhancing lesion involving left nasal cavity, maxillary and ethmoid sinuses with mucosal thickening and hyperdense contents. Bony thicknening and mass effect with extraconal extension of left retrobulbar region was also seen. Followed which, an FNAC was done

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which suggested a low grade mesenchymal lesion and a biopsy which revealed that tumor is comprised of spindle cells with cellular atypia on a background of myxoid tissue and vessels with the features of spindle cell neoplasm.

On IHC, the tumor stayed positive for vimentin. Thereafter, a surgery was done involving left total maxillectomy with maxillary and orbital floor reconstruction using titanium mesh. The tissue mass resected was sent out for biopsy detecting myxofibrosarcoma.

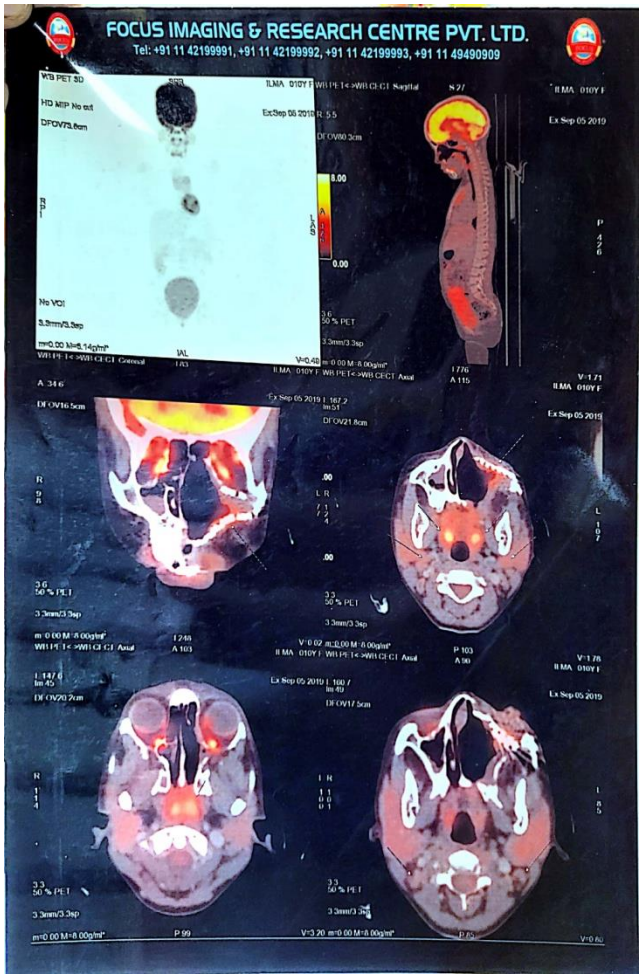

Fig. 2: PET-CT Scan showing the primary disease area

Post-operatively, CECT scan of face detected enlarged cervical lymph node with no residual disease and the patient underwent PET-CT scan after 5 months which showed mild, metabolically active bilateral cervical lymph nodes for which IMRT was started with a Planning target volume (PTV) 66Gy was given to local site in 33 fractions over a period of 2 months as radical dose.

Subsequently, the patient was advised to follow-up after 1 month but defaulted for 2 years; after which a PET-CT scan was done finding low-grade heterogeneously enhancing thickening in left buccal mucosa, maxillary sinus and extraconal compartment of left orbit suggesting a recurrent disease on left side.

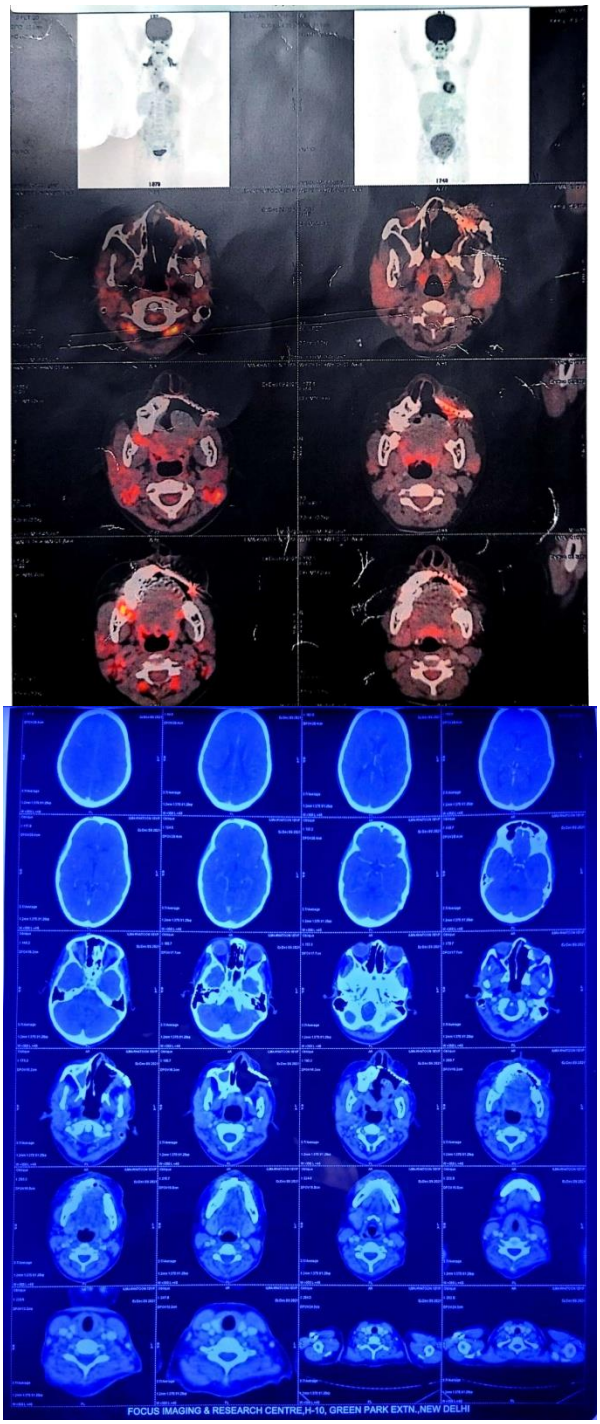

Fig. 3: PET-CT Scan revealing recurrent disease on left side of face

Following which, another default happened due to COVID-19 of 10 months duration, now the patient presented with a swelling on right cheek area for which a repeat PET-CT scan done revealing a recurrent disease on left side. Also, an ill-defined, metabolically active soft tissue density lesion in seen involving right buccal mucosa, pterygoid muscle, retromolar trigone and gingivobuccal sulcus suggesting disease progression; along with the involvement of bilateral cervical lymph nodes.

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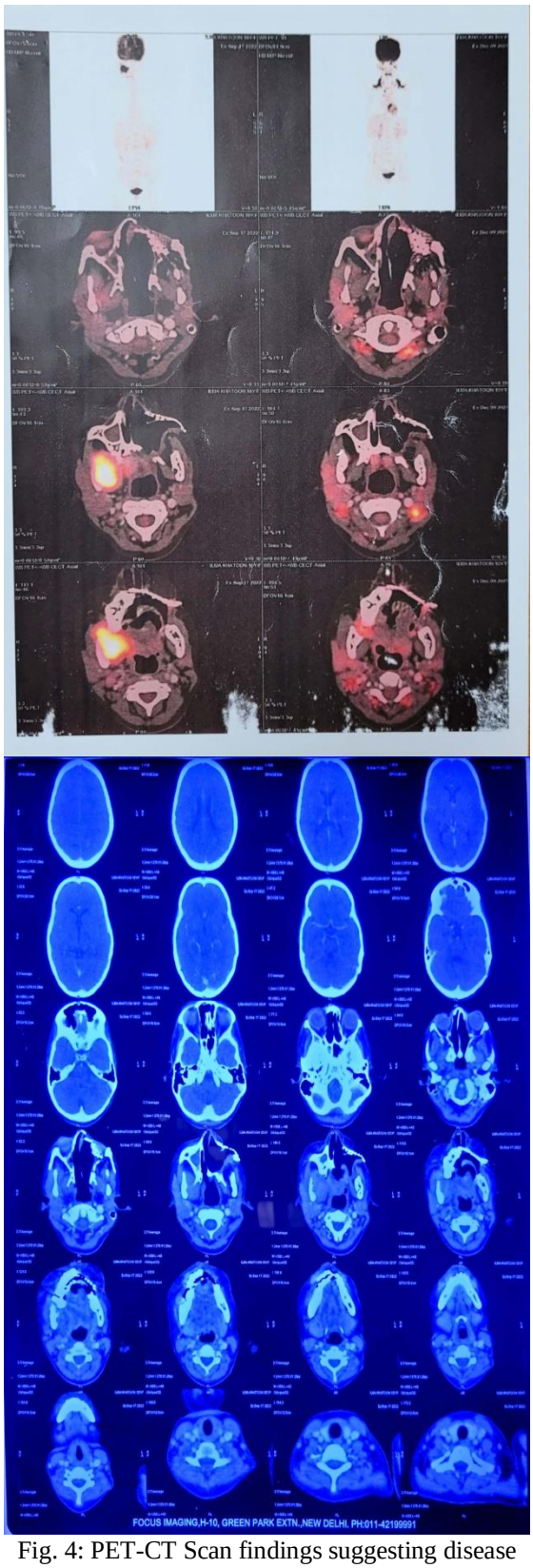

Fig. 4: PET-CT Scan findings suggesting disease progression towards right side along with nodal involvement

A biopsy was taken from right maxillary area revealing a diagnosis of moderately differentiated squamous cell carcinoma; thereby, an inference of secondary malignancy induced by radiotherapy.

IV. DISCUSSION

Radiotherapy continues to be a critical component of oncological care. As cancer survival improves, the late effects of radiotherapy can impact long-term patient health. The most significant and life-threateninglate effect is the development of RTIM. A review of the literature demonstrates that radiation-induced tumors develop after relatively long latencies of often several years, but that this risk often persists for decades without a plateau. (6)

The secondary malignancies reported post RT includes sarcomas, carcinomas, leukaemias, and mesotheliomas. An interplay of host factors (example- age, type of primary cancer, and hereditary predisposition), environmental factors (i.e., smoking), and type of RT determine the risk of RTIMs (7) (8) (9). RTIMs are typically biologically aggressive and carry a worse prognosis than that of the corresponding primary malignancy (4) (7).

Cahan et al gave the criteria to diagnose RTIMs. The modified Cahan criteria state that *(a)* RTIMs must arise in an irradiated field; *(b)* a sufficient latency period, preferably more than 4 years, must have elapsed between the initial RT and the alleged induced malignancy; *(c)* the treated tumor and the alleged induced tumor must have been biopsied, and the two tumors must be different histologically; and *(d)* the tissue in which the alleged induced tumor arose must have been metabolically and genetically normal before RT exposure (10) (11).

There has been an increased risk of secondary malignancies after chemoradiotherapy for paediatric cancer patients as compared to general population (12). In the 1980s, the prominent role of the irradiated volume was demonstrated, as well as the higher risk of radio-induced cancers in young adults, and even more in children (13).

RT for mucosal cancers in the head and neck region (most commonly oropharyngeal and laryngeal carcinomas) can lead to the development of secondary tumors (14). The majority of RTIMs are squamous cell tumors and are commonly seen in the head and neck and thoracic regions (15) (14). In 1989, a study by Cooper et al showed 110 second, independent, malignant tumors out of 928 patients with squamous cell carcinoma of head and neck (16).

The first experimental study conducted by Gomarteli et al. testing the dogma that the low-dose IMRT induces more cancers than conventional treatment. (17)There are two reasons why the change from 3D-CRT to IMRT may result in an increase in second malignancies. First, it involves the use of more fields, and as a consequence, a bigger volume of normal tissue is exposed to lower doses. Second, delivery of a specified dose to the isocenter from a modulated field, delivered by IMRT, will require the accelerator to be energized for longer; therefore the total body dose due to leakage radiation will be increased. (18)

To reduce RTIMs, a careful selection of patients for radiotherapy and RT treatment techniques and subsequent vigilant follow-up and investigations can be proved helpful in early diagnosis and, hence, resulting in successful treatment. (19) Proposed recommendations to reduce the risk of radio-induced cancer after radiotherapy: (1) adapting the irradiation technique; (2) reducing the target volumes; (3) adapting to patient's age; (4) adapting to specific organs; (5) and optimizing the imaging dose (20).

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