ORIGINAL RESEARCH PAPER

Volume-8 | Issue-4 | April-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

MALIGNANT MELANOMA IN A PATIENT OF XERODERMA PIGMENTOSUM TREATED WITH RADIATION THERAPY: A CASE REPORT

Oncology

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ABSTRACT

Xeroderma Pigmentosum(XP) is a rare, autosomal recessive disorder characterized by photosensitivity, cutaneous pigmentary changes, premature skin ageing, and the development of various cutaneous and internal malignancies at an early age. The basic underlying genetic abnormality is a nucleotide excision repair (NER) defect leading to defective repair of DNA damaged by ultraviolet(UV) radiation.most patients with XP are not abnormally sensitive to therapeutic radiation. We herein describe the clinical response with radiation therapy for malignant melanoma in a child with XP. This case is being presented because of rare association of Malignant Melanoma with Xeroderma Pigmentosum patients in India. However, radiation therapy should be used with caution in XP patients with an anticipated prolonged life expectancy, because the late side effects of ionizing radiation in XP are not well known. This case is reported to illustrate the use of ionizing radiation in the treatment of malignancies in XP patients in addition to other management strategies available for this incurable disease entity.

KEYWORDS

XP, malignant melanoma, radiotherapy.

CASE REPORT:

A 10 year old girl presented to us with pigmented lesions over the skin since early childhood. Patient also complained of a large mass over nose for past 6 months. Patient complained of multiple swellings in the neck for last 2 months (fig 1). There was no history of consanguinity and both parents and siblings were normal

Hyperpigmented macules were seen all over the body mainly over sun exposed areas (face and upper neck). A large mass of 5x5x2cm^3 was seen over the left side of nasal ala with ulceration, areas of haemorrhage and blackish pigmentation. There were bilateral cervical lymph nodes palpable. One was 4x4 cm, hard, fixed, non-tender, in the left post-auricular site. One right sided level II cervical lymph node, 2x2 cm, non tender and mobile was also palpable. Systemic examination showed no abnormality. Ophthalmic examination revealed conjunctival chemosis.

Biopsy from hyper-pigmented macular lesions on skin showed features of Xeroderma Pigmentosum (fig 2). FNAC of left post-auricular lymph node also suggested Metastatic Melanoma.

She underwent wide local excision with naso-labial flap cover (fig 3). Gross pathology revealed a tumour measuring 6x6x3 cm^3 with areas of necrosis and haemorrhage. Cut section revealed a solid black surface. Microscopic examination showed ulcerated epidermis with sheets of tumour cells beneath it. Cells were epithelioid-spindloid with vesicular pleomorphic nuclei and melanin pigment. All resection margins were free (fig 4).

Patient was given external beam radiation therapy by Cobalt-60 unit to the left post auricular node by 5x5 cm en-phase field at depth of 3 cm in a hypofractionated schedule to a total dose of 25 Gray in10 fractions (fig. 5).

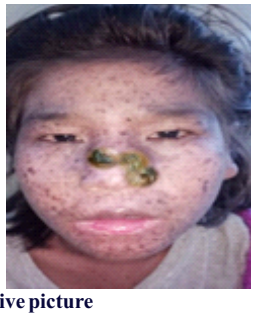

Fig 1:Pre-operative picture

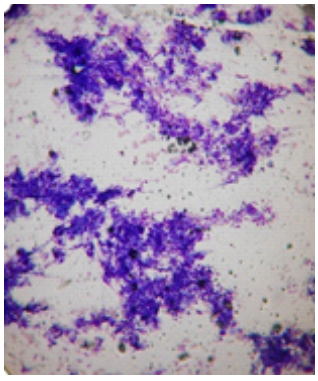

Fig 2-Cells arranged in groups clusters.

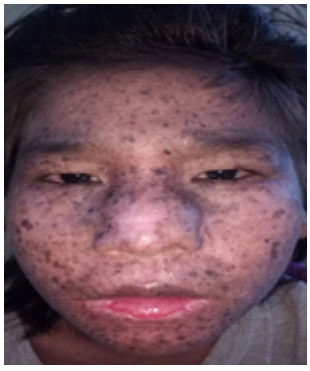

Fig 3: post surgery and reconstruction.

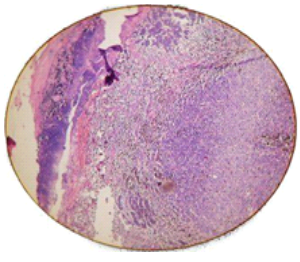

Fig4: tumor tissue with hyperchromatic nuclei and melanin.

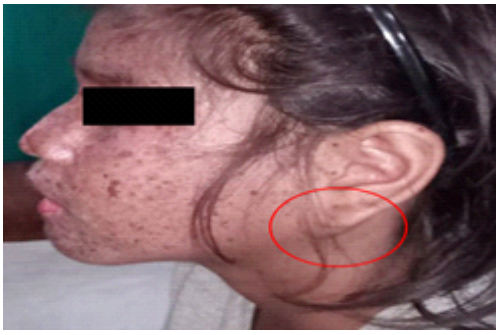

Fig 5: pre-auricular lymph node irradiated.

DISCUSSION:

XP (XerodermaPigmentosum) is an autosomal recessive disease caused by defects in the normal repair of the DNA of various cutaneous and ocular cell types damaged by exposure to sunlight. First described in 1874 by Hebra and Kaposi, it occurs with an estimated frequency of 1:100,000 in the US and Europe, more commonly in Japan(1:400000), Middle East, North Africa.[1] Incidence in India is not well reported. It has equal sex predilection and significant parental consanguinity. Patients with XP develop multiple malignant neoplasms at an early age. The tumours include squamous cell and basal cell carcinoma. In 3% of the patients, Malignant Melanoma develops. Patients younger than 20 years have a 1000-fold increase in the incidence of non-melanoma skin cancer and melanoma. The mean patient age of skin cancer is 8 years in the patients with XP compared to 60 years in the healthy population. Actinic damage occurs in the age range of 1-2 years of age.[5]The reported incidence of melanoma arising in XP is approximately 2,000 times greater than normal.[2]

There are seven XP complementation groups(A-G) which define defects in nucleotide excision repair(NER) responsible for excising U-V(less than 280 nm) induced DNA photo damage.[3]

XP patients develop sensitivity to sunlight as early as 6 months of age with actinic keratosis, xerosis, poikilodermaocular abnormalities, neurodegeneration, malignant neoplasms of skin in the sun exposed areas especially head and neck region. [8]

The diagnosis of XP can be established with studies of cellular hypersensitivity to UV radiation, chromosomal breakage studies, complementation studies, gene sequencing, exon analysis. Prenatal diagnosis is possible by amniocentesis or chorionic villous sampling. Unfortunately all these investigations could not be carried out for our patient.[4]

Surgical excision is the most common modality used for the treatment of XP-related malignant melanoma.[7] However; lesions at some sites may not be amenable to adequate surgical intervention. Again, significant aesthetic deformities may result from multiple excisions. In such instances radiation can be offered as an alternate modality of treatment.[6]

In mammalian cells, Non Homologous End Joining (NHEJ) is the predominant mechanism of repair of ionizing radiation induced double stranded DNA breaks. Any defect in any component of NHEJ can lead to hypersensitivity to Ionizing Radiation, genome instability and cancer.[9]Literature review showed that patients of XP (Nucleotide Excision Repair defect) show difference in sensitivity to ionizing radiation. Some patients develop severe radiation-induced reactions during radiotherapy and some tolerate complete tumoricidal doses well with minimal reactions. Arlett CF et al[10]examined the ionizing radiation survival data for 33 XP primary fibroblast lines and compared the data to that of 53 normal fibroblast lines. Although there were differences in radiosensitivity between cell lines, there was no convincing evidence that XP lines as a group were more sensitive to ionizing radiation than the general population.

Keeping in mind the poor overall survival of such patients, radiation was offered for palliation instead of re-surgery or radical neck dissection, which would be a more mutilating option with high morbidity. Patient had partial response with improvement in quality of life without any undue toxicity. Being malignant melanoma which acts like late reacting normal tissue with low α/β ratio, and poor long term survival, a hypofractionated schedule (large dose per fraction) was adopted.

The schedule for radiotherapy may be individualized based on the clinical presentation and the number, type, size, and the site of the lesion. In view of short survival of these patients, long-term clinical outcome and late effects of radiation therapy remain to be elucidated.

CONCLUSION:

XP patients are predisposed to develop skin malignancies. In contrast to exaggerated sensitivity to UV radiation, XP patients may tolerate therapeutic doses of Ionizing Radiation. Radiotherapy is a possible and effective therapeutic alternative in cases of XP with Malignant Melanoma even though reports of such treatment in India are rare. Dose and methods are not defined for XP. While planning treatment by ionizing radiation, detailed counselling regarding the possibility of severe acute radiation reactions during the course of treatment is needed. Every case being reported might help us to learn about the incidence and prevalence of XP as well as association with malignant melanoma in India, which is yet unknown.

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