Re-irradiation of metastatic disease in the neck from xeroderma pigmentosum

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ABSTRACT

Background

Xeroderma pigmentosum, an autosomal recessive disease that occurs with a frequency of 1:250,000, is caused by a genetic defect in nucleotide excision repair enzymes. Mutation of these enzymes leads to the development of multiple basal cell and squamous cell carcinomas.

Objectives

We present a case of xeroderma pigmentosum in a patient with cervical and intraparotid metastatic disease from recurrent cutaneous squamous cell carcinomas of the face and scalp, treated with neck dissection and re-irradiation. With the illustrative case report, we include a literature review of diagnosis, prognostic factors, and treatment, with emphasis on surgical and radiation treatment of cervical metastatic disease from recurrent skin carcinomas.

Case Presentation

A xeroderma pigmentosum patient presented to our clinic with a 2-cm right submental and 1-cm right infra-auricular mass after resection of multiple squamous cell carcinomas of the scalp and face, and external-beam radiation therapy to the right face and neck. Fine-needle aspiration biopsy of the submental mass revealed poorly differentiated squamous cell carcinoma. The patient was brought to the operating room for a right modified radical neck dissection and excision of the right submental and intraparotid mass. Surgical pathology revealed 3 level IA and supraclavicular lymph nodes that were positive for metastatic squamous cell carcinoma. Re-irradiation to the entire right hemi-neck and left submandibular nodal region was performed using opposed oblique portals for the upper neck and a low anterior en face hemi-neck portal. The left parotid region was also included in the re-irradiation volume. Treatment was completed without delayed complications or recurrences to date.

Conclusions

To our knowledge, this is the first case report in the literature of a patient with xeroderma pigmentosum who subsequently developed metastatic disease from recurrent cutaneous squamous cell carcinoma. Because of the rarity of xeroderma pigmentosum, this case report is also the first to describe re-irradiation to treat cervical and intraparotid metastatic disease in a xeroderma pigmentosum patient.

KEY WORDS

Xeroderma pigmentosum, radiation, head-and-neck cancer, re-irradiation

1. CASE PRESENTATION

A 17-year-old male adolescent with xeroderma pigmentosum (XP), on routine follow-up for multiple excisions of squamous cell carcinoma of the scalp and face, presented to our head-and-neck clinic with a 1-cm right submental firm mass. His previous surgeries included excisions of squamous cell carcinomas of the right parietal, left frontal, and midline scalp, and left forearm in 2004. He underwent radiation therapy to the right face and neck in 2005. A total of 59.4 Gy using 9 MeV electrons was given because of the finding of a 1.2×0.6-cm moderately differentiated invasive squamous cell carcinoma of the right temporal skin, with extensive perineural invasion and metastasis to one of four cervical lymph nodes. Tumour was present at less than 1 mm from the deep margin in that specimen. The radiation dose was prescribed to the 90% isodose line, and no bolus was used.

On examination, diffuse freckling and areas of cutaneous hypo- and hyperpigmentation were noted throughout this young man's face and scalp. He had bilateral pterygia and multiple healed scalp incisions. He had a firm right submental mass 2.5×1.5 cm, a

firm right infra-auricular mass 1.5×1.0 cm, and a firm, mobile, discrete right supraclavicular lymph node 2.0×1.0 cm on palpation. A fibre-optic examination of the nasopharynx, oropharynx, and larynx was unremarkable.

A fine-needle aspiration biopsy of the submental neck mass was performed. Cytology revealed poorly differentiated carcinoma consistent with squamous cell carcinoma. Positron-emission tomography imaging demonstrated a hypermetabolic focus in the right parotid region approximately 2.0 cm inferior to the external auditory meatus, with a standardized uptake value (SUV) of 5.5, which corresponded to a hyperdense 1.4-cm nodule within the parotid. A hypermetabolic focus with an SUV of 3.2 was found near the inferior tip of the right parotid gland, corresponding to a 0.8-cm soft-tissue nodule. In addition, a circular density measuring 1.5 cm in diameter, with an SUV of 3.6 and a relatively radiolucent centre, was found in the right submental region, suggestive of a lymph node with central necrosis.

The patient was brought to the operating room and a right modified radical neck dissection was performed. Following development of subplatysmal and submandibular gland flaps, the submental mass was identified and removed. Multiple lymph nodes at all levels of the neck dissection, particularly at level IIB, appeared suspicious for malignancy and were excised. A right intraparotid lymph node was also removed. Surgical pathology identified 30 cervical lymph nodes within the right neck lymph node dissection, 3 of which were positive for metastatic squamous cell carcinoma: 1 of 4 level IA lymph nodes, and 2 of 2 right supraclavicular lymph nodes. In addition, the right intraparotid mass was positive for moderately differentiated invasive squamous cell carcinoma within a predominating lymphoplasmacytic background. This patient's disease was staged as TxN2cM0, and he was referred to radiation oncology for radiation therapy to the right neck.

Given the high-risk features of this lesion (namely, multiple positive lymph nodes), re-irradiation was recommended. The patient received 54 Gy in 30 fractions to a comprehensive volume that included the entire right hemi-neck and left submandibular nodal region. Calculation of cumulative doses to normal structures was performed using computed tomography planning. Left anterior and right posterior oblique portals with 30-degree wedges were used for the upper neck. A right low anterior hemi-neck portal was matched with asymmetric collimation for coverage of the supraclavicular fossa. All treatments used 6 MV photons, without bolus. The re-irradiation course used maximum and minimum doses of 62.6 Gy and 51.9 Gy respectively. The left parotid region, which received the previous radiation dose of 59.4 Gy in 33 fractions, was also fully included in the re-irradiation volume because of the presence of intraparotid disease. Thus, the cumulative total dose to this volume was 113.4 Gy. Assuming an alpha:beta ratio of 3 for normal tissues, the biologically equivalent doses were 95 Gy and 86.4 Gy for first and second courses of radiation therapy respectively.

Given the concern for radiation-induced complications in patients with XP, this patient was counselled extensively on possible complications. However, he tolerated treatment without any interruption. He experienced grade 3 oral mucositis, which was managed with topical rinses and which resolved 1–2 months after treatment. He also had grade 1 dermatitis, which was similarly managed with topical agents and which resolved spontaneously. Treatment was completed in September 2007, and during an 18-month follow-up since re-irradiation completion, no recurrences or delayed complications have been seen.

2. DISCUSSION AND CONCLUSIONS

Xeroderma pigmentosum is an autosomal recessive disease that occurs with a frequency of approximately 1:250,000. It is caused by a deficiency in nucleotide excision repair or post-replication repair. Individuals with XP have an incidence of skin cancers 2000 times that of the population at large before the age of 20. Predisposition to severe actinic changes leads to the development of multiple basal cell and squamous cell carcinomas in these patients. In one retrospective study, a 57% lifetime prevalence of non-melanoma skin cancer was found, with a median age of 8 years at initial diagnosis of a cutaneous malignancy [1].

Treatment of patients with XP is based on prevention: protection from ultraviolet radiation and close surveillance for skin lesions. A review of the otolaryngology and dermatology literature revealed only one report of a patient with XP who subsequently developed metastatic disease from recurrent cutaneous squamous cell carcinoma—in that case, treated successfully with cetuximab [2]. In addition to close monitoring of a patient's entire skin surface by family members, examination by a physician should be conducted every 3–6 months.

Patients at high risk for cutaneous neoplasms treated with oral retinoids were shown to have significantly lower rates of new cutaneous squamous cell carcinoma. Premalignant lesions should be treated expeditiously with liquid nitrogen freezing or topical 5-fluorouracil. Cutaneous neoplasms should be treated with electrodessication or surgical excision, depending on location and depth of cutaneous invasion. The prognosis is poor; most patients with XP die of skin cancer early in adulthood.

Clinical experience of radiation therapy in patients with XP is limited. In a review from St. Bartholomew's Hospital, London, over 20 years, 4 of 2000 children exhibited a severe reaction to radiation therapy, of which only 1 had XP [3]. Arlett and colleagues [4] described a XP case with angiosarcoma of the scalp treated with surgical excision and radiotherapy. After 38 Gy in 19 fractions with 6-MeV electrons, severe desquamation

and necrosis of the underlying bone ensued, and death followed 4 years later. The cell line was correspondingly hypersensitive to the lethal effects of gamma irradiation. Other case reports suggest that radiation can be tolerated in patients with XP. A 21-year-old XP patient with multiple skin cancers was treated successfully with radiation for a spinal cord astrocytoma and did not have recurrence after 9 years [5].

To our knowledge, re-irradiation has been described in 1 patient with recurrent squamous cell carcinoma of the nose treated with 2 courses of electron-beam irradiation, each delivering a dose of 30 Gy in 10 fractions. The investigators used amifostine, a cytoprotective agent, during the second course, and treatment was well tolerated. We also found that re-irradiation was well tolerated without employing cytoprotection [6].

No consensus has yet been reached on the appropriate dose for re-irradiation in head-and-neck cancer, but doses of 50–60 Gy have typically been delivered, because tumour control requires such doses and because complications generally increase after a cumulative dose of 120 Gy [7]. Our cumulative dose of 113.4 Gy was within this broadly acceptable range.

3. REFERENCES

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