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Case Report

ORAL CAVITY SQUAMOUS CELL CARCINOMA IN A CASE OF ICHTHYOSIS FOLLICULARIS, ALOPECIA, AND PHOTOPHOBIA SYNDROME WITH CHRONIC MYELOID LEUKEMIA ON LONG-TERM HYDROXYUREA: A RARE PRESENTATION

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ABSTRACT

We report a case of a patient in his early 30s who presented with an ulceroproliferative growth over the left buccal mucosa; he was also on treatment for chronic myeloid leukemia in blast crisis on hydroxyurea and a known case of ichthyosis follicularis, alopecia, and photophobia syndrome. Although a working diagnosis of chloroma/hydroxyurea-induced erosive lichen planus was suspected, the histopathological examination of the lesion was suggestive of squamous cell carcinoma. He was subsequently planned for palliative radiotherapy.

Keywords: Hydroxyurea, Ichthyosis follicularis; alopecia; and photophobia, Myeloid leukemia.

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INTRODUCTION

The ichthyosis follicularis, alopecia, and photophobia (IFAP) syndrome is a rare X-linked genetic disorder which is characterized by the triad of IFAP from birth [1-3].

Our case with IFAP syndrome had a complex presentation with chronic myeloid leukemia (CML) in blast crisis and squamous cell carcinoma of the oral cavity. This case had a remarkable response to radiation therapy but at the cost of severe mucosal and skin reactions. This is a rare case which brings together the disciplines of dermatology, medical oncology, and radiation oncology.

CASE REPORT

The patient was diagnosed with IFAP syndrome by the Department of Dermatology at Kasturba Medical College in 2004 and was managed symptomatically for the same.

In 2008, he was evaluated under the department of medicine for generalized weakness; upon further evaluation and bone marrow studies, he was diagnosed with CML in chronic phase.

The translocation assay studies revealed a BCR/ABL-negative disease; thus, he was started on hydroxyurea after an oncology consultation.

Within 2 weeks of therapy, patient developed diffuse oral ulceration warranting a drug-free interval of 1 week; subsequently, hydroxyurea was restarted at a lower dose. Within 3 weeks of restarting hydroxyurea, patient developed generalized hyperpigmentation and hyperkeratosis of skin and diffuse oral mucositis for which a dermatology opinion was sought, it was diagnosed as hydroxyurea-induced erosive lichen planus of oral cavity. He was managed conservatively for the same.

Patient received hydroxyurea for approximately 5 years till June 2013 when a bone marrow biopsy revealed the progression of the disease to blast crisis. He was subsequently started on vincristine and prednisolone chemotherapy regimen for a duration of 6 weeks. A repeat bone marrow biopsy was suggestive of regression of CML to the chronic phase, and he was restarted on hydroxyurea. However, within a span of 1 month, he relapsed into blast crisis phase. Thereafter, since October 2013, he was on supportive care alone.

It was during this phase, he developed a painful oral ulcer over the left buccal mucosa, which subsequently progressed to an ulceroproliferative lesion within a span of 2 weeks (Fig. 1), with a working diagnosis of chloroma or hydroxyurea-induced erosive lichen planus, a biopsy was undertaken.

Patient was referred to the Department of Radiation Oncology, Kasturba Medical College, Manipal in October 2013 with biopsy reports suggestive of squamous cell carcinoma.

On local examination, there was ulceroproliferative growth of 4 cm × 3 cm over the left buccal mucosa about 2.5 cm posterior to the commissure and 2 cm anterior to the left retromolar trigone, involving the inferior gingiva buccal sulcus; skin over the lesion was freely pinchable. There was no trismus at presentation.

Systemic examination revealed features consistent with IFAP syndrome and myeloproliferative disorder. Remarkable findings included generalized icthyosisatrichia, palmoplantar keratoderma, and total nail dystrophy (Figs. 2 and 3).

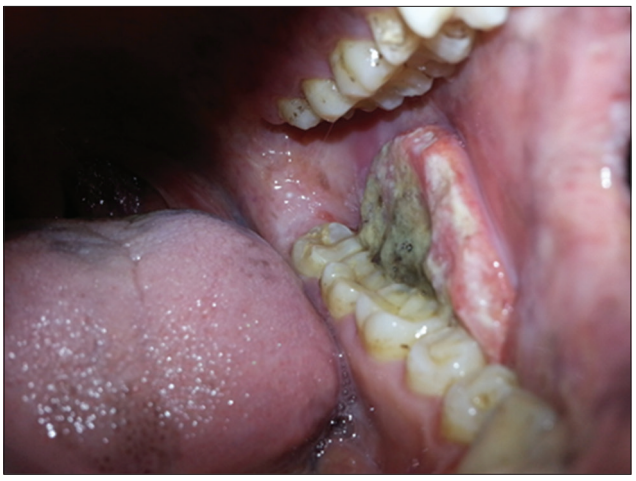

Fig. 1: The primary tumor at presentation

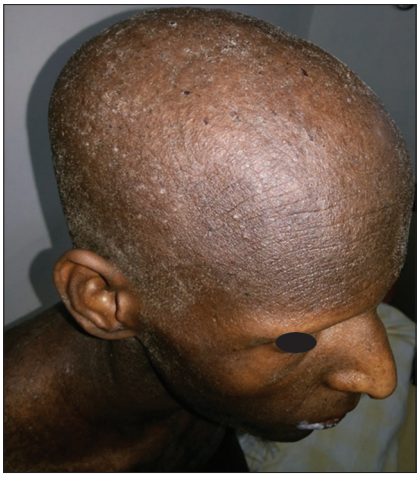

Fig. 2: Atrichia, a component of ichthyosis follicularis, alopecia, and photophobia

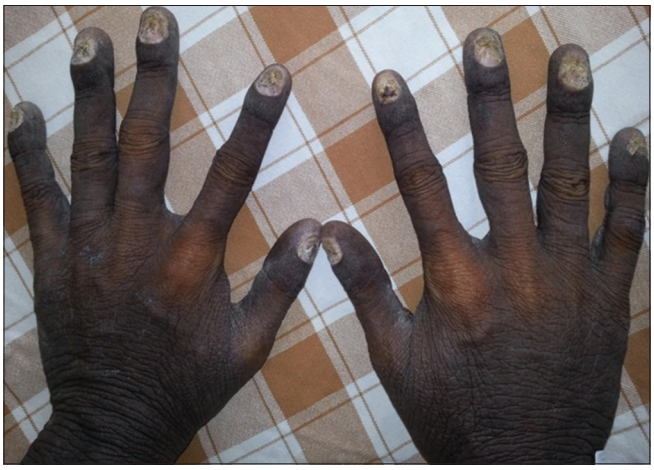

Fig. 3: Onycholysis a component of ichthyosis follicularis, alopecia, and photophobia

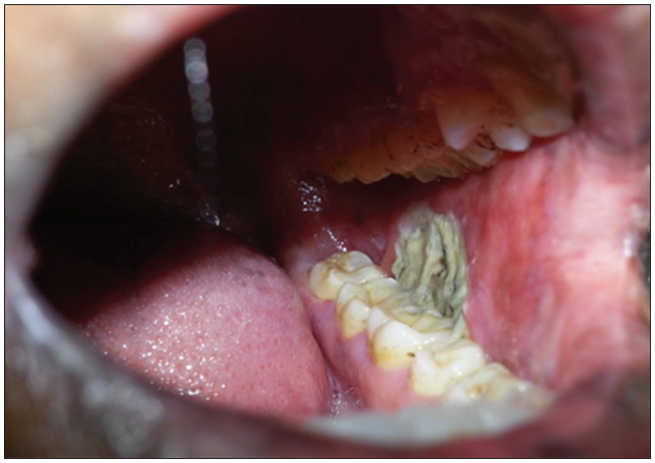

Fig. 4: The primary tumor after four fractions of radiotherapy

Fig. 5: The mucosal and skin reactions after 1 week of radiotherapy

A per abdominal examination revealed a hepatosplenomegaly.

The surgical option was ruled out in view of his guarded prognosis; he was thus planned for palliative radiotherapy.

He was prescribed to a dose of 30 grays in 10 fractions of radiotherapy over a 2-week period, only to the primary tumor site.

There was near total response with just four fractions of radiotherapy (Fig. 4), but before the completion of the prescribed dose, he developed Grade 3 skin and Grade 4 mucosal reactions (Fig. 5).

The treatment was thus stopped only after eight fractions of radiotherapy as the skin and mucosal reactions failed to subside even after 1 week of treatment stoppage.

He was on follow-up for 3-month post-treatment completion with no evidence of local recurrence of the oral cavity lesion. He eventually succumbed to his illness in March 2014.

DISCUSSION

There are <50 cases with IFAP syndrome reported in literature [1], and the oldest reported patient was 33 years old [2]. There is no reported case of IFAP syndrome in literature complicated by CML and squamous cell carcinoma of the oral cavity.

The literature review of patients with CML [4,5] and other myelogenous disorders on treatment with hydroxyurea revealed that oral cancer following long-term treatment with hydroxyurea has been reported only in a few instances, once in a patient with concomitant multiple skin tumors and the other instance in a patient with polycythemia vera who developed oral cancer after 15 years of hydroxyurea therapy [6]. There is no reported correlation between the onset of this complication to the dose and duration of therapy.

Patients with CML are at a considerable risk of developing second primary neoplasms. However, mucosal squamous cell cancers (SCCs) of the head and neck have only been reported in a study by Budrukkar *et al.* [7] where seven patients with mucosal SCC of the head and neck that presented as metachronous second primary tumors were reviewed. The median interval between diagnosis of CML and head neck cancer was 6 years (range: 2-15); in our report, the time lag was between the diagnosis of the two was 5 years.

Whether this entity can be attributed totally to CML or hydroxyurea will be hard to decipher.

The exquisite radiosensitivity of the tumor and that of the normal tissue could possibly suggest that this rare syndrome with its poorly understood molecular genetics might render the patient inherently susceptible to radiation exposure.

CONCLUSION

Apart from reporting the rare syndrome, our case report aims to highlight the fact that hydroxyurea-induced oral cancer though rare should be considered as a differential diagnosis in patients with oral lesions on long-term hydroxyurea.

Any oral lesions in patients with long-term hydroxyurea should warrant discontinuation or use of alternative medication.

The treating clinician must bear in mind that mucosal squamous cell carcinomas of the head and neck are a rare but a reported complication in patients who are long-term survivors of CML and whenever feasible a biopsy should be undertaken to ascertain the diagnosis.

REFERENCES

1. Mégarbané H, Mégarbané A. Ichthyosis follicularis, alopecia, and photophobia (IFAP) syndrome. Orphanet J Rare Dis 2011;6:29.
2. Keyvani K, Paulus W, Traupe H, Kiesewetter F, Cursiefen C, Huk W, *et al*. Ichthyosis follicularis, alopecia, and photophobia (IFAP) syndrome: Clinical and neuropathological observations in a 33-year-old man. Am J Med Genet 1998;78(4):371-7.
3. Boente MC, Bonet HB, Coronel AM, Asial RA. Atrichia, ichthyosis follicular hyperkeratosis, chronic candidiasis, keratitis, seizures, mental retardation and inguinal hernia: A severe manifestation of IFAP syndrome? Eur J Dermatol 2000;10:98-102.
4. Darji AA, Bharadia PD. Chronic myelogenous leukemia: A review and update of current and future therapy. Int J Pharm Pharm Sci 2016;8:35-46. Available from: http://www.innovareacademics.in/journals/index.php/ijpps/article/view/12124.
5. Ting CY, Shamsuddin AF. Optimized RNA extraction for detection of BCR-ABL transcripts in chronic myeloid leukemia patients during treatment. Int J Pharm Pharm Sci 2014;6(1):415-8.
6. De Benedittis M, Petruzzi M, Giardina C, Lo Muzio L, Favia G, Serpico R. Oral squamous cell carcinoma during long-term treatment with hydroxyurea. Clin Exp Dermatol 2004;29(6):605-7.
7. Budrukkar A, Muttagi S, Shahid T, Chatturvedi P, Banavali S, Laskar SG, *et al.* Second primary head and neck squamous cell cancers with aggressive behavior in patients with chronic myeloid leukaemia. Br J Oral Maxillofac Surg 2012;50(6):504-7.