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Case Report

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Skin Hypopigmentation in a Patient with Papillary Carcinoma Thyroid Treated with Sorafenib

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ABSTRACT

Sorafenib is an oral multikinase inhibitor approved for the treatment of advanced renal cell carcinoma, hepatocellular carcinoma and thyroid cancer. The dermatological side effects of sorafenib include palmar-plantar erythrodysesthesia, alopecia, skin rash, pruritus, xeroderma and erythema. Here we report a case of skin hypopigmentation related to sorafenib therapy.

A 60 year old male with papillary carcinoma of thyroid with cervical lymph nodal metastasis, post thyroidectomy and Iodine-131 ablation therapy developed lung metastasis. As the lesions were not iodine avid, he was started on sorafenib. After 4 months of treatment with 800 mg/day he developed hypopigmentation of the skin, prominently on the forehead, neck, hands and feet. He was also having grade 2 mucositis, so dose was reduced to 400 mg/day. Later his disease progressed, so sorafenib was discontinued. However, the hypopigmented lesions persisted.

Hypopigmentation as a potential side effect of sorafenib has rarely been reported in literature. Close collaboration between oncologists and dermatologists is needed to improve in the characterization and the management of cutaneous side effects of Sorafenib.

KEYWORDS: Thyroid Carcinoma; Sorafenib; Hypopigmentation.

INTRODUCTION

Sorafenib is an oral multikinase inhibitor which has antiangiogenic and proapoptotic activity. Sorafenib is a potent inhibitor of the C-RAF and B-RAF kinases, as well as the Vascular Endothelial Growth Factor Receptor-2 (VEGFR-2) and Platelet-Derived Growth Factor Receptor (PDGFR).[1] Such an inhibition works in two way- anti-proliferative activity targeting the tumor cell and indirectly through the inhibition of angiogenesis.[2] The mutational events in some genes including BRAF and RET that affect early stages of thyroid carcinogenesis has opened up new avenues for the use of targeted therapies.[3]

Sorafenib causes a variety of side effects including: gastrointestinal (diarrhea, nausea, vomiting, constipation), dermatological (rash, facial erythema), constitutional (fatigue, weight loss), cardiovascular (hypertension) and pulmonary events.[3,4] In most of the cases, the adverse events are grade 1-2 and decrease over time.[5] Observations from clinical trials and clinical practice with the long-term use of sorafenib suggests that unexpected adverse events and

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cumulative toxicity are of no major concer.[6] The cutaneous manifestations of sorafenib with its long-term use include rash/ desquamation, hand foot skin reactions, splinter subungual hemorrhages, pruritus, alopecia and xerosis. Dermatological events probably represent the main problem in the case of sorafenib-treated patients because of their higher frequency and negative impact on quality of life.[1]

CASE REPORT

A 60 year old male presented to the Head and Neck Department with complaints of a right sided neck swelling of 1 year duration. Physical examination showed a 2×1 cm hard nodule in the right lobe of thyroid. Ultrasound guided Fine Needle Aspiration Cytology (FNAC) of the thyroid was suggestive of papillary carcinoma of thyroid. He underwent total thyroidectomy after 1 month. The histopathology revealed multifocal papillary thyroid carcinoma, the tumor sizes being 4 cm × 3 cm × 2 cms on the right, 1 cm × 1 cm × 0.8 cms on the left lobe along with extrathyroidal extension, lymphovascular emboli and lymph node metastasis involving one node. A whole body Iodine scan showed presence of moderate residual thyroid tissue. Post operatively, he underwent radioiodine ablation with 1998 MBq of I-131, post therapy whole body imaging showed significant I-131 uptake in thyroid bed. He was then given external beam radiotherapy (60 Gy) to thyroid bed. After three months of radiotherapy, the patient was diagnosed with lung metastasis. So he was put on sorafenib 800 mg daily, after 3 months of therapy he developed mucositis, and hand foot syndrome. Then dose was modified to 400 mg/daily. After about one month he developed hypopigmented lesions on neck, back (Figure 1) and other sites like lips, forearms (Figure 2) and feet. Later he developed breathlessness and chest discomfort. Chest X-ray showed right sided pleural effusion. As it was recurring fast after tapping, it was decided to insert a flexible drain for draining pleural fluid. In view of progressive disease, sorafenib was discontinued and decided to put him on supportive care alone.

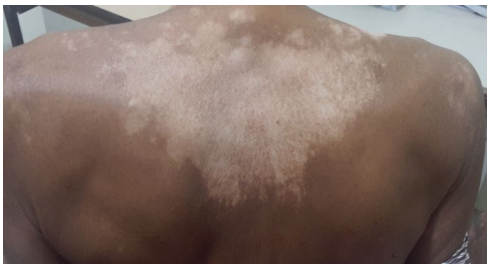

Figure 1: Hypopigmented patches over the back.

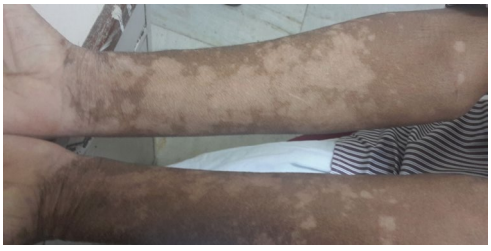

Figure 2: Hypopigmented patches over the forearm.

DISCUSSION

Sorafenib is mainly used for the treatment of hepatocellular carcinoma, renal cell cancer, thyroid cancer and gastrointestinal stromal tumor. The commonly reported dermatological side effects of sorafenib are HFS, erythema, itching, follicular rash and xerosis or skin dryness. Pigmentary changes have rarely been reported in literature.[7] The mechanism behind sorafenib induced hypopigmentation is poorly understood. Previously only one such case has been reported.[8] They reported hypopigmentation of skin induced by sorafenib along with diarrhea, desquamation of hands and feet, loss of hair over scalp, eye brows and moustache. It normalised after discontinuation of the drug. But in our patient the reaction did not resolve even after the complete discontinuation of sorafenib. A number of hypotheses have been proposed for the dermatologic side effects. But the exact pathogenesis these adverse events is still unclear.[3,9-11] One of the initial theories suggested that tyrosine kinase inhibition may affect keratinocyte proliferation and differentiation. These keratinocytes are highly proliferative cells in the epidermis that constitute an essential barrier against environmental injuries and prevent water loss from the body. Histological examination of specimens from patients who developed HFS, reveal keratinocyte damage and the presence of intracytoplasmic eosinophilic bodies and vacuolar degeneration eventually leading to necrosis.[12] Higher serum concentrations of the drug and its longer half life in the skin is responsible for cutaneous toxicities associated with sorafenib. Blockade of c-kit signaling in hair cause depigmentation and the active metabolite of the drug causes yellowish discoloration of skin.[13,14]

CONCLUSION

In the present era of targeted therapy, sorafenib is a widely used drug. Among the plethora of adverse events reported with sorafenib, hypopigmentation of skin is probably the rarest. A good understanding of the possible adverse events of the drug is essential in clinical practice. Although not alarming as some of the other adverse effects of sorafenib, hypopigmentation of skin can certainly affect the quality of life in our patients.

CONFLICTS OF INTEREST

There are no conflicts of interest.

CONSENT

The patient has provided written permission for publication of the case details.

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