INTRODUCTION

Sunitinib is a multikinase inhibitor approved for treatment of metastatic renal cell carcinoma (mRCC) in the first line and advanced gastrointestinal stromal tumor (GIST) in the second line. It is generally well tolerated, but sometimes, it exhibits a distinct pattern of novel side effects that require monitoring and management. Important known side effect of sunitinib includes fatigue, diarrhea, anorexia, skin toxicity, and hypertension which need special mention. Considering its effectiveness in first-line setting in mRCC and paucity of other good options, utmost efforts are made to continue it with identification of side effects which may require only slight dose modification or no dose alteration. We report here a 38-year-old male who was diagnosed as a case of mRCC and started on sunitinib at the diagnosis and developed whitish discoloration of eyebrows and body hairs after 3 months of starting sunitinib. In view of good overall response to treatment and no other significant toxicity, sunitinib was continued with good tolerability.

CASE REPORT

A 38-year-old male patient with no prior known medical or dermatological comorbidities or any drug allergy was diagnosed as a case of Stage IV renal cell carcinoma, clear cell type with multiple lung metastases. He underwent right nephrectomy followed by palliative therapy with sunitinib 50 mg OD in 4 weeks on and 2 week off therapy schedule (the dose approved by food and drug administration for the treatment of renal cell carcinoma and gastrointestinal stromal tumors). During outpatient...
follow-up, 3 months after starting the drug reevaluation revealed a radiological partial response to treatment on whole body positron emission tomography with marked clinical improvement, however, patient incidentally noticed discoloration of eyelashes while combing hairs. There was alternating band of depigmented and normally pigmented eyebrows correlating with on and off schedule of the drug [Figure 1]. Routine laboratory investigations including liver and renal function tests were normal. A clinical diagnosis of sunitinib-induced hair depigmentation was considered, and in view of no evidence of other toxicities and a clinical as well as radiological response, the patient was advised to continue on same treatment schedule and a more stringent monthly follow-up plan is advised.

DISCUSSION

Sunitinib is a multikinase inhibitor that selectively targets platelet-derived growth factor receptor α and β and Vascular endothelial growth factor receptor (VEGFR) 1, 2 and 3, the stem cell factor receptor c-Kit (CD117), Fms-like tyrosine kinase-3 receptor, and the RET receptor. It is currently approved as first-line therapy for the treatment of advanced RCC and for the treatment of advanced or recurrent GISTs in second-line therapy for those who failed imatinib in the first line. The relatively long half-life of sunitinib and its major metabolite allow for a once-daily dosing schedule. Considering toxicity profile, fatigue is the most common adverse effects of sunitinib seen in 50-70% of patients with advanced RCC and GIST. Other common adverse effects are diarrhea, anorexia, nausea and vomiting, oral changes, and bleeding events. Hypothyroidism has been described usually within the first 2 weeks of sunitinib therapy and its incidence increases progressively with the duration of therapy warranting close monitoring of thyroid functions during sunitinib therapy. Sunitinib may exert its hypertensive activity through a direct effect on the vasculature, while the most important cardiac adverse effect is left ventricular dysfunction. A variety of skin adverse effects have been described with the use of sunitinib such as hand-foot syndrome, yellow discoloration of the skin, dry skin, subungual splinter hemorrhages, acral erythema, and generalized skin rashes. Sometimes, these patients have yellowish discoloration of hair as well as urine. Hair depigmentation as a side effect of sunitinib therapy has been very unusual and has been reported very infrequently in past. Most of its toxicities are reversible and usually do not require discontinuation of drug however dose adjustments or interruptions may be required as per clinical demands. Similarly, cutaneous reactions are often seen within 3rd to 4th week of treatment and are usually dose dependent and reversible. Our patient developed hair discoloration after 3 months of starting sunitinib, and it was noticed incidentally without any other accompanying toxicity.

Mechanism of sunitinib-induced hair discoloration has not been clearly understood. Disruption of the interaction between the ligand stem cell factor with its class III receptor tyrosine kinase c-Kit (also called as stem cell factor receptor) has been shown to be associated with hair depigmentation. Experiments with mice suggested that sunitinib directly inhibits melanocytes function rather than their migration, development, or survival. Similar pattern of hair discoloration has been well described previously in literature with other tyrosine kinase inhibitors such as dasatinib. Interestingly similar pattern of hair discoloration has been described with anticytotoxic T-lymphocyte antigen 4 inhibitors used in the treatment of metastatic melanoma, and in those patients, hair discoloration was associated with significant durable treatment response as compared to those who did not have such discoloration. There is no such correlation described in past with anti-VEGF agents however succession of depigmented and normally pigmented bands of hair may correlate with on and off periods of treatment. Our patient was continued on same treatment in view of clinical and radiological response.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.
Agrawal, et al.: White eyebrows as a side effect of sunitinib therapy

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Faivre S, Delbaldo C, Vera K, Robert C, Lozahic S, Lassau N, et al. Safety, pharmacokinetic, and antitumor activity of SU11248, a novel oral multitarget tyrosine kinase inhibitor, in patients with cancer. J Clin Oncol 2006;24:25-35.
2. Papaetis GS, Syrigos KN. Sunitinib: A multitargeted receptor tyrosine kinase inhibitor in the era of molecular cancer therapies. BioDrugs 2009;23:377-89.
3. Wolter P, Stefan C, Decallonne B, Dumez H, Bex M, Carmeliet P, et al. The clinical implications of sunitinib-induced hypothyroidism: A prospective evaluation. Br J Cancer 2008;99:448-54.
4. Kapiteijn E, Brand A, Kroep J, Gelderblom H. Sunitinib induced hypertension, thrombotic microangiopathy and reversible posterior leukencephalopathy syndrome. Ann Oncol 2007;18:1745-7.
5. Pragasam V, Verma R, Vasudevan B. Sorafenib and sunitinib: A dermatologist's perspective. Indian Dermatol Online J 2014;5:1-3.
6. Moss KG, Toner GC, Cherrington JM, Mendel DB, Laird AD. Hair depigmentation is a biological readout for pharmacological inhibition of KIT in mice and humans. J Pharmacol Exp Ther 2003;307:476-80.
7. Sun A, Akin RS, Cobos E, Smith J. Hair depigmentation during chemotherapy with dasatinib, a dual Bcr-Abl/Src family tyrosine kinase inhibitor. J Drugs Dermatol 2009;8:395-8.
8. Pavlick AC, Ott PA, Kammaj R, Madden KM, Sorfic C, Escano C, et al. Hair depigmentation as an indicator of durable response to CTLA-4 therapy. J Clin Oncol 2010;28 15 Suppl:8571.