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Rapid Hair Depigmentation Following Treatment with Pazopanib for Metastatic Renal Cell Carcinoma: Case Report

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***Abstract*— Pazopanib is an orally available multietyrosine kinase inhibitor that is able to counteract angiogenesis and reduce cell growth and survival. The therapeutic efficacy and safety of pazopanib in patients with metastatic renal cell carcinoma (mRCC) were demonstrated in phase 3 randomized controlled trials versus placebo or sunitinib.**

Pazopanib is generally well tolerated, with an acceptable and manageable safety profile in this population. Hair hypopigentation is a common side effect of pazopanib therapy which usually develops gradually during few months of therapy.

In this review, we will describe one case of rapid hair depigmentation associated with pazopanib supplemented with pictures.

***Index Terms*— Pazopanib, Renal cell carcinoma, tyrosine kinase inhibitor, hair depigmentation.**

I. INTRODUCTION

Pazopanib is an oral, small-molecule tyrosine kinase inhibitor (TKI) targeting vascular endothelial growth factor (VEGF) receptors (VEGFR-1, − 2, and − 3), platelet-derived growth factor (PDGF) receptors (PDGFRalpha and -beta), fibroblast growth factor receptor, and KIT [1].Pazopanib is approved by the Food and Drug Administration (FDA) as a first and second line treatment for late stages of RCC and nonadipocytic soft-tissue sarcoma, respectively [2-3].
Treatment with pazopanib has also been explored in a range of other tumor types, such as thyroid cancer [4], gastrointestinal stromal tumors [5] and ovarian cancer [6].
Pazopanib provides a higher quality of life and lower incidence of side effects compared to other VEGF inhibitors. The most common adverse events related to pazopanib include fatigue, nausea, diarrhea, hypertension, anorexia, hair depigmentation, and hepatic toxicity [8-3]. Pazopanib can also cause a variety of adverse reactions including, hypothyroidism, bone marrow toxicity, heart failure, myocardial ischemia, and arterial thromboembolic events [9].
We report a case of a patient with mRCC who experienced rapid hair depigmentation after the second cycle of pazopanib.

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II. CASE REPORT

A 26-year-old male patient presented to the consultation with pain in the right hypochondrium that had been evolving for 3 months and was associated with an deterioration of general condition.
Computed tomography (CT) of the chest, abdomen, and pelvis showed a 10.5 × 9.2 × 8.5 cm irregular mass of the left kidney associated with multiple bone and hepatic metastasis.
The patient underwent a liver biopsy and was diagnosed with renal clear cell carcinoma with hepatic and bone metastasis.
He was treated with pazopanib 800 mg once daily, two months after the beginning of treatment with pazopanib, the patient began to develop hair depigmentation (figure 1), he has now been treated with pazopanib for 9 months, although no other adverse events associated with pazopanib were observed. His hair stayed depigmented throughout this period.

Figure1. Hair depigmentation was observed 2 months after the initial treatment with pazopanib.

III. DISCUSSION

Pazopanib is a TKI that inhibits vascular endothelial growth factor (VEGF) and platelet-derived growth factor receptors on cancer cells and vascular endothelial cells. Hence, stopping the proliferation of tumor cells and development of tumor blood vessels [10]. In patients with locally advanced or metastatic RCC, pazopanib increased progression-free survival (PFS) from 4.2 to 9.2 months compared with placebo, with a hazard ratio of 0.46 (95% confidence interval 0.34–0.62; p\0.0001) [8].

Most of the adverse events resulting from the treatment are of grade 1/2 , among those with toxicity of grade 3 or higher, most frequent are diarrhea, hypertension, fatigue, and, above all, hepatic toxicity [11-8]. Hair depigmentation has been reported in response to therapy with multitargeted receptor TKIs such as sunitinib, pazopanib and imatinib due to their inhibition of c-kit [12-13].

Hair pigmentation is dependent on the transfer of melanin produced in the neural crest derived melanocytes to precortical hair matrix keratinocytes, which are then incorporated into the growing hair shaft [14]. Hair pigmentation is tightly regulated by several factors [15-16]. Stem cell factor (SCF) and its tyrosine kinase receptor c-kit are critically important for the migration, proliferation, and differentiation of melanoblasts during embryogenesis [17-18].

Hair depigmentation is thought to be caused by blockade of c-Kit signaling, which is important for melanocyte proliferation, differentiation, and proper pigment production [10]. This is supported by the observation that human mutations in the encoded tyrosine kinase region of c-kit cause piebaldism, an autosomal dominant disorder characterized by white hair and hypopigmented skin patches on the forehead, torso, and extremities [19].

Reported incidence of hair colour changes in patient treated with pazopanib is about 35% according to drug-safety studies. In a few reported cases, hypopigmentation was first noted after 1–5 cycles of therapy and it gradually developed to maximum after 6–10 cycles [20].TKI therapy associated hypopigmentation appears to represent a dose and duration of therapy dependent phenomenon in response to TKI therapy and an indicator of successful targeting of c-Kit [21].

Hair hypopigmentation can impair psychosocial functioning and negatively impact on patients quality of life, sometimes leading to dose reduction or even discontinuation of therapy. This is one of the clinical case reports to make aware about this side effect of pazopanib to the treating oncologist.

IV. Conclusion

Pazopanib is a molecular targeted drug approved for the treatment of advanced RCC. Although pazopanib exhibits efficacy in patients with advanced RCC, it is associated with various adverse events, including cutaneous complications, with hair depigmentation being one of the most common symptoms. Exact pathophysiology of this phenomenon is still not clear. Knowledge and management of its side effects are essential to reduce patient's discomfort and avoid unnecessary treatment interruption.

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