infection and predominantly occur in children and adolescents. However, HV-like eruption is occasionally observed in adults aged older than 60 years: one case was that of a 65-year-old woman with orogenital ulcer, whose symptoms were well controlled with corticosteroid and famciclovir[3], whereas the other was a case of a 74-year-old man whose condition deteriorated rapidly and who died within 3 months of diagnosis[4]. Thus, we report a case of HV-like eruption in an older adult manifesting chronic feature. Furthermore, the disease entity needs to be clarified and the disease properties need to be investigated in future studies.

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Gray Hair Associated with the Multitargeted Receptor Tyrosine Kinase Inhibitor Pazopanib

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Dear Editor:

A 38-year-old man was referred to our hospital with a left renal mass and multiple paraspinal and rib masses. The diagnosis was clear cell renal cell carcinoma with multiple bone metastases with soft tissue formation, and multiple lymph node metastases in both histological and radiological evaluations. He was treated with 800 mg pazopanib once daily. During the treatment, he began to notice a gradual increase in scalp hair loss and a change in his hair texture. Before starting the therapy, he had coarse, black hair (Fig. 1A), and denied ever dying his hair or having a history of alopecia. By the fifth month of therapy, nearly all of his scalp hair had turned white, whereas his other body hair had changed little (Fig. 1B, C). In addition, his hair texture changed from coarse to fine. The therapy was discontinued after 8 months because of disease progression, and the new hair growth was pigmented. On the basis of these findings, we concluded that the hair de-

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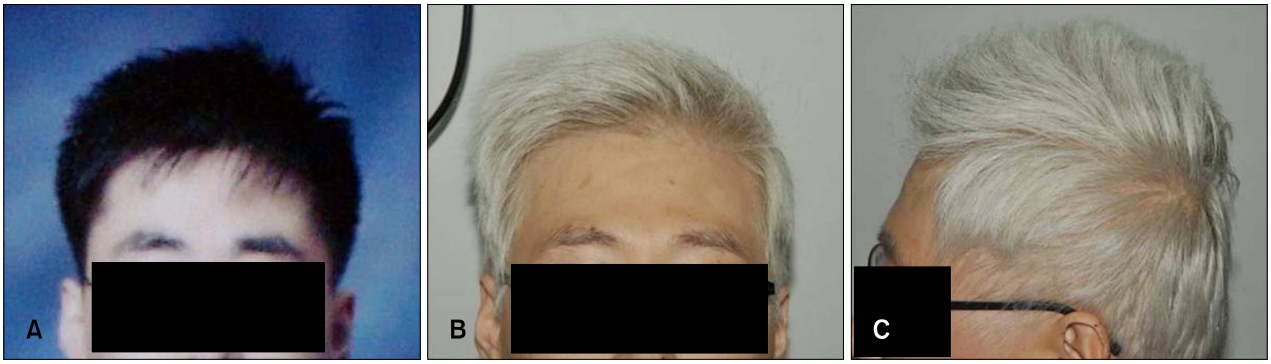

Fig. 1. Hair changes before (A) and after (B and C) the treatment with pazopanib.

pigmentation and changes were induced by pazopanib.

Hair pigmentation is finely regulated by several factors including the interaction of the ligand stem cell factor with its receptor tyrosine kinase, c-kit. The stem cell factor/c-kit interaction is crucial for embryonic pigment development. The stem cell factor and c-kit map to the steel and the white spotting loci, respectively, and mutations in either of these genes result in hair depigmentation in mice. Treatment with anti-c-kit antibody during murine embryogenesis also leads to coat depigmentation. In humans, c-kit mutation is associated with an autosomal dominant disorder of melanocyte development, piebaldism, which is characterized by leukoderma and poliosis. An interruption of stem cell factor/c-kit signaling pathway could result in hair depigmentation and texture change, although the exact mechanism is yet unkown[1,2]. In addition, Moss et al.[2] demonstrated that hair depigmentation can serve as a biological readout for c-kit inhibition in mice and humans.

Pazopanib, which has been approved for the treatment of patients with metastatic renal cell carcinoma, is an orally bioavailable molecule that inhibits multiple receptor kinases, including c-kit[3]. The incidence of hair color changes in patients treated with pazopanib is about 30% in metastatic renal cell carcinoma[4,5]. In addition, another multitargeted receptor tyrosine kinase inhibitor, sunitinib, which also inhibits c-kit, induces changes in hair color in 10% of patients taking sunitinib[4]. Hartmann and Kanz[6] reported periodic hair depigmentation in a patient treated with sunitinib (the depigmented part corresponded to the sunitinib treatment schedule: 4 weeks-on during the growth of the depigmented part of the hair followed by 2 weeks-off during the growth of the pigmented part of the hair), suggesting that the recurrent change in hair pigmentation might be due to the temporary inhibition of c-kit throughout the sunitinib treatment. As the use of pazopanib and other multitargeted kinase inhibitors is increasing in oncology patients, clinicians need to be familiar with various cutaneous toxicity effects, including hair changes.

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