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CASE REPORT

A Case Report of Multiple Capillary Hemangioma in a Chronic Myeloid Leukemia Patient Taking Tyrosine Kinase Inhibitors

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A capillary hemangioma is a vascular tumor with small capillary sized vascular channel. Multiple capillary hemangioma in relation with drugs have been rarely reported. Here in, we report a case of multiple capillary hemangioma in patient diagnosed with chronic myeloid leukemia who received tyrosine kinase inhibitors (TKIs). Histopathological findings have shown capillary proliferation in the upper dermis, which is consistent with capillary hemangioma. Since TKIs can paradoxically activate the MEK/ERK pathway which is required for angiogenesis, we presumed that the lesions as the cutaneous side effects of TKIs. **(Ann Dermatol 33(3) 278～280, 2021)**

-Keywords-
Capillary hemangioma, Chronic myeloid leukemia, Dasatinib, Imatinib, Nilotinib

INTRODUCTION

Hemangioma is a benign blood containing vascular tumor that shows proliferation of the endothelial cells[1]. Depending on the size of the vascular channel, a tumor with small capillary sized vascular channel is classified as a capillary hemangioma[1]. A capillary hemangioma is primarily papular or nodular in shape, and multiple capillary hemangioma in relation with drugs have rarely been reported[2]. In the present case, we report multiple capillary hemangioma developed after taking bcr-abl tyrosine kinase inhibitors (TKIs).

CASE REPORT

A 57-year-old male presented with multiple erythematous papules and plaques on the trunk, which developed two months ago. Ten months ago, he was diagnosed with bcr-abl positive chronic myeloid leukemia (CML) and was treated with nilotinib (300 mg twice daily for 7 weeks), a bcr-abl TKI. Seven weeks later, nilotinib was changed to dasatinib, an inhibitor of bcr-abl kinase and SrC family kinase, due to the exfoliative skin rash. Dasatinib was administered 50 mg once daily for 10 weeks. Dasatinib treatment was then interrupted because of neutropenia for a month, and then treatment was restarted with imatinib mesylate, which binds to an ATP-binding site on bcr-abl, KIT, and platelet-derived growth factor receptors[3]. Imatinib mesylate was administered 100 mg once daily for two weeks. Multiple erythematous papules and plaques were found by the time around the start of imatinib treatment. Physical examination revealed approximately 75 erythematous to violaceous round or rod-shaped papules or plaques mainly on the anterior and lateral trunk (Fig. 1). We received the patient's consent form about publishing all photographic materials. According to the patient, the lesions grew bigger over time, with no specific symptoms.

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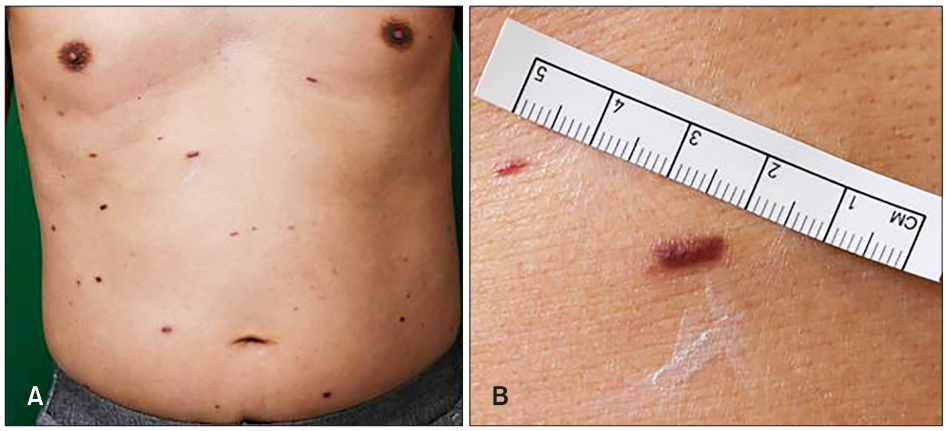

Fig. 1. (A, B) Multiple round or rod-shaped erythematous papules and plaques on the trunk.

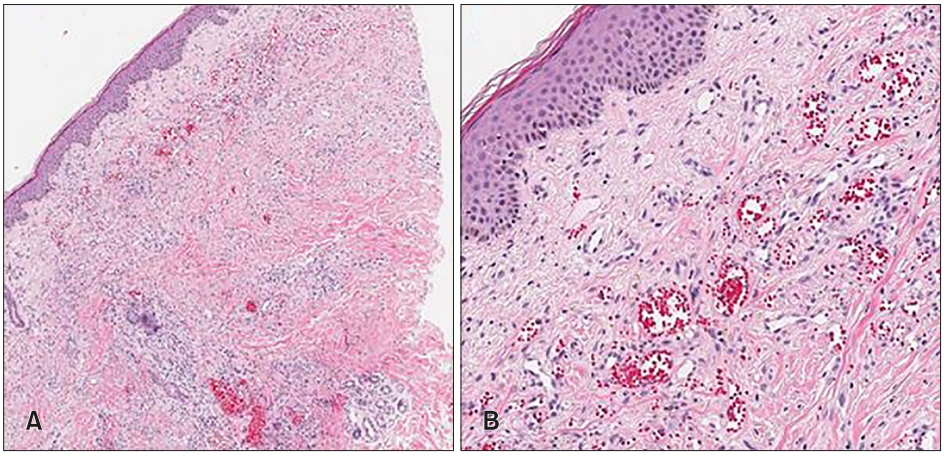

Fig. 2. (A) Diffuse capillary proliferation in the upper dermis, and vascular dilatation involving mid-dermis (H&E, ×40). (B) Capillary proliferation involving the upper dermis (H&E, ×200).

The lesions were not in the typical nodular shape, but rather rod like, and that made us suspect the lesions as scars. However, the fact that multiple lesions developed without trauma was inconsistent with the clinical manifestations of scars. Therefore, biopsy was performed for accurate diagnosis. Skin biopsy was done for the erythematous plaque on the chest. The biopsy revealed capillary proliferation in the upper dermis, which is consistent with capillary hemangioma (Fig. 2). No other capillary hemangioma were found in the abdomen and pelvic computed tomography scan. The cutaneous lesions were gradually improved without any special treatment.

DISCUSSION

The cutaneous side effects of TKIs include superficial edema, maculopapular eruptions, and pigmentary changes etc[4]. Also, few cases of capillary proliferative lesions caused by these drugs have been reported. A case of scrotal hemangioma developed after taking sunitinib[5], and a case of periungual pyogenic granuloma following imatinib administration[6] had been reported. In the present case, multiple capillary hemangioma, which had never occurred before, developed after taking TKIs. As the lesions began to develop after taking TKIs, cutaneous side effects of the drugs were suspected. We suspect that the TKIs caused paradoxical angiogenesis. Nilotinib, dasatinib, and imatinib are all drugs with anti-angiogenic effect, which are usually used as a treatment for angiogenic CML cells[7,8]. They are known to reduce angiogenic factors such as vascular endothelial growth factor in CML patients[7]. However, it is reported that TKIs can paradoxically activate the MEK/ERK pathway, which is required for angiogeneseis[9]. In an experiment that studied whether various protein kinase inhibitors affected MEK/ERK pathways, the authors found that imatinib, nilotinib, dasatinib paradoxically stimulated MEK/ERK phosphorylation[10]. Since Raf-MEK-ERK signal transduction pathway is required for angiogenesis[11], we could consider the possibility that such mechanism have induced paradoxic angiogenesis, causing multiple capillary hemangioma. As a similar case, previous literature has reported an occurrence of Kaposi sarcoma following an imatinib mesylate administration in a CML patient[12]. The mechanism underlying the develop-

ment of Kaposi sarcoma was not clear. However, according to the adverse drug reaction probability scale, the score estimated that the development of Kaposi sarcoma was probably associated with the imatinib treatment[12]. In the present case, Kaposi sarcoma could be excluded, because only the capillary proliferation in the upper dermis was observed in the biopsy, and no tissue findings that would suspect Kaposi sarcoma such as slit like vascular space, and proliferating spindle cells were found. In addition to TKIs, factors that may have caused hemangioma in this case include history of exfoliative dermatitis and leukemia. We cannot exclude these factors, because there was a case report of multiple hemangioma in relation with exfoliative dermatitis, and another report with underlying leukemia[13,14]. These reports however, did not clarify the mechanism of development of hemangioma by the underlying diseases. The lesions developed after the administration of TKIs, and they gradually improved after drug discontinuation. Considering this temporal relationship, it is reasonable to consider the possibility that the secondary neoplasms were caused by TKIs. To the best of our knowledge, this is the first case to report of multiple hemangioma occurred after the use of TKIs. It is meaningful that we added possible cutaneous side effects of TKIs.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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DATA SHARING STATEMENT

Research data are not shared.

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