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LETTERS TO THE EDITOR

Oral itraconazole for the treatment of giant tufted angioma with hair loss arising during pregnancy: A case report

Dear Editor,

Tufted angioma or Nakagawa angioblastoma is a benign angiogenic neoplasm of pediatric populations rarely reported in adulthood and pregnancy.[1,2] We report a case of huge tufted angioma arising during pregnancy with severe pain and hair loss, resulting in the improvement of the symptoms and hair regrowth by oral itraconazole.

A 35-year-old Chinese woman 1 month after her third childbirth presented with progressive papules and plaques on the nape and occiput, accompanied by severe pain for 3 months. She started developing papules and plaques at the nape during her 8-month pregnancy, which proliferated and extended to the occiput with hair loss and severe pain. She vaginally delivered a healthy girl. The lesions and pain persisted after delivery. She reported no drug history during gestation and post-partum. Physical examination revealed a cluster of fuscous infiltrating plaques and nodules sized approximately 4 cm × 10 cm, annularly and unevenly distributed over the nape and occiput with hair loss (Fig. 1a). Histopathology showed a "cannon ball-like" appearance (Fig. 1b), demonstrating many scattered, clearly limited, round cellular lobules in the dermis, and subcutaneous area composed of hyperplastic vascular endothelial cells and perivascular cells surrounding dilated lymphatic vessels (Fig. 1c). Immunohistochemistry revealed positive capillary aggregates for CD31 (Fig. 1d), CD34 (Fig. 1e), D2-40 (Fig. 1f) and positive perivascular cells for smooth muscle actin (Fig. 1g), but was negative for desmin and S100 protein. Diagnosis of tufted angioma was confirmed.

After detailed explanation and signed informed consent was obtained, itraconazole capsules (Xi'an Janssen Pharmaceutical, Xi'an, China) 200 mg twice daily and quitting of breast-feeding was initiated. The pain was significantly relieved after 3 days.

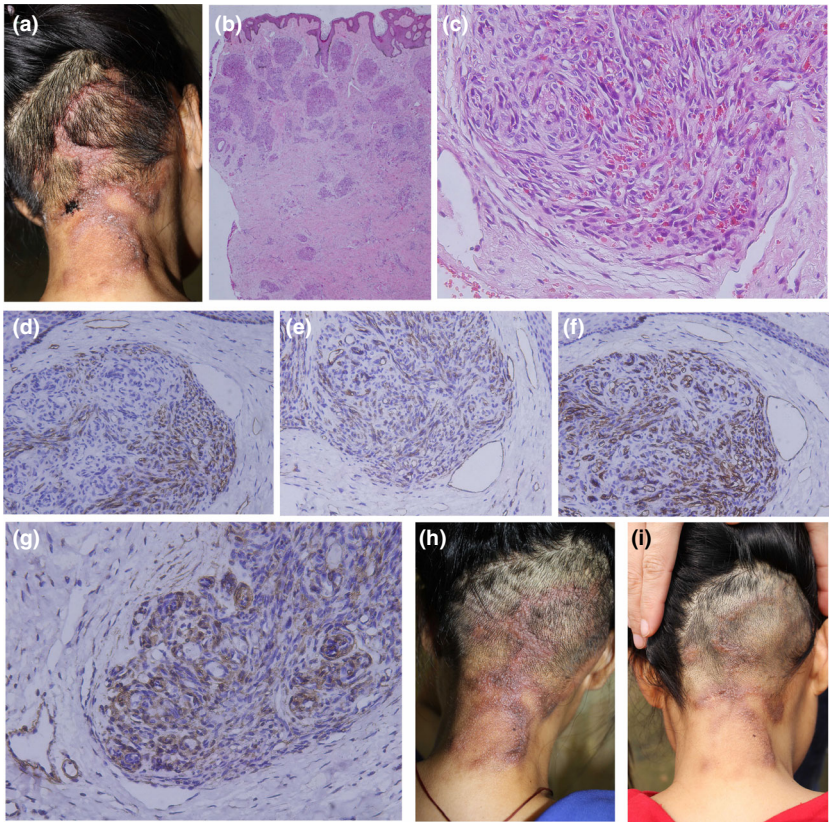

Figure 1. (a) Lesions prior to treatment. (b) Histopathology showing a "cannon ball-like" appearance (hematoxylin–eosin [HE], original magnification ×20). (c) Vascular tufts composed of hyperplastic vascular endothelial and perivascular cells (HE, ×200). Immunohistochemistry showing the spindle tumor cells positive for (d) CD31 and (e) CD34 (×200). (f) Lymphatic vessels were positive for D2-40 (×200). (g) Perivascular cells were positive for smooth muscle actin (×200). (h) The lesions improved after 2 weeks of oral itraconazole. (i) Sustained clinical improvement with hair regrowth after 6 months of itraconazole withdrawal was achieved.

Correspondence: Yuping Ran, M.D., Ph.D., Department of Dermatovenereology, West China Hospital, Sichuan University, 37 Guoxue Alley, Xiao Tian Zhu, Wuhou, Chengdu, Sichuan 610041, China. Email: ranyuping@vip.sina.com

Two weeks later, the plaques slightly flattened (Fig. 1h) and the pain disappeared. Hair regrowth was observed after 1 month. Itraconazole was discontinued after 3 months. Significant portions of the lesions disappeared. Liver function and blood routine were normal before and after the treatment. After 6 months of itraconazole withdrawal, sustained clinical improvement (Fig. 1i) was observed.

The pathogenesis of tufted angioma is unclear and may be associated with some vascular growth factors. Pregnancy could be a predisposing factor for vascular proliferation, indicating estrogen promoting its development.[1,2] Tufted angioma may occur in hypertrichosis and hyperhidrosis;[2] however, hair loss was never reported. It was regretful that the histopathology of hair loss was not collected. Complete surgical excision is recommended for a small lesion. Topical rapamycin, cryotherapy, electron beam radiation and pulsed dye laser are also applied. Systemic administration includes corticosteroid, aspirin, propranolol, interferon (IFN)-α, rapamycin and vincristine. Ran *et al.*[3,4] first reported successful treatment of oral itraconazole with 5 mg/kg per day for infantile hemangiomas, and found that itraconazole significantly reduced platelet-derived growth factor (PDGF)-D level, resulting in suppression of PDGF receptor-β activation, and inhibition of its downstream effectors, such as PI3K, Akt, 4E-BP1 and p70S6K.[5] However, the therapeutic effect of itraconazole for tufted angioma is still unclear. Itraconazole is an antifungal drug with good tolerance, unlike corticosteroid, propranolol and IFN-α which have side-effects, and rapamycin being an infrequent drug. Therefore, itraconazole can be used for the treatment of large areas and painful tufted angioma.

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Wei WU,[1] Jianqiang SHI,[1] Zhaojun LI,[1] Ding LI,[1] Shuhui DOU,[1] Sushmita PRADHAN,[2] Xin RAN,[2] Yuping RAN[2]

[1]*Department of Dermatovenereology, Affiliated Hospital of Guangdong Medical University, Zhanjiang, and* [2]*Department of Dermatovenereology West China Hospital, Sichuan University, Chengdu, China*

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Amelanotic melanoma of the nail apparatus with regression previously diagnosed as melanoma of unknown primary site with a lymph node metastasis: A case report

Dear Editor,

Subungual melanoma is a distinct type of acral melanoma, and its incidence is higher in the Asian population than in others.[1,2] Common manifestations are melanonychia, periungual pigmentation and dystrophic nail change. However, there are diagnostic challenges after spontaneous regression. The management of such cases has not been fully discussed. Here, we present a case of amelanotic subungual melanoma with regression, previously diagnosed as melanoma of unknown primary site with a regional metastasis.

A 68-year-old Japanese man was referred to us with a diagnosis of nodal melanoma of unknown primary site. Computed tomography for staging his prostate cancer had revealed an enlarged right axillary node in the previous hospital. Histopathological diagnosis was melanoma (Fig. 1a–c) and the *BRAF* was wild-type, but no primary lesion was found.

Careful physical and dermoscopic examination showed a thin and faint melanonychia with mild onycholysis in the right thumb (Fig. 1d,e). We administered a precise interview and the patient remembered a previous history of onychomycosis in the thumb. Indeed, a picture from 3 years ago showed severe nail dystrophy without pigmentation (Fig. 1f). As the amelanotic and dystrophic nail had been in part resolved after application of a topical antifungal agent, he believed it was onychomycosis. Considering left nail lesions and the presence of the regional metastasis, we suspected them as the primary site of amelanotic subungual melanoma.

Correspondence: Yo Kaku, M.D., Department of Dermatology, Kyoto University Graduate School of Medicine, 54 Shogoin-Kawahara, Sakyo, Kyoto 606-8507, Japan. Email: montreux77@live.jp