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Multifocal Infantile Hemangiomas Treated by Oral Itraconazole: A Case Report

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Abstract

We describe a case of a 2-month-old girl presented with more than 60 papules and nodules of hemangiomas involving the skin of the sclera, endocanthion, lower lip, and labium majus pudenda without visceral hemangiomas and laboratory abnormality. A skin biopsy showed numerous scattered, clearly limited, irregular cellular lobules in the dermis circumvoluted into capillaries comprising incomplete vessel walls, which was consistent with a diagnosis of multifocal cutaneous infantile hemangioma. Oral treatment with itraconazole (5mg/kg/day) for 26 weeks resulted in predominantly involution of the skin hemangiomas. We would like to report a rare case of multifocal cutaneous infantile hemangioma, successfully treated with oral itraconazole.

Key words: Infantile hemangiomas; Itraconazole; Propranolol.

Introduction

Infantile Hemangioma (IH) is a benign angiogenic neoplasm of pediatric populations. Infantile hemangiomas are categorized into localized, segmental, and multifocal types, the latter subtype occurring rarely. Infants with multifocal IHs are recognized to have a higher risk of extracutaneous hemangiomas, with the liver being the most affected organ. Propranolol is the first-line therapy for IH, and recent evidence suggests that a dose of 3 mg/kg per day for an average of 6 months is the most effective and well tolerated.[1] We report a 2-month-old girl presented with more than 60 lesions of IH involving the skin of the sclera, endocanthion, lower lip, and labium majus pudenda without visceral hemangiomas, successfully cured by oral itraconazole.

Case Report

A 2-month-old girl was presented at birth with beefy red papules and plaques on the scalp, face, trunk, extremities, and foot soles without abnormal development. She was born full-term natural delivery, weighing 3 kg. Skin lesions rapidly enlarged in size and increased in numbers over time. Physical examination revealed more than 60 red, isolated, 0.5- to 2-cm soft papules and plaques all over the body, including the

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sclera, endocanthion, lower lip, and labium majus pudenda (Fig. 1a). Histopathology showed numerous scattered, clearly limited, irregular cellular lobules in the dermis circumvoluted into capillaries comprising incomplete vessel walls. Blood coagulation, blood routine, thyroid function tests, liver and renal function examinations were within normal limits. The brain's magnetic resonance imaging and B-mode ultrasound of the liver and spleen showed no active vascular tumors. Multifocal IHs was diagnosed.

In view of the multiple involvements of hemangiomas on the lower lip and labium majus pudenda, resulting in ulceration; and hemangiomas on the sclera causing vision impairment, systemic therapy was chosen. Oral propranolol, commonly used for the treatment of IH is considered the first-line treatment since 2008.[1] However, they may present with possible side-effects that need to be monitored by an electrocardiogram. In view of a 2-month-old infant, treatment with Oral Itraconazole (Xi'an Janssen Pharmaceutical, Xi'an, China) 5 mg/kg per day was initiated after a detailed explanation to her mother and signed informed consent. 4 weeks later, the papules and the plaques all over the body slightly flattened and darkened without new involvement of hemangiomas. Hemangiomas flattened and shrank after 12 weeks. However, the parents refused to follow-up examining. Itraconazole was discontinued after 26 weeks, and until then, the cumulative dose was 5600 mg. The major portion of the lesions disappeared, as known through frequent telephone consultations. After 16 weeks of itraconazole withdrawal, a significant portion of the lesions disappeared without recurrence. Blood routine and liver function examinations were normal before, during and after the treatment. After 66 weeks of Itraconazole withdrawal, hemangiomas still regressed persistently (Fig. 1b).

Discussion

Propranolol is the first choice for the systemic treatment of infantile hemangiomas. However, it is presented with intolerance, poor effectiveness, and recurrence.[1-3] In recent years, there have been reports about oral itraconazole successfully treating IH. [4-8] It was found that down-regulation of the PDGF-D/PI3K/Akt/mTOR pathway with regression of infantile hemangioma may correlate to itraconazole's effective treatment.[9] Two prospective parallel clinical trials,[7,8]

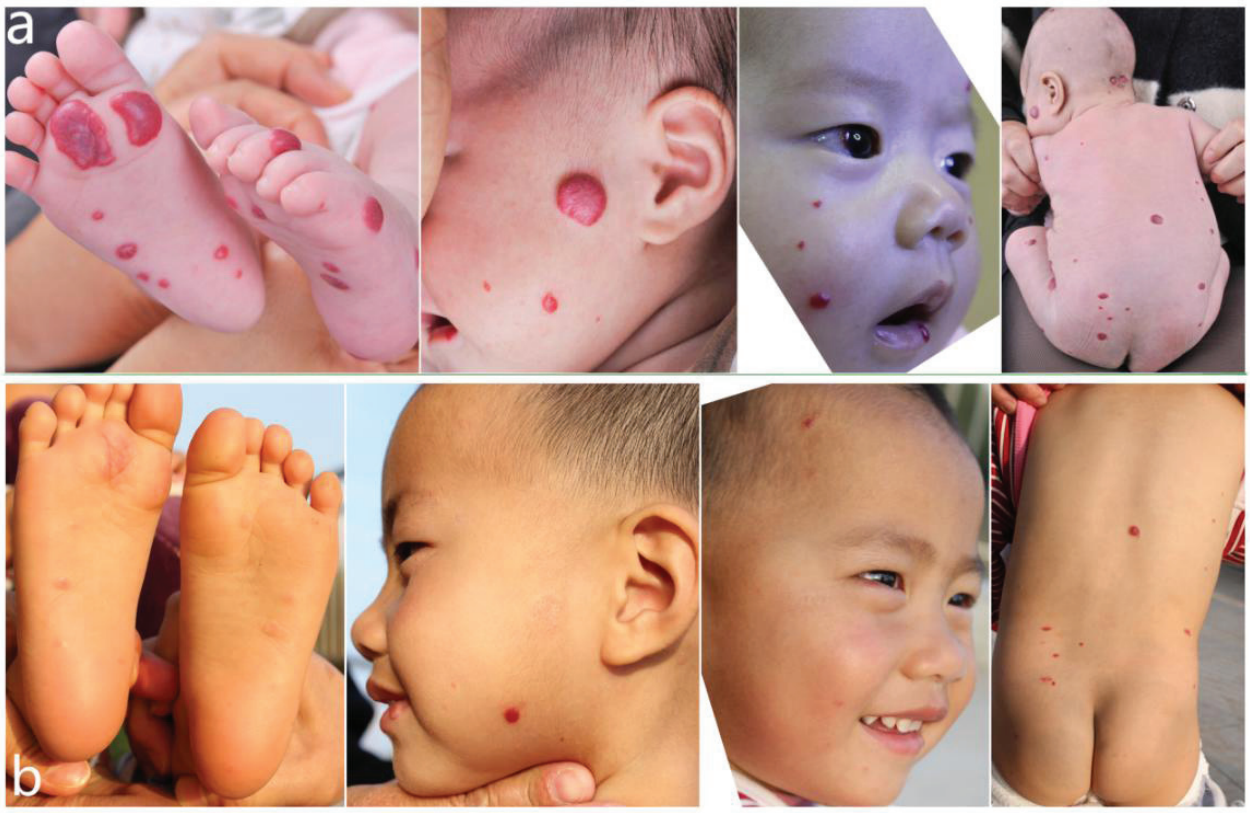

Figure 1: Clinical response of a 2-month-old girl with multiple infantile hemangiomas to oral itraconazole therapy. (a) Patient at baseline. From left to right: feet, left cheek, right cheek and back of trunk. (b) After 66 weeks of itraconazole withdrawal. From left to right: feet, left cheek, right cheek and back of trunk.

(oral itraconazole versus oral propranolol) showed that oral itraconazole and propranolol are effective and safe in treating hemangioma. Despite the biggest challenge of more than 60 multiple papules and plaques all over the body in a 2-month-old child, remarkable achievements after oral itraconazole were acquired. The possible side-effects of propranolol include hypotension, bradycardia, hypoglycemia, acrocyanosis, sleep disturbances, diarrhea, emesis, restlessness, etc.[1] Contraindications of propranolol are cardiac diseases and bronchial asthma. ECG monitoring, blood sugar, blood pressure and pulse are monitored in each visit. However, itraconazole is a common triazole antifungal drug that has been applied clinically for more than 20 years and has confirmed its safety in infants.[10] Itraconazole only requires routine monitoring of liver function, which is considered a more convenient and safe treatment for multiple IH.

Conclusion

This case is noteworthy for its multiple infantile hemangiomas in an infant successfully treated by oral itraconazole without any side effects. Therefore, we suggest itraconazole could be a safe choice to replace propranolol to treat multifocal IH to avoid possible intolerance and frequent monitoring, especially in remote areas with inadequate medical facilities, lack of infant ECG monitoring and other necessary equipment.

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