Itraconazole Oral Solution Cured a Case of Infantile Hemangioma on Scrotum and Penis with Ulcer: Monitoring by Dermoscopy

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Abstract

Infantile hemangiomas (IHs) are characterized by endothelial cell hyperproliferation and blood vessel architecture. Itraconazole (ITR), a clinically used antifungal drug, was found to possess potent antiangiogenic and anticancer activity that is unique among theazole antifungals.

Herein, we describe a case of a male infant who presented with hemangiomas on his scrotum and penis with ulceration and pain and was successfully treated, which was monitored by dermoscopy, with itraconazole oral solution.

Keywords: Infantile Hemangioma; Itraconazole Oral Solution; Dermoscopy; Ulcer

Abbreviations

IHs: Infantile Hemangiomas; ITR: Itraconazole

Introduction

Infantile hemangiomas (IHs) are the most common soft tissue tumors of infancy and occur in 4% - 10% of children younger than 1 year of age [1]. Spontaneous regression can be expected in the majority of hemangiomas, so watchful waiting without any medical intervention is the best management. However, medical treatment is required in 10% - 20% of cases due to the presence of complications such as ulcerations, infections, hemorrhage and so on [2,3]. Early recognition and treatment of critical lesions help in preventing or minimizing complications. As a series of cases were successfully treated with Itraconazole (ITR) in our clinic [4,15], we attempted to use ITR, after signing informed consent, in the treatment of IH with complications or in children whose parents requested treatment.

In this report, we describe a case of an IH in a 2-month-old boy who presented with a 40 days history of an ulcer on his hemangioma and was successfully treated with ITR oral solution 5 mg/kg per day.

Reported Case

A 2-month-old boy, weighing 5 kg, presented with a 40 days history of an ulcer on the hemangioma, which was a little red dot on his left scrotum 10 days after birth and then kept growing and involved the penis (Figure 1a1). Before visiting our clinic, the baby was treated with povidone-iodine topically but the ulcer did not improved. The baby always cried when it was touched. The microscopic examination and culture of fungi infection were negative. Dermoscopic examination, which fixed on the same target (Figure 1a, black arrow), was used as an indicator for evaluation of treatment efficacy showing more intensive vascular network and outward capillary branches which were the hints of growing trend (Figure 1a2). After detailed explanation to the parents, they signed informed consent and agreed to treat both ulcer and hemangioma of the baby by ITR oral solution (Belgium Janssen Pharmaceutical Company) with a dosage of 5 mg/kg per day.

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ITR oral solution was given for 2 months and topical wet dressing with saline was administrated for 2 weeks. After 30 days of treatment, the erythema faded partly and the ulcer healed mostly (Figure 1b1). Dermoscopic feature showed darker vascular network and less capillary branches (Figure 1b2). After 50 days, the ulcer healed, the erythema on the scrotum had mostly disappeared and dermoscopy showed instict vascular network (Figure 1c1 and 1c2). After 60 days of a bottle of ITR oral solution (a total dose of 1500 mg) the lesion was seen degrading obviously, then the treatment ended. More than 3 months after the end of the treatment, the erythema on the scrotum had significantly disappeared and the vascular network involuted mostly under dermoscopy. In addition, the hemangioma on the penis became smaller than before (Figure 1d1 and 1d2). In the course of oral ITR, the patient’s hepatic and renal function remained normal and no adverse reaction was observed.

**Figure 1:** Clinical response and dermoscopic presentation of the patient to itraconazole oral solution therapy. (a1) (a2) baseline, (b1) (b2) 30 days of treatment, (c1) (c2) 50 days of treatment, (d1) (d2) 3 months after the end of treatment.

**Conclusion**

The seminal studies of the natural history of untreated IH showed that involution is completed in 50% by 5 years, 70% by 7 years, and 90% by 9 years. There is a wide variation in what remains after involution, ranging from complete disappearance, telangiectasia, or more commonly a fibro-fatty residuum. Sites such as the lips, nose, and cheeks leave cosmetically more disfiguring residua. IHs with ulceration tend to leave white or yellow scars. So, early treatment of critical lesions, especially with complications, is required [5].

IH are treated with a wide range of medications. Several therapeutic regimens, covering beta-blockers, corticosteroids, angiotensin-converting-enzyme inhibitors (ACEI), immune modulators and chemotherapy have been used to treat these benign tumors. From the many therapeutic options, propranolol is the first-line approach for IH, predominantly based on clinical observation, efficacy and tolerability in the short-term. But only 7 years after the first report of Léauté-Labrèze., et al. [6], little is known about the long-term outcome and safety when used in infants.

ITR, an active triazole antifungal drug, has demonstrated good tolerance from its world-wide application over 20 years [7]. The efficacy and safety of ITR are widely recognized. ITR is versatile for use at a dose of 5 mg/kg per day in infants who have normal liver function. There are mild to moderate gastrointestinal diseases (nausea, vomiting, diarrhea and constipation), elevated transaminases, headache, abdominal pain, fever, rash and epistaxis. The range of adverse events noted with ITR capsules or oral solution use in children is similar to the range in adults [8-10]. It is important to monitor liver function for infants before and during the treatment with ITR as in adults. In addition to antifungal effects, ITR was found to have antiangiogenic activity in recent antitumor study. Nacev BA., et al. showed that ITR
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inhibits vascular endothelial growth factor receptor 2 (VEGFR2), which is expressed mostly on the surface of vascular endothelia cells and has a major role for vascular endothelial cell development and angiogenesis [11]. Sertan Goktas., et al showed that ITR inhibits experimental corneal neovascularization and could be considered as a novel pharmacotherapy to prevent corneal neovascularization [12].

The effect of ITR on this case supports the good clinical efficacy and tolerability for IH. The treatment duration of ITR was 60 days (a total dose of 1500mg), which was shorter than the course of propranolol (the median duration of therapy is 7.1 months reported by Chang L., et al. in China [13], 372 days reported by Sawa K., et al. in London [14]). The treatment of IH lesion achieved partial efficacy during the medication days and obtained significant improvement after 3 months of drug withdrawal, which explained the post effect of ITR. No adverse effects were observed during the days of treatment. Liver function and blood routine examination before and after treatment were both normal. The baby patient and parents showed good compliance. Dermoscopy played a key role in vivo accurate observation of the hemangioma changes with vascular regression during the treatment process.

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Conflicts of Interest

None declared.

Bibliography


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