Successful treatment of ulcerated haemangioma with propranolol

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Abstract

Background Ulceration is a frequent complication of proliferating haemangioma.

Methods Four patients with ulcerated hemangioma aged 2, 4, 5 months and 5 weeks were treated with 2 mg/kg KG propranolol.

Results Efficacy and safety of propranolol were excellent in all four cases.

Conclusions Propranolol may be the first-choice therapy for ulcerated haemangioma.

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Conflicts of interest

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Introduction

Haemangioma is the most frequent vascular tumour in early childhood. The presentation is unique, with an initial phase of proliferation, then a phase of slow, spontaneous regression after the age of 1 year.1,2 Most haemangiomas are uncomplicated and do not need any intervention. Therapy is needed for localization at special sites of the body such as the face and/or functional handicap as a result of the haemangioma, such as eye opening, as well as for ulceration in rapidly growing haemangioma.3

Ulceration occurs in about 16% of patients with haemangioma. Additional complications with ulceration can be bleeding in 41% or infections in 16%.4 Wound therapy with different dressings, compresses or topical antibiotics has been used, but ulcerated haemangiomas can respond to flashlamp pulsed-dye laser (FPDL) or drug therapy with steroids, chemotherapeutic agents or interferon, for example.5

Propranolol has shown excellent response in complicated proliferating haemangioma, and its use has rapidly entered the field of haemangioma therapy.6 Propranolol seems to be safe, with high efficiency and acceptable toxicity. However, a scientifically driven clinical study of propranolol for haemangioma is still lacking, and the mechanism of its action is speculative.

Here, we present four cases from two centres in France and Germany for which therapy involved the ‘off-label’ use of propranolol in children with ulcerated haemangioma.

Case reports (Table 1)

Case 1

A 2-month-old girl presented with a voluminous haemangioma, 10 × 6 cm in diameter, on her back, which had developed during the first weeks after birth and continued to proliferate. The haemangioma had ulcerated a few days before presentation. Ulceration covered the entire surface of the haemangioma; parts of it were bleeding and it was painful (Fig. 1a). First-line therapy was an antiseptic and lipido-colloid dressing (Urgotul®; URGO GmbH, Sulzbach, Germany). One month later, the patient received treatment with FPDL (Cynosure, V-Star, Westford, MA, USA) with the following settings: fluence 8 J/cm², pulse duration 0.5 ms, and 10-mm spot diameter. Because of the haemangioma’s large size, treatment with propranolol [1 mg/kg body weight (BW) twice a day] was added after the patient underwent blood pressure determination, electrocardiography and echocardiography. Treatment led to immediate cessation of bleeding (Fig. 1b).
Pain disappeared after 3 weeks, and a scar completely covered the haemangioma after 8 weeks (Fig. 1c), with the tumour size reduced considerably. Propranolol was discontinued after 3 months (Fig. 1d). Two weeks after cessation of treatment, the haemangioma had again increased in size and darkened (Fig. 1e). Propranolol (1 mg/kg BW twice daily) was re-introduced, which led to a lightening in colour and decrease in size of the haemangioma after a few weeks.

Treatment was discontinued again 3 months later. After 2 months of no therapy, the previous features of the haemangioma recurred, which led to re-introduction of the same dosage of propranolol. When the patient was 15 months old, treatment with propranolol was still ongoing (Fig. 1f).

**Case 2**

A 5-week-old girl presented with a haemangioma at the left part of the lower lip (Fig. 2a). The haemangioma was noticed immediately after birth and proliferated thereafter. To stop the growth, immediate treatment was with FPDL (V-Beam, 595 nm; Candela Corp., Wayland, MA, USA, twice during 6 weeks, with the following settings: fluence 7 J/cm², pulse duration 1.5 ms, 7-mm spot diameter. However, the haemangioma continued to increase in size and finally ulcerated (Fig. 2b). Additionally, intermittent bleeding was observed. When the patient was 3 months old, she began to receive propranolol (1 mg/kg BW twice daily) after blood pressure examination, electrocardiography and echocardiography. After 2 weeks, the size of the haemangioma diminished and the bleeding stopped (Fig. 2c). However, the patient did not gain weight and underwent intermittent tube feeding for 6 weeks (Fig. 2d). The propranolol dosage was adjusted to the weight gain. When the patient was 6 months old, the size of the haemangioma was considerably reduced, and bottle drinking was possible without any problem. The haemangioma continued to shrink in size and lighten in colour (Fig. 2e). When the patient was 9 months old (Fig. 2f), treatment with propranolol was still ongoing.

**Case 3**

A 4-month-old girl presented with a haemangioma on the skull that showed ulceration and necrosis, with bleeding and pain for several days (Fig. 3a). The haemangioma was first observed when

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**Table 1** Characteristics of infant cases with ulcerated haemangioma

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Sex</th>
<th>Localization</th>
<th>Haemangioma size (cm)</th>
<th>Ulceration size (cm)</th>
<th>Therapy other than propranolol (age at beginning and end)</th>
<th>Propranolol (age at beginning and end)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>Back</td>
<td>10 × 6</td>
<td>9 × 5</td>
<td>Lipido-colloid dressing (Urgotul®) (2 weeks) 1 × FPDL (2 months)</td>
<td>2 mg/kg BW (2–5, 5.5–9 and 11–15 months, ongoing)</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>Lower lip</td>
<td>3 × 2</td>
<td>1 × 1.5</td>
<td>2 × FPDL (1 and 2 months)</td>
<td>2 mg/kg BW (from 2 months, ongoing)</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>Skull</td>
<td>5 × 4</td>
<td>4 × 3</td>
<td>Wound care, polihexanid gel (Lavasept®; 0.04%) intravenous/oral antibiotics (3 and 4 months)</td>
<td>2 mg/kg BW (from 4 to 8 months)</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>Right arm</td>
<td>5 × 5</td>
<td>3 × 3</td>
<td>Wound care, oral antibiotics (1 month) 1 × FPDL (5 months)</td>
<td>2 mg/kg BW (6–14 months)</td>
</tr>
</tbody>
</table>

FPDL, flashlamp pulsed-dye laser; BW, body weight.
The patient was 2 weeks old, and it proliferated after that. The wound was treated for 4 weeks with polihexanid gel (Lavasept\textsuperscript{®}, 0.04%; B. Braun Melsungen AG, Melsungen, Germany). When the patient was 5 months old, superinfection with staphylococcus and proteus necessitated systemic antibiotic therapy for 10 days (Fig. 3b). Thereafter, propranolol was started at 1 mg/kg BW twice daily after examination ruled out cardiovascular diseases (Fig. 3c). The ulceration healed completely after 2 weeks. The haemangioma continued to lighten in colour and decrease in size (Fig. 3d). During propranolol therapy, the parents observed a more quiet child. When the patient was 9 months old, propranolol treatment was discontinued, and results were excellent (Fig. 3e).

### Case 4

A 5-month-old boy presented with a haemangioma of the right arm measuring 5 cm in diameter and with ulceration of 3 cm. The patient presented superinfection, bleeding and pain. First-line therapy was oral antibiotics (cloxacillin, 25 mg/kg BW) and antisepsics for 2 weeks. Further treatment was FPDL (Cynosure, V-Star) with the following settings: fluence 8 J/cm\textsuperscript{2}, pulse duration 0.5 ms, and 10-mm spot diameter. Therapy with propranolol (1 mg/kg BW twice daily) was started after cardiology examination. After 4 weeks, bleeding and pain disappeared and healing was observed. Propranolol was administered for 9 months until the patient was 14 months old.
Discussion

Ulcerated haemangiomas are often painful in infants and incur risk of local or systemic infection. Ulceration may also be the cause of permanent, unsightly scars. Therefore, ulcerated haemangiomas require treatment independent of their localization or any functional discomfort. In addition to therapy aiming to stop proliferation and further ulceration, supportive therapy such as local wound care, pain medication and antibiotics may be necessary.

None of the published studies of ulcerated haemangioma has defined a single effective treatment. Usually, a combination of therapies is required. Besides FLPD laser therapy, systemic steroid therapy has been effective. In our own retrospective analysis of steroid therapy for proliferating haemangiomas, two of 42 haemangiomas presented with ulceration and responded satisfactorily to long-term steroid therapy.

Two of the cases of ulcerated haemangioma we report here underwent treatment with a single course of FLPD and propranolol as first-line therapy. Therapy was accompanied by drugs for pain and antibiotics. Both haemangiomas responded well without the need for further FLPD. The good effect of propranolol was further shown by the recurrence of growth of the haemangioma in patient 1 who received treatment for only 3 months: propranolol was re-introduced when the haemangioma re-grew after medication was discontinued and the patient was 5 months old. In case 3, with localization of the haemangioma at the lower lip, two courses of FDLP resulted in ulceration at the lower lip, two courses of FDLP resulted in ulceration and responded satisfactorily to long-term steroid therapy.

We found no side-effects with propranolol among the four cases. The pre-treatment assessment and the safety of beta-blockers for infants are still controversial. Nevertheless, no serious complications with the therapy have been reported, and beta-blockers may have a more secure profile than the therapy previously used for the treatment of proliferating haemangiomas.

Conclusion

Propranolol is highly effective and a safe new treatment modality for ulcerated haemangioma in infants, as we show in our four cases. A clinical trial of the preferred dosage and duration of therapy, as well as side effects and the mechanism, is urgently needed.

References