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Innovative Multimodal Management with Propranolol, Prednisone, and Pulsed Dye Laser for Ulcerated Infantile Hemangiomas: A Case Series

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Abstract

Infantile hemangiomas (IHs) are the most common benign vascular tumors of infancy, yet a clinically important subset develops ulceration during the proliferative phase, causing significant morbidity including pain, bleeding, infection, and permanent scarring. Traditional monotherapy is often insufficient for these complicated lesions, particularly in the setting of syndromic conditions such as PHACE syndrome (Posterior fossa anomalies, Hemangioma, Arterial anomalies, Cardiac defects, and Eye anomalies), where cerebrovascular co-morbidities add further complexity to management. We present three infants with ulcerated IHs treated with a simultaneous multimodal regimen comprising weight-based systemic propranolol, a tapering course of oral prednisone, and adjunctive pulsed dye laser (PDL) therapy. One patient carried a confirmed diagnosis of PHACE syndrome with significant cerebrovascular anomalies and bilateral ocular findings. Treatment was initiated with oral prednisone at 1–2 mg/kg/day alongside propranolol at 1–2 mg/kg/day, with PDL sessions administered every 2–4 weeks. All three patients achieved complete re-epithelialization, marked lesion regression, and favourable long-term cosmetic outcomes. The combination was well tolerated across all cases, including the infant with PHACE syndrome, in whom propranolol was introduced cautiously following multidisciplinary clearance with no adverse neurological events. To our knowledge, this is among the first case series to describe the simultaneous use of all three modalities in ulcerated IHs, including in a syndromic setting. These findings support early multimodal therapy as a promising strategy for complex ulcerated hemangiomas and provide a practical treatment framework for future clinical practice.

Key Summary Points

- Ulcerated infantile hemangiomas are challenging lesions associated with pain, bleeding, and risk of scarring.
- Combining propranolol, short-course corticosteroids, and pulsed dye laser achieved rapid re-epithelialization and excellent cosmetic outcomes in three complex cases, including one with PHACE syndrome.
- This multimodal approach was well tolerated and effective even in severe or syndromic hemangiomas.
- Early combined therapy may reduce morbidity and improve long-term aesthetic results compared with monotherapy.

Introduction

Infantile hemangiomas (IHs) are recognized as the most common benign vascular tumors of infancy, with reported incidences ranging from 2% to 10% [1]. Although most IHs follow a benign course, with a rapid proliferative phase during the first few months of life followed by spontaneous involution over several years, a subset of lesions can be particularly problematic due to their size, location, or associated complications [1]. This is especially true in the context of PHACE syndrome, a rare

multisystem disorder defined by the presence of Posterior fossa anomalies, Hemangioma, Arterial anomalies, Cardiac defects, and Eye anomalies [2]. The hallmark of PHACE is a large segmental IH, typically over 5 cm in diameter, affecting the face, scalp, or neck [3]. Among infants with large segmental IHs of the head or neck, the estimated risk of PHACE syndrome is approximately 30% [4]. In these patients, hemangiomas are at an increased risk of ulceration, which can lead to significant morbidity including severe pain, infection, and permanent scarring [5]. Large facial IHs warrant investigation for PHACE syndrome, while IHs located on the lumbosacral region should raise suspicion for LUMBAR syndrome, which encompasses lower body IHs associated with cutaneous, urogenital, neurologic, skeletal, and renal anomalies [1].

In recent years, treatment strategies for IHs have evolved considerably. A pivotal report in 2008 demonstrated that propranolol could effectively suppress the proliferation of IHs, fundamentally changing clinical practice [6]. Nonetheless, in patients with PHACE syndrome, where hemangiomas are often large and complicated by ulceration, propranolol monotherapy may not achieve optimal outcomes. Studies have shown that adding a short course of oral corticosteroids can accelerate lesion regression by modulating inflammatory and pro-angiogenic pathways [7]. In addition, pulsed dye laser (PDL) therapy leverages the principle of selective photothermolysis to target and thermally damage superficial vascular tissue [8]. This modality not only has shown efficacy as a stand-alone treatment for superficial infantile hemangiomas but also enhances treatment outcomes when used as an adjunct [9]. PDL therapy can improve cosmetic results by reducing residual erythema and promoting lesion flattening while minimizing damage to surrounding healthy tissue [8–10].

Despite these advances, the literature remains sparse regarding a comprehensive multimodal approach that integrates systemic propranolol, oral corticosteroids, and tailored PDL therapy simultaneously. To our knowledge, this is among the first case series to describe simultaneous use of propranolol, corticosteroids, and PDL therapy in ulcerated hemangiomas, including one with confirmed PHACE syndrome. This gap is noteworthy, given that each modality targets different aspects of hemangioma pathophysiology.

In this report, we present our experience with a novel multimodal treatment approach in three infants with ulcerated hemangiomas. By providing detailed treatment parameters and clinical outcomes, we aim to contribute preliminary evidence that may inform future studies and support the development of standardized protocols for managing these challenging lesions.

Case Presentations

Case 1

A 3 month old girl presented with a large, segmental IH involving the right side of the face, specifically the periorbital region and the lip, accompanied by a cleft palate. Abnormal red vascular markings were noted near the lip at birth. By one month of age, ulceration developed over the lip, and the lesion

progressively enlarged (Fig. 1). Her past medical history is unremarkable, with no known allergies or prior surgeries.

On examination, the hemangioma measured 14 × 10 cm, presenting as an erythematous plaque with ulceration over the right periorbital area and lip. Comprehensive evaluations were performed to rule out syndromic associations or systemic involvement. Neurology, cardiology, ophthalmology, and otorhinolaryngology examinations were all normal.

Treatment was initiated with oral prednisone at 1 mg/kg/day, which was increased to 2 mg/kg/day after one month and maintained until complete re-epithelialization, followed by a weekly taper of 0.5 mg/kg/day. Propranolol was started at 1 mg/kg/day and increased to 2 mg/kg/day after one month, based on tolerance and clinical response. PDL therapy was administered every 2–4 weeks, and medical honey under occlusion was applied as adjunctive wound care.

This patient's hemangioma regressed significantly over the treatment period, with complete healing of ulcerations and improved feeding (Fig. 2). The combination therapy was well tolerated, with dose adjustments made appropriately as the patient grew.

Case 2

A 4 month old previously healthy girl presented with a hemangioma on the left upper extremity with extension to the left shoulder and left chest that had been present since birth (Fig. 3). Initial workup performed at an outside facility included laboratory investigations, cardiac ultrasound, and brain and body MRI, all of which returned normal results, ruling out any associated syndromic features or extracutaneous involvement.

Treatment was initiated with oral prednisone at 1 mg/kg/day, which was increased to 2 mg/kg/day after one month and continued until complete re-epithelialization of the ulcer. The steroid was then tapered by 0.5 mg/kg/day each week. Propranolol was started at 1 mg/kg/day and titrated to 2 mg/kg/day after one month based on tolerance and clinical response. In addition, PDL therapy was administered every 2–4 weeks, and medical honey under occlusion was used for local wound care.

Significant improvement was noted after six months of combination therapy, with rapid healing of ulcerated areas and reduction in lesion size (Fig. 4). The patient tolerated treatment well, and regular follow-ups were conducted to monitor weight and adjust medication dosages appropriately.

Case 3

A 1-month-old girl presented with a sizable right-sided facial hemangioma measuring approximately 9 cm × 7 cm, with upper lip ulceration, ultimately confirmed as PHACE syndrome (Fig. 5). Initial evaluations revealed significant extracutaneous findings: an ophthalmology examination showed bilateral "morning

glory" disc anomaly with severe retinal involvement and optic nerve hypoplasia in the left eye; neurological assessment demonstrated normal developmental milestones, and an MRA revealed vascular abnormalities of the polygon of Willis (hypoplasia and stenosis affecting the carotid, sylvian, and posterior cerebral arteries) as well as a left intraocular "rope-like structure" consistent with retinal vascular malformation. Cardiology evaluation (including echocardiography and ECG) and otorhinolaryngology examination (including laryngoscopy) were both normal.

Following neurological and cardiological clearance, treatment was initiated with prednisone at 0.5 mg/kg/day, one week prior to starting propranolol, to reduce the risk of ulceration. Propranolol was then introduced at 0.5 mg/kg/day and gradually increased in tandem with prednisone over one month, reaching 2 mg/kg/day for both medications. The patient was closely monitored through follow-up visits, with regular weight checks guiding dose adjustments. By the end of the first month, the upper lip ulceration had resolved, and prednisone was tapered gradually while propranolol was maintained.

PDL therapy was initiated two months after the start of systemic treatment and administered every 2–4 weeks to promote ulcer healing and improve the cosmetic outcome. Medical honey under occlusion was also applied for local wound management during the early phase of treatment.

By the sixth month of treatment, the patient demonstrated excellent clinical progress, with visible reduction in hemangioma size, healing of the ulceration, and no adverse effects reported throughout therapy (Fig. 6). She continued to thrive with normal growth and developmental milestones. Multidisciplinary follow-up was maintained, particularly with ophthalmology and neurology, in view of the underlying PHACE syndrome.

Discussion

The three cases presented here illustrate how a multimodal approach, integrating systemic propranolol, short-course oral corticosteroids, and PDL therapy, can effectively manage complicated hemangiomas, particularly in infants with PHACE syndrome. Each component of this regimen targets a different aspect of hemangioma biology and pathophysiology, resulting in more rapid and sustained clinical improvements than might be achieved with monotherapy alone.

Role of propranolol

Within multimodal regimens, propranolol remains the systemic backbone because of its well-documented efficacy in ulcerated IHs. Saint-Jean et al. [11] demonstrated that ulcerated lesions treated with propranolol achieved complete re-epithelialization within a few weeks, alongside rapid pain control, with minimal adverse effects. More recently, Marquart *et al.* [12] reported sustained healing of a completely ulcerated hemangioma within three weeks of propranolol initiation, with remission maintained at long-term follow-up. These findings highlight propranolol's central role in promoting ulcer healing and alleviating morbidity.

The therapeutic action of propranolol results from several complementary mechanisms rather than a single pathway. By blocking β-adrenergic receptors, propranolol disrupts signalling cascades that normally enhance endothelial survival and angiogenesis, including those mediated by cyclic adenosine monophosphate, protein kinase A, mitogen-activated protein kinase, and phosphoinositide 3-kinase–Akt [13]. Its impact also differs across the main cellular populations within the tumour. In hemangioma-derived endothelial cells, propranolol activates intrinsic apoptotic pathways, suppresses vascular endothelial growth factor receptor 2 signalling, and slows proliferation through downregulation of cyclins. In hemangioma stem cells, the drug does not induce apoptosis but instead reduces vascular endothelial growth factor (VEGF) secretion, causes cell cycle arrest, and promotes adipogenic differentiation, mirroring the natural regression phase of hemangiomas [14]. In hemangioma-derived pericytes, propranolol diminishes proliferative activity and prevents adrenergic-mediated relaxation, leading to increased vascular constriction and reduced blood flow within the lesion. Together, these mechanisms limit angiogenesis, destabilize the vascular framework, and reduce the tumour's capacity to persist, explaining both the rapid improvement in ulcer healing and the longer-term involution observed clinically [13, 14].

Despite its excellent efficacy, propranolol is not without risk. Ji *et al.* [15] noted that a small proportion of children developed problems shortly after starting treatment, most often related to sleep disturbance or irritability. Less frequent but more serious complications included respiratory difficulty, such as hyperreactivity or bronchospasm, and episodes of hypoglycemia, usually in association with poor feeding or concurrent illness. Although uncommon, these reactions highlight the importance of close observation during the early stages of treatment. Early concerns suggested that its use in PHACE syndrome might increase the risk of arterial ischemic events due to underlying cerebrovascular anomalies [16]. Recent evidence has dispelled these concerns by showing no serious adverse events associated with propranolol therapy in this population [17]. In our series, propranolol was well tolerated, with no instances of stroke or other severe complications, even as its dosage was carefully adjusted according to weight gain.

Role of corticosteroids

Systemic corticosteroids, most commonly prednisone or prednisolone, were considered the standard therapy for complicated infantile hemangiomas for several decades prior to the introduction of propranolol, and although their role has diminished, they continue to provide useful benefit in multimodal regimens, particularly in ulcerated lesions where rapid suppression of inflammation and pain is desirable [18]. Our observations are consistent with the findings of Aly *et al.* (10), who demonstrated that a short course of corticosteroids used alongside propranolol enhanced the speed of lesion regression and symptom relief. They recommended this regimen particularly for life or function-threatening lesions, such as those affecting the airway, eyelids, or those complicated by ulceration. In our series, prednisone had a similar effect, contributing to faster re-epithelialization when combined with propranolol and PDL therapy. This supports the view that corticosteroids retain value as an adjunct in multimodal protocols, particularly in ulcerated hemangiomas where rapid clinical improvement is required.

Prednisone acts through several pathways that together limit the progression of IHs. After binding to glucocorticoid receptors in the cytoplasm, the receptor–drug complex moves into the nucleus where it influences gene transcription. This can involve the activation of anti-inflammatory genes but also the suppression of transcription factors such as nuclear factor kappa B and activator protein 1, which normally drive angiogenesis and inflammation [13, 19]. One of the key consequences is seen in hemangioma stem cells, where corticosteroids markedly reduce their ability to form new blood vessels. In experimental models, systemic steroids inhibited vasculogenesis in vivo and strongly decreased secretion of VEGF-A through a receptor-dependent mechanism [19]. Rather than eliminating cells, this effect stems from disrupting the signalling pathways that sustain abnormal vascular growth. Other pro-angiogenic mediators associated with the proliferative phase, including monocyte chemoattractant protein 1, interleukin 6, matrix metalloproteinase 1, and urokinase-type plasminogen activator receptor, are also suppressed in this process [13]. Corticosteroids may additionally counteract estrogen activity, which is thought to support vascular proliferation and endothelial survival during early growth. Acting across these molecular and cellular targets, prednisone contributes to reduced angiogenesis, dampened inflammation, and improved healing of ulcerated lesions [13, 19].

Prednisone is associated with a wide range of adverse effects when used systemically in infants with hemangiomas [18]. Reported complications include hypertension, often occurring early in treatment and sometimes requiring pharmacological management, and hypothalamic–pituitary–adrenal axis suppression, which can persist for weeks to months after discontinuation. Growth retardation is another concern, with reduced weight and height gain observed during therapy, although many infants demonstrate catch-up growth once steroids are tapered. Additional complications described include Cushingoid features, irritability and sleep disturbance, gastrointestinal upset, and increased susceptibility to infection. These risks emphasize that prednisone should be reserved for short courses in selected cases, with careful monitoring throughout treatment [20].

Role of PDL

PDL therapy has an important role in the management of ulcerated IHs, especially for lesions with a marked superficial component. PDL therapy has been shown to accelerate ulcer healing, alleviate pain and bleeding, and promote earlier re-epithelialization. Beyond acute healing, it also improves the quality of long-term outcomes by lessening residual redness and reducing the risk of visible scarring. For this reason, PDL therapy not only addresses immediate complications but also contributes to cosmetic improvement as lesions involute [10]. In our experience, when used alongside systemic therapy, it complemented the effects of propranolol and corticosteroids by promoting quicker recovery and more favourable aesthetic results.

PDL achieves its effect through a combination of precise vascular targeting and modulation of angiogenic pathways [8, 10]. By exploiting the absorption of light by hemoglobin, it produces controlled photothermal injury to abnormal vessels while preserving the surrounding skin, making it most effective for superficial hemangiomas. Its penetration is limited, and for deeper or mixed lesions, PDL is often

combined with systemic therapy to achieve optimal outcomes [10]. Importantly, the benefits extend beyond photothermal injury alone. Clinical observations and experimental studies show that treatment is accompanied by a reduction in angiogenic activity, with downregulation of VEGF expression and evidence of endothelial apoptosis. These biological changes, alongside direct vascular ablation, help to explain the rapid relief of ulceration and the improved long-term cosmetic results seen in practice, supporting PDL therapy as a valuable adjunct within multimodal regimens for complex hemangiomas [21].

Although PDL therapy is generally considered safe in the treatment of infantile hemangiomas, adverse effects have been documented. Most are mild and transient, such as erythema, edema, and purpura that resolve within days [8]. More serious complications, though rare, have been reported. One paper described cases of deep ulceration resulting in significant pain, permanent atrophic scarring, and even a life-threatening hemorrhage following early PDL treatment of superficial facial hemangiomas [22]. These events remain uncommon with modern devices and improved cooling systems, but they underscore the need for cautious parameter selection and close monitoring, particularly when treating ulcerated or delicate anatomical sites.

Proposed management strategy

From our experience, we propose a practical treatment protocol that can be adapted for infants with ulcerated hemangiomas, including those associated with PHACE syndrome. Treatment may begin with oral prednisone at 1 mg/kg/day, increased to 2 mg/kg/day after one month if clinically indicated and well tolerated. Propranolol can be introduced in parallel at 1 mg/kg/day, with careful monitoring and escalation to 2 mg/kg/day if tolerated. Once systemic therapy has achieved initial control, PDL sessions may be introduced approximately one month later, at intervals of every 2–4 weeks, to target residual erythema, accelerate wound healing, and improve long-term cosmetic outcomes. This stepwise approach allows close observation of treatment response and maximizes the complementary effects of each modality.

Strengths and Limitations

The strength of this case series lies in its comprehensive documentation of a multimodal regimen combining propranolol, corticosteroids, and pulsed dye laser, supported by serial clinical photographs and inclusion of a syndromic PHACE case. Strengths also include detailed treatment parameters and longitudinal follow-up demonstrating sustained remission and favourable cosmetic outcomes. Limitations include the small number of patients and the absence of a comparator or control group. Future multicentre studies with larger cohorts are warranted to further validate the safety and efficacy of this integrated therapeutic approach.

Conclusion

A multimodal approach combining systemic propranolol, oral corticosteroids, and PDL therapy presents a promising strategy for managing complex hemangiomas, including in infants with PHACE syndrome. This regimen not only enhances treatment efficacy but also minimizes risks associated with monotherapy. Our findings highlight the importance of individualized treatment plans and multidisciplinary collaboration in optimizing outcomes. Further research is needed to refine protocols and establish long-term safety and efficacy guidelines.

Abbreviations

ECG
Electrocardiogram
IH
Infantile hemangioma
MRA
Magnetic resonance angiography
MRI
Magnetic resonance imaging
PDL
Pulsed dye laser
PHACE
Posterior fossa anomalies, Hemangioma, Arterial anomalies, Cardiac defects, and Eye anomalies
VEGF
Vascular endothelial growth factor

Declarations

Ethics approval and consent to participate

This study protocol was reviewed, and the requirement for ethics approval was waived by the Lebanese American University Institutional Review Board. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Consent for publication

Written informed consent was obtained from the parents or legal guardians of all patients for publication of the details of their medical cases and any accompanying images.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing Interests

The authors declare that they have no competing interests.

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Authors' contributions

Julia Ali and Ahmad Berjawi contributed equally to the conception, data collection, and drafting of this manuscript. Zeina Tannous supervised the work, provided critical revision for important intellectual content, and approved the final manuscript. All authors read and approved the final manuscript.

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Figures



Figure 1

Facial ulcerated infantile hemangioma before initiation of combination therapy (Case 1).



Figure 2

Same lesion seven months after systemic propranolol, oral prednisone, and pulsed dye laser therapy showing excellent cosmetic recovery (Case 1).



Figure 3

Ulcerated hemangioma of the left upper extremity prior to treatment (Case 2).



Figure 4

Six months after multimodal therapy demonstrating significant ulcer healing and marked reduction in lesion size (Case 2).



Figure 5

Right-sided facial hemangioma with upper-lip ulceration in an infant with PHACE syndrome before treatment (Case 3).

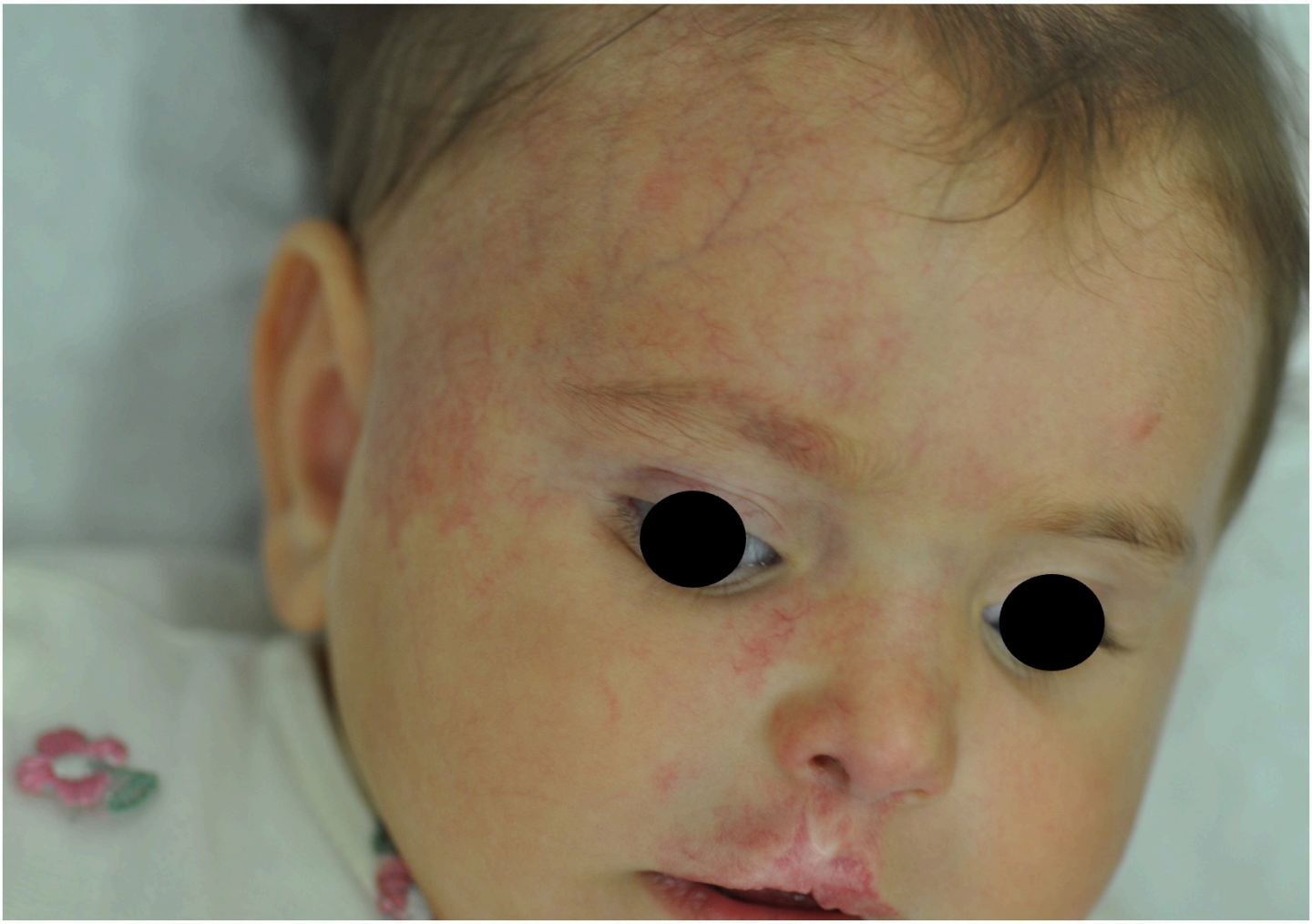


Figure 6

Six months post-treatment demonstrating near-complete lesion involution with minimal residual erythema (Case 3).