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Modern Management of Nasal Hemangiomas

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IMPORTANCE Current treatment approaches for infantile hemangiomas of the nose include observation, pharmacologic agents, surgery, and/or laser therapy. Because of the known functional, social, and cosmetic effect of nasal deformities, obtaining the best possible result is critical. Optimal timing, type, duration, and extent of therapy remain unclear.

OBSERVATIONS Results of a review of 86 patients (64 females and 22 males; mean age, 4.8 months [range, 2 days-23 years]) with infantile hemangiomas of the nose treated from January 1, 1999, to December 31, 2015, and a review of the literature are presented to gain insight into the preferred approach to the treatment of these lesions. Patients underwent single-modality and multimodality treatment with pulsed-dye laser (n = 73), oral corticosteroids (n = 11), intralesional corticosteroids (n = 2), propranolol hydrochloride (n = 30), and surgery (n = 50). The treatment decision algorithms and outcomes based on tumor phase and infantile hemangioma subtype are reviewed in detail. Nine articles met the criteria to be included in the literature review. Literature from the era before the approval of propranolol advocates for early use of oral or intralesional corticosteroids followed by surgery or pulsed-dye laser in cases of unacceptable outcomes. Literature from the era after the approval of propranolol supports early initiation of oral β-blockers until proliferation ceases or until additional intervention is necessary.

CONCLUSIONS AND RELEVANCE Despite a lack of higher levels of evidence, there exists a general consensus between the literature and clinical experience advocating for early multimodality treatment to achieve the best result possible by the time the children reach certain sociodevelopmental milestones.

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Supplemental content

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There is a wealth of literature dedicated to the pathogenesis, diagnosis, and clinical behavior of infantile hemangiomas (IHs), which are the most common benign tumors of infancy. Therapeutic strategies, however, are less well studied, and continue to evolve as laser, surgical, and medical interventions are refined to attain the best cosmetic and functional outcomes. Infantile hemangiomas of the nose (IHNs) comprise a special subset of these tumors owing to their effect on a structure with known functional, aesthetic, and psychosocial importance. Because of the relatively low incidence of IHNs, the timing, type, duration, and extent of treatment are topics of debate. Recently, a more aggressive approach for a wider range of tumors has been gaining strength because of the excellent efficacy and safety profile of β-blockers and the availability of a US Food and Drug Administration–approved formulation for infants with IHs.[1-3] The paucity of outcomes data for management of IHN, however, makes planning of generalized treatment difficult. Because of this difficulty, we hypothesized that a standardized therapeutic protocol for IHNs that is capable of achieving acceptable aesthetic and functional outcomes by 2.5 to 3 years of age (when a sense of self begins to form) could be developed from consensus literature reports and personal experience.[1,4] To address this hypothesis, we performed a retrospective record review of treatment approaches and outcomes in our patient population and compared this experience with that in the literature.

Methods

Primary Study

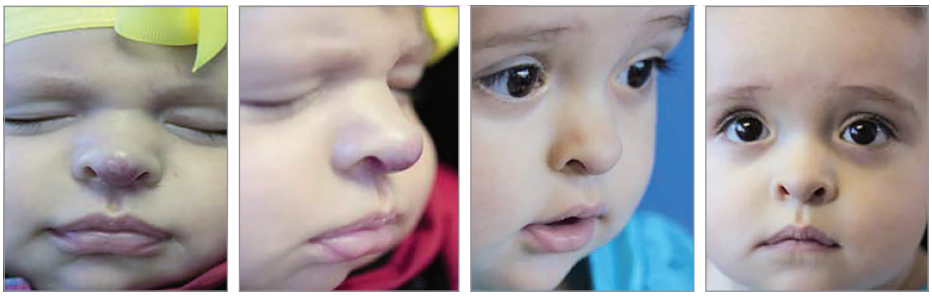
We performed a retrospective review of all patients with IHNs treated by a single surgeon (M.H.) in a tertiary referral private practice between January 1, 1999, and December 31, 2015. Inclusion criteria were diagnosis of IHN, documentation of medical and/or surgical interventions, and duration of follow-up of 1 year or more. Patients were excluded if management consisted solely of observation for tumors or anomalies other than IHNs and if the IHN was confined solely to the glabella. Patient records were mined for demographic data, tumor-specific variables, clinical data, therapeutic interventions, and outcomes. Tumor-specific variables were as follows: (1) depth of involvement, characterized as superficial lesions extending to the dermis only, deep lesions confined to the subcutaneous or subdermal tissue, and compound lesions with simultaneous superficial and deep components; (2) tumor distribution, characterized as focal tumors involved in solitary nasal subunits and segmental tumors involved in multifocal and/or dermatomal distributions; and (3) tumor life

Table. Treatment Modality Dosing and Administration Algorithms

Modality	Dose	Frequency	Duration	Comments
Observation	NA	NA	Arbitrary length of time until intervention is deemed to be necessary	NA
Pulsed-dye laser	7-10-mm spot size, 7-9 j/cm^2, 1.5-6-msec duration, DCD 30:20	Monthly for superficial components, every 10 d for ulceration	3-8 Treatments for superficial lesions, 2-4 treatments for ulcerated lesions	NA
Systemic corticosteroids	3-5mg/kg/d	Daily	Based on response during proliferation only	Prior to 2008
Intralesional corticosteroids	Triamcinolone acetonide 20-40 mg/mL	Based on response	Based on response	Prior to 2008
Propranolol hydrochloride	2 mg/kg/d	Twice daily	Proliferation through early involution	Until acceptable result or change in modality
Surgery	NA	Until acceptable result	NA	NA

Abbreviations: DCD, dynamic cooling device; NA, not applicable.

Figure 1. Treatment of Infantile Hemangiomas of the Nose (IHNs) With Propranolol



A, Proliferating compound IHN before 6 months of treatment with propranolol hydrochloride. B, Total resolution of the deep and superficial components of the tumor after treatment.

cycle, characterized as the defined phases for the purposes of this study of early proliferation (≤3 months), late proliferation (3 to ≤6 months), plateau (6 to ≤9 months), early involution (9 to ≤24 months), and late involution (>24 months).

Treatment outcomes were assessed subjectively via 2 mechanisms. First, the surgeon and parents completed a generalized posttreatment assessment rating their satisfaction with the overall outcome as very satisfied, satisfied, or unsatisfied. Second, the surgeon completed a post hoc analysis addressing tumor response (complete or incomplete), detailed posttreatment cosmesis (residual scarring and/or deformity), and degree of functional improvement (when relevant).

We additionally performed a review of the literature. Eligible for inclusion were all studies reviewing treatment algorithms for IHNs, excluding those without clearly defined outcome measures, with mean follow-up of less than 6 months, and with discussions of other types of vascular anomalies.

Results

A total of 122 patients received a diagnosis of IHN during the study inclusion period. Of those, 86 patients (64 females and 22 males) met all criteria to be included in the study. Mean age of the study population at presentation was 4.8 months (range, 2 days-23 years). Mean follow-up was 3.5 years (range, 12-180 months). All lesions were typed by presenting tumor characteristics. There were 12 (14%) superficial, 13 (15%) deep, 59 (69%) compound, and 2 (2%) complicated IHNs at presentation. The nasal lateral wall was the subsite most often involved in IHNs (30 [35%]), followed by the nasal tip (25 [29%]), nasofacial region (12 [14%]), nasofrontal region (8 [9%]), nasal ala (5 [6%]), dorsum (4 [5%]), and columella (2 [2%]).

A summary algorithm for each treatment modality is presented in the **Table**. The most commonly used modality in our cohort, either alone or in combination therapy, was the 585-nm pulsed-dye laser (PDL) (73 [85%]), with propranolol hydrochloride (after 2008) being the most popular medical modality, used in 30 patients (35%) (**Figure 1**). Surgery was performed in 50 patients (58%). Oral corticosteroids were used in 11 patients (13%), and intralesional corticosteroids were used in 2 patients (2%). The tumor phase during which treatment was most frequently initiated was proliferation (46 [53%]), followed by the involution (31 [36%]) and plateau (9 [10%]) phases (eTable 1 in the Supplement).

Two primary factors influenced treatment decision making: tumor phase at presentation and the degree of cutaneous involvement (superficial, deep, or compound; hereafter known as *type of IHN*). Whereas observation, propranolol, and intralesional and oral corticosteroids were treatment options prescribed during proliferation, surgery was reserved for postproliferative lesions only. Similarly, medical interventions (corticosteroids and β-blockers) were not typically used for postproliferative lesions. However, because propranolol treatment has some putative effect on apoptosis,[1,4,5] it was occasionally continued through the plateau and early involutional periods.

Type of IHN also largely influenced choice of treatment modality. All 12 superficial focal and segmental hemangiomas were treated

with PDL. Surgery was the most common treatment for deep focal tumors (10 of 13 [77%]), but propranolol was also used in 5 patients with deep focal tumors (38%) and oral or intralesional corticosteroids were also used in 4 patients with deep focal tumors (31%). All 59 patients with compound focal and segmental lesions were treated with a combination of PDL, and some received systemic medical therapy (either propranolol [n = 25] or corticosteroids [n = 9]). Ulcerative lesions were treated with PDL monotherapy or with medical and PDL therapy until the ulceration healed (eFigure in the Supplement).

Treatment complications varied depending on the modality used. There were no observed complications associated with use of PDL. Typical systemic sequelae of oral corticosteroid use were observed in many patients, although the incidence was not categorized formally except that no complications were associated with their use.

These systemic sequelae of oral corticosteroid use most commonly included cushingoid facies, gastric irritation, and "fussiness," all of which resolved after discontinuation of the drug. All patients were treated with H_2 receptor antagonists for the duration of therapy. Two patients treated with propranolol experienced diarrhea and significant sleep disturbance, requiring temporary discontinuation of therapy. No patient experienced any adverse cardiovascular events. Among the patients who received surgical treatment, 4 experienced unacceptable scarring requiring revision surgery, including scar revision, laser resurfacing, further debulking, and PDL treatments. Three of these patients were dark-skinned babies with incisional hypertrophy and unfavorable cosmetic outcomes. The scars were revised with simple re-excision. The other patient with unacceptable scarring had partial thickness skin sloughing at the nasal tip caused by injudicious use of bipolar cautery on the undersurface of the nasal tip flap, which was apparent by intraoperative blanching and eventual partial sloughing of the skin. The wound was managed with local wound care and eventual scar revision. The final result was deemed to be cosmetically acceptable and satisfactory to the parents and surgeon.

Overall, 100% of parents expressed being very satisfied or satisfied with treatment outcomes after completion of therapy. Surgeon assessment demonstrated very satisfied responses in 72 cases (84%), satisfied responses in 8 cases (9%), and unsatisfied responses in 6 cases (7%). All cases with unsatisfied reponses were compound segmental lesions with either residual tumor left behind or poor scarring.

Literature Review

Of 376 abstracts reviewed, 9 studies ultimately met all criteria for inclusion (eTable 2 in the Supplement).[6-14] All reports were retrospective case series representing level 4 evidence with the exception of a single level 3 retrospective cohort study.[14] In total, 261 patients among these 9 studies were treated for IHNs. Four studies discussed management of nasal tip hemangiomas only,[6,8,9,13] and the remaining studies discussed hemangiomas of any nasal subsite. Among these studies, the nasal tip was still the most common subsite affected, involving 147 of 181 treated tumors (81%).[6,8,9,13] Mean follow-up among the studies in which these data were reported ranged from 25 to 69 months. Only 3 of the articles discussed treatment of patients in the era after propranolol was approved.[6,7,14] For the 261 patients included in the literature review, observation (26 [10.0%]), systemic and intralesional corticosteroids (43 [16.5%]), propranolol (37 [14.2%]), cryotherapy (6 [2.3%]), surgery (157 [60.2%]), and laser treatment (PDL and Nd:YAG) (55 [21.1%]) were used in the management of their IHNs.

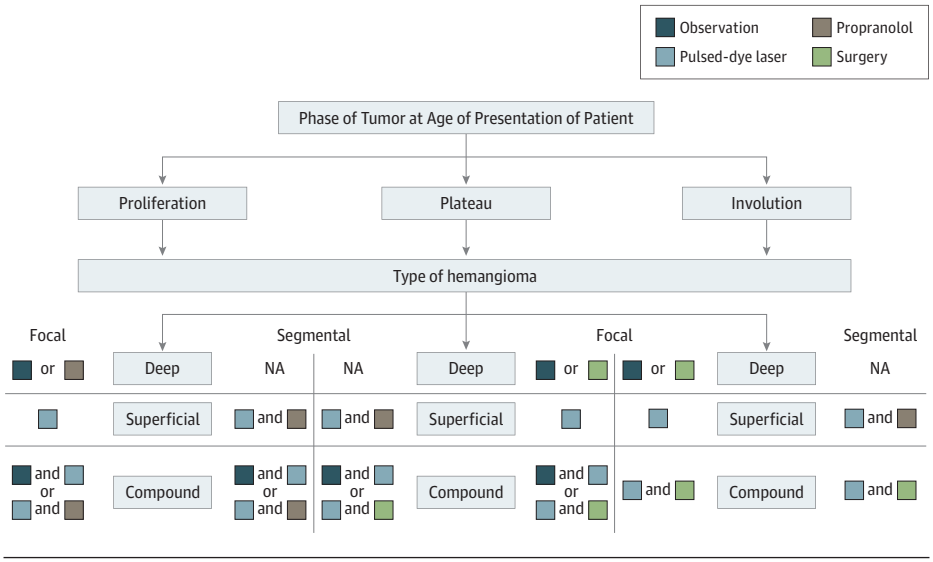
Discussion

The management of IHNs remains a difficult task for even the most skilled and experienced physicians because of the associated cosmetic, functional, and psychosocial implications. We performed a review of our own clinical experience, which is currently the largest review of treated IHNs in the literature, to our knowledge, and compared results of this review with results of similar reports, with the objective of identifying consensus on the management of IHNs. Although there was significant heterogeneity in reporting of quantitative data that precluded a meta-analysis, there were obvious trends in management approach and rationale that agreed with our own algorithms. An important point generally agreed on by all authors is that IHNs deserve aggressive attention and intervention. The morbidity associated with failure to adequately treat a proliferating IHN can make subsequent attempts at treatment substantially more challenging. Therefore, early and active management is encouraged.

Authors generally agreed that the 2 most important factors influencing choice of treatment modality were IHN type and phase of the tumor life cycle. For example, small, superficial, uncomplicated, proliferating IHNs were considered to be limited lesions by Eivazi et al,[7] who found good to excellent outcomes in these patients with observation alone. Although we did not include patients in our study who underwent only observation, we generally do not disagree with the approach of closely observing small, superficial, proliferating IHNs. More typically in our experience, however, these small lesions are treated with the PDL because morbidity is minimal and the chance of attaining complete resolution, at least anecdotally, is higher. If at any point during active observation rapid thickening of the tumor occurs, a deep component grows, functional issues arise, or concern for destruction of the nasal architecture or skin develop, initiation of systemic propranolol treatment, PDL therapy, or surgery would be options to consider. Furthermore, if the lesion has not involuted to an acceptable degree by the time the patient is approximately 2 to 3 years of age, PDL and surgery should, again, be considered as options to treat the residuum (**Figure 2**).

For proliferating deep or compound IHNs, most authors agreed with a dual-modality approach of early initiation of medical therapy followed by more invasive modalities (laser or surgery) beginning in the plateau or involution phases. Ben-Amitai et al[6] found that early initiation of propranolol treatment for IHNs prevented lesion proliferation, reduced lesion volume, and prevented nasal and facial deformation. Arneja et al[8] agreed that early medical therapy optimized conditions for later surgery if indicated. Perkins et al[14] provided additional evidence for early initiation of propranolol for IHNs, showing a significant decrease in the need for future invasive therapies in patients treated with propranolol vs those who were not treated with a β-blocker. Some experimental and anecdotal evidence exists supporting β-blocker therapy for IHNs in the plateau or involution phases, and in our own experience, we will occasionally extend use of a β-blocker into the early involution phase; however, this modality is typically discontinued at cessation of proliferation.[5]

Figure 2. Treatment Algorithm for the Management of Infantile Hemangiomas of the Nose (IHNs)



Generalized management algorithm for the treatment of IHNs. Key features influencing treatment decision-making rationale are phase of tumor life cycle and type of IHN. This flowchart represents a generalized algorithm that is most often consistent with our approach, but frequent deviation is the norm when specific case scenarios demand unique treatment approaches. Because none of the patients in our cohort were treated with topical β-blockers (timolol maleate), this modality was not included in the algorithm. However, timolol has more recently been included in our practice as an important modality mainly in the management of focal, superficial IHNs and superficial components of compound hemangiomas. NA indicates not applicable.

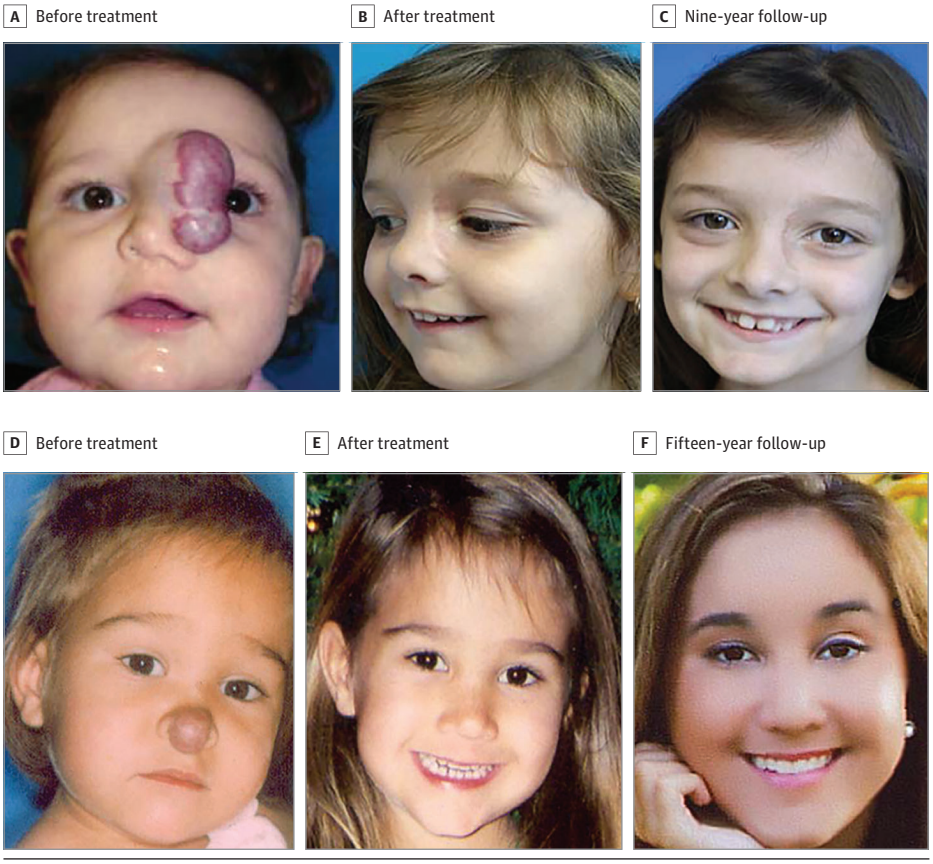
More invasive treatments for IHNs, such as surgery, are generally used in the context of failed medical therapy or incomplete involution. In a study by Simic et al,[12] among 9 patients treated with surgery alone, results were very good in 2, good in 6, and unsatisfactory in 1. The authors advocated for early surgery in the immediate postproliferation phase. Hamou et al[13] treated 39 IHNs with surgery and stressed the importance of early surgery to avoid nasal cartilage distortion, which was seen in 29 patients before surgery in their series. Eivazi et al[7] posited that surgery should be reserved for advanced lesions after prior therapy, highly proliferative or destructive tumors not controlled with medical therapy, and/or for residuum. In our own series, surgery was considered an option beginning in the plateau phase (>6 months) and extending through the postinvolution phase. Surgery was performed only for deep or compound IHNs in our series; this was often done as part of a multimodality approach in conjunction with laser and/or medical therapy (**Figure 3**).

Surgical techniques differ substantially, as previously mentioned, and because of the variability in outcomes reporting, it is impossible to directly compare outcomes by surgical technique or approach. Our technique modifies an external approach[15] that spares the soft-tissue triangles, with skin excision along subunit junctions or nonanatomical lines for resection of severe skin expansion (**Figure 4**).[16] By placing the incision along the caudal edge of the nasal tip subunit, the opportunity to drape and resect the expanded skin of the IH arises. The traditional open rhinoplasty marginal incision does not allow for the redraping over the 3-dimensionally curved margin with ease. In addition, by avoiding the soft-tissue triangles of the subtip, we avoid risking "notching" of an area that is difficult to reconstruct. The transcolumellar incision is patterned after the usual open approach incisions. Exposure of a nasal tip IHN requires continuing the caudal incisions laterally along the alar groove to varying lengths. The length is determined by the amount of exposure needed to show the entire tumor. These alar groove incisions are continued only as far as the lateral aspect of the tip subunit and then are directed superiorly. Again, the length is determined by the need to expose the tumor and allow redraping of the expanded skin laterally and inferiorly. The incisions may be asymmetric in length in cases in which the tumor is not midline. In severely expanded nasal tip skin that has been so distorted that there is no ability to redrape through these incisions or in the case of a compound lesion with scarred skin that needs to be removed, a vertical incision can be used through the tip skin. We are extremely conservative in resecting skin and will err on the side of needing a later definitive procedure than risk stunting of nasal growth due to scar contracture. For nasal dorsal or lateral wall IHNs, the incisions are typically centered on the nasofacial junction and extended superiorly onto (what will become later in life) a glabellar rhytid in the manner of a reverse dorsal nasal or Reigert flap. Inferiorly, the incision is extended as needed to the junction of or onto the alar groove as described above.

The complexity of surgery required to treat these lesions cannot be overstated, and authors frequently stress the importance of setting clear preoperative expectations with parents that mention the likelihood of additional surgery. Revision rates in the literature range between 11% and 32%,[6-14] whereas our study had a revision rate of 8% for the 50 patients who underwent surgery. We defined *revision* as surgery for an unsatisfactory or failed result, rather than for a planned, staged set of procedures. This definition probably accounts for the wide range in reported revisions among experienced surgeons. Ultimately, surgeon comfort and experience with a given technique is probably the most important factor that portends favorable outcomes.

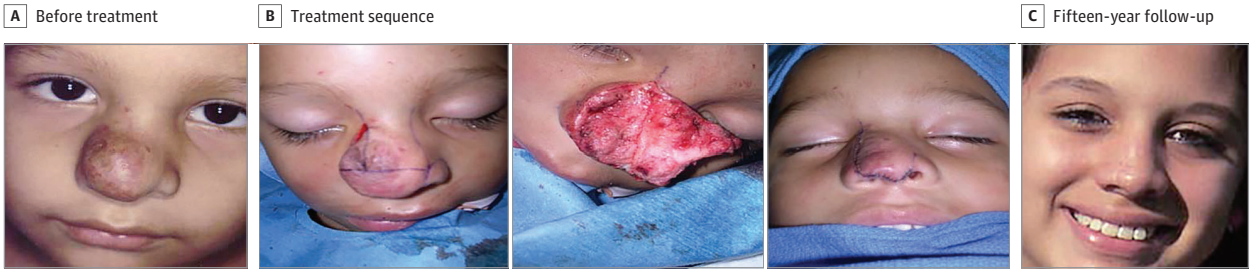
A paucity of data exists on the outcomes of PDL therapy specifically for IHNs, although this was the most common treatment modality used in our series (85% of patients). In our experience, PDL therapy is rarely used as a single modality (other than for small, superficial IHNs) but is used more often in conjunction with systemic propranolol treatment (when a deep component is present) or surgery (typically used after surgery for improvement of scar erythema or residual superficial component). Pulsed-dye laser was used for 100% of tumors in our series other than deep IHNs, and no complications were seen with its use. Pulsed-dye laser was also the treat-

Figure 3. Multimodality Approach to Infantile Hemangiomas of the Nose (IHNs)



Compound early involuting IHN of the lateral wall and nasofacial junction before treatment (A) and after treatment with 2 serial excisions followed by 4 pulsed-dye laser (PDL) treatments (B). C, Nine-year follow-up. D, Compound, early involuting IHN of the nasal tip before treatment with PDL and surgery before approval of propranolol hydrochloride. The tumor was removed in 1 operation, taking advantage of the expanded skin and the PDL used to treat the residual superficial component. E, After treatment. F, Fifteen-year follow-up.

Figure 4. Multimodality Approach to Management of Infantile Nasal Hemangioma (IHN)



A, Compound involuting IHN involving several subunits before treatment. B, Treatment sequence showing initial redraping of the skin after debulking of the deep component. The incisions are asymmetrically extended onto the alar grooves and superiorly along the nasofacial junction on the involved side. The residual superficially involved skin was treated with sequential pulsed-dye laser treatments until acceptable resolution. C, Fifteen-year follow-up.

ment of choice for ulcerative lesions. Although treatment protocols lacking cooling technologies may have been associated with complications, more recent studies have shown that ulcerating IHs respond well to PDL, typically requiring no more than 2 to 3 treatments for healing of the ulcer.[17-20]

Overall outcomes in our study and others are reported with varying measures, most commonly subjective, and thus must be viewed with reservation. Outcomes for our general treatment approach were reported in terms of parent and surgeon satisfaction. Parents tended to be less critical than the surgeon of posttreatment results: 100% of parents were very satisfied or satisfied with treatment, whereas the surgeon was very satisfied in 84%, satisfied in 9%, and unsatisfied in 7% of cases. Unsatisfactory cases were all more advanced, compound IHNs posing significant therapeutic challenges. More objective outcome measures using established grading schemes remain necessary.

Limitations

The retrospective review presented here is not without limitations. A confounding factor that affects any review spanning the introduction of propranolol in 2008 is the significant shift away from the use of corticosteroids and observation of IHNs to a more ag-

gressive approach with early initiation of propranolol, rendering obsolete most data and outcomes from before propranolol was introduced for the treatment of IH.[21] An additional limitation to our study was the substantial subjectivity in outcome measure reporting. In both our primary report and the literature review, parent satisfaction and surgeon opinion were often the only variables examined, leaving significant room for bias. More uniform and objective outcomes data reporting in the literature is needed for the management of IHNs.

Conclusions

Although higher levels of evidence supporting optimal treatment algorithms for IHNs remain absent, the best available evidence supports a general consensus advocating for multimodality approaches to treatment. Specifically, initiation of medical therapy early during the proliferation phase, alone or with concomitant PDL therapy, followed by more invasive options if necessary after proliferation has ceased, is generally supported. An individualized approach that primarily considers IHN type, phase of tumor life cycle at presentation, developmental and social milestones, and parent preferences is reflected in the literature and our experience. Assuming that IHs of other cutaneous sites are similar to those of the nasal tip in terms of natural history, response to therapies, and outcomes, it seems to be reasonable to extrapolate our findings to the management of other cutaneous IHs. Clinical trials of newer medical agents (eg, mechanistic target of rapamycin inhibitors and topical β-blockers), technologies, and techniques would be the definitive way to test that hypothesis. Until then, other reviews of clinical experience and the best available evidence should be encouraged and the old management dogma of "leave it alone, it will go away" should be abandoned as universal advice for infantile hemangiomas.

ARTICLE INFORMATION

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