Hemangiomas in Infants and Children

An Algorithm for Intervention

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Considerable confusion exists with the diagnosis and management of vascular birthmarks. For this article we reviewed charts for the diagnosis and recommended management of 208 new patients with vascular birthmarks presenting to the Albany Medical Center Vascular Malformation Clinic, Albany, NY, over a 26-month period from October 1995 through December 1997. Based on our patient population, data available, and the current literature, we concluded that an early evaluation and an accurate diagnosis in infants with a vascular birthmark are important. Furthermore, intervention by way of systemic steroids, laser therapy, or surgical debulking is appropriate and safe in a select group of patients presenting with a proliferating hemangioma and in patients with an involuting but disfiguring hemangioma. Also in this article we present an algorithm to assist the clinician with the management of the pediatric patient with a diagnosis of a hemangioma.

The earliest attempts to treat infants and children afflicted with vascular tumors were based on anecdotal case reports and included treatment modalities of cryotherapy, electrolysis, thermocautery, vessel ligation, and/or surgical excision.1-6 Unfortunately, a lack of classification and a poor understanding of the natural history of vascular anomalies often resulted in treatment that was inappropriate or more disfiguring than the original deformity.7,9 Many physicians in the early 1900s noted that children afflicted with vascular tumors often had gradual improvement or resolution of their deformity in later childhood. However, it was not until 1938, when Lister and Camb published an article in Lancet titled “The Natural History of Strawberry Nevi,” that recommendations became uniformly agreed on. In this communication, Lister and Camb concluded that of 92 lesions in 77 children with the diagnosis of hemangioma, all but 2 underwent complete involution within 5 years. They made an argument for “watchful waiting,” and other authors supported a very conservative approach.11-14 It is because of the benign nature of this vascular neoplasm, the risk of anesthesia, and the limited available treatment modalities that the dogma of watchful waiting was propagated in the pediatric and plastic surgery literature.

In a series presented by Bowers et al,11 the authors state that perhaps insufficient emphasis is placed on the fact that a small but appreciable number of nevi persist after age 7 or 8 years and cause substantial deformity.11 In reality, reports advocating no intervention may have underemphasized the fact that most hemangiomas will leave a residuum that can take the form of epidermal atrophy, persistent telangiectasia, residual fibrofatty tissue, excess skin, or a combination of the above.

More contemporary studies have attempted to quantify the proportion of children who do not experience complete involution.15 In a retrospective review, Finn et al demonstrated that only 50% of 298 hemangiomas completely involuted by age 6 years. Of the remaining 50% that did not involute, 80% left a substantial residual cosmetic deformity. For the 50% that did involute completely by age 6 years, 38% also left substantial residual cosmetic deformity.

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PATIENTS AND METHODS

The charts of all patients presenting to the clinic between October 1, 1993, and December 31, 1997, were reviewed and used as the primary source of information for this retrospective review. A comprehensive history and physical examination were performed, including photographs. For the purpose of medical and/or surgical management, hemangiomas were divided into either the proliferative or involutive phase. Proliferation was considered to begin at birth and by definition continued until the neoplasm no longer increased in size. The proliferative phase usually continued until age 9 to 12 months and rarely continued past 12 to 13 months. The involutive phase began at the end of the proliferative phase and continued for months to several years (Figure 1). After the initial evaluation and diagnosis, hemangiomas were characterized based on proliferation or involutive phase, the location, and/or whether functional problems (ie, visual impairment or ulceration) were of concern. Recommendations for either treatment or observation were made and patients were seen monthly or twice a month during the proliferative phase and annually or twice a year during the involutive phase.

MANAGEMENT DURING PROLIFERATION

During the proliferation phase, treatment options consisted of observation, intralesional steroid injection, systemic steroid therapy, treatment with a pulse-dye laser alone, surgical debulking alone, or laser and surgical therapy in combination. Patients chosen for treatment with the pulse-dye laser included those with actively proliferating hemangiomas with superficial components in a cosmetically sensitive area (Figure 2). The Candela STP1-b (Wayland, Mass) pulse-dye laser was used in all patients at the appropriate start safe fluence parameters for spot size 2 to 10 mm. During the rapidly proliferating phase, treatment was repeated at a 4- to 6-week interval when it was thought to be indicated. The pulse-dye laser was also used in the ulcerating hemangioma (Figure 3). The ulcerating hemangioma was treated over its entire surface, excluding the ulceration, and at a slightly higher fluence than a standard treatment. Retreatment was performed at a 4- to 6-week interval only in rapidly proliferating or impending ulcerating hemangiomas. However, most ulcerating hemangiomas required only 1 or 2 treatments. Surgical debulking during the proliferating phase was considered in the patient with a hemangioma causing a functional impairment (ie, airway disruption or visual disruption) that created an impending medical situation or in the patient who did not respond to systemic steroid therapy.

Intralesional steroid injection was recommended and used in localized subcutaneous (deep) proliferating facial hemangiomas. Intralesional steroid injection was also recommended in an area of potential functional impairment when it was thought that the risk-benefit ratio was not favorable for systemic steroids. Intralesional steroid injection was performed with 10 mg/mL of kenalog for a total of 10 to 15 mg, depending on the size of the hemangioma. In all cases, the needle placement and deposition was confined to the hemangioma proper, and in patients undergoing periorbital injection, care was taken not to violate the orbital septum. Treatment was repeated at 4- to 6-week intervals.

Intralesional steroid injection therapy was also used in patients who had recently been tapered from systemic steroid therapy and who were responding with a rebound proliferation at the end of the proliferation phase (aged 10-12 months) if it was determined by the attending staff that the risk-benefit ratio for intralesional steroid injection was favorable compared with another course of systemic steroids. For the rapidly proliferating, poorly localized, potentially large disfiguring hemangioma, or a lesion that did not respond to intralesional injection, a low threshold existed for recommending systemic steroid therapy.

In our vascular malformation clinic, systemic steroids were chosen for those patients younger than 14 months with a rapidly proliferating hemangioma. These hemangiomas were primarily on the face, including, in order of frequency, the lips, cheeks, nose, eyelids, and ears (Figure 4). Before the infants began treatment with steroids, their hemangiomas were evaluated, and treatment options were discussed with the family by the entire attending staff. Our starting dose of steroids was 4.0 mg/kg per day in a single dose. The patients' hemangiomas were reevaluated in 1 week for steroid response. If shrinkage or stabilization was noted at this time, the treatment was maintained at the initial dose for 3 weeks. On follow-up examination at 3 weeks, the steroids were tapered over 4 to 8 weeks. The patients were observed closely by their primary care physicians or pediatricians for anti-reflux management and frequent well-baby checks. All patients were observed by an endocrinologist. A follow-up examination for patients treated with systemic steroids was performed every 4 weeks, or sooner if parents noted problems. During treatment, no live vaccines were given. Parents were informed that the infants were immunocompromised and day care and foreign travel were not advised.

One month after steroid treatments were discontinued, the patients were reevaluated. If the hemangioma exhibited proliferation, as determined by the team of attending physicians, systemic steroid treatments were resumed at a dose of 3 to 4 mg/kg per day; the hemangiomas were reevaluated at 1 week and, if improvement had occurred, systemic steroid treatments were tapered over 4 weeks. Alfa interferons were not used in our patients, given the favorable responses to other available treatments and the substantial associated risks and reported serious complication rates in infants and children treated with alpha-interferons for rapidly proliferating life-threatening hemangiomas.15

MANAGEMENT DURING INVOLUTION

By definition, the cessation of proliferation coincides with the commencement of involution. This usually occurs by age 9 to 12 months but as late as age 13 to 15 months in some patients. No attempt at treatment was made in early involution because in this phase one cannot differentiate between a treatment response and the natural history of the hemangioma. While all hemangiomas involute, each lesion is different with regard to the rate of involution and residual deformity following involution. Based on more contemporary literature, it seems that all hemangiomas follow 1 of 2 different patterns of involution, as seen in Figure 1.

Patients were seen in follow-up at age 24 to 28 months, at which time the hemangioma would be classified as an early involuter or a late involuter by asking the question,
“Over the past 2 or 3 months have you noticed any significant decrease in size in your child’s hemangioma?” For patients whose parents’ answer was affirmative, the hemangiomas were considered early involuters, and no intervention was offered at that time. These children were observed during the period of natural involution and size reduction, which usually continued until the child was almost ready to enter school. If a substantial deformity still existed prior to the child entering school (aged 4-4½ years) surgical and/or laser correction was offered and recommended.

Patients whose hemangiomas experienced no involution or reduction in size by age 2 years were considered to have late involuters. Surgical and/or pulsedye laser treatment was offered at this time because, statistically, these children would enter school with substantial deformities if their hemangiomas were left untreated.16

Surgical correction in all cases consisted of incision placement at the junction of aesthetic facial units, subunits, or in a relaxed skin tension line. A conservative debulking of tissue volume was performed, with extreme care taken to err, if at all, on the side of under-resection without the sacrifice or distortion of any surrounding normal tissue or anatomical landmarks, as shown in Figure 5. The goal of surgical correction was merely volume reduction and removal of distorted or excess skin. No attempt was made at removal or resection of all abnormal skin. During the surgical debulking, if given the choice between removing normal skin or atrophic and/or scarred skin, we would include the abnormal skin in the surgical excision. Laser treatment was preferred over surgical resection for the component of the anatomic deformity that was amenable to treatment with a pulse-dye or carbon dioxide laser (ie, persistent dermal ecstasia or uneven texture). At 4 to 6 weeks after surgery, all patients with residual dermal ecstasia were recommended for treatment with the pulsedye laser. If the response was not complete with 1 treatment, the pulse-dye laser treatment was repeated 4 to 6 weeks later.

Treatment with the pulse-dye laser was usually not offered in early involution because in this phase one cannot differentiate between a response to laser treatment and the natural history of the hemangioma. With patients seen in follow-up at ages 24 to 48 months, the pulse-dye laser was recommended as the only treatment modality when the deformity was primarily a superficial vascular ecstasia as opposed to a deformity also characterized by redundant skin and/or excess tissue volume (Figure 6). Laser treatment was administered at the start safe fluence parameters given the appropriate spot size and repeated at 4- to 6-week intervals when indicated.

Systemic and/or intralesional steroids were not recommended or used in our patients during involution because the involuting hemangiomas did not seem to respond to steroid therapy. In contrast to the rapidly proliferating hemangiomas. When it was determined by the attending staff that treatment was complete or that no further benefit could be realized by additional treatment, patients were photographed and discharged from the clinic. Based on these data and our experience, we have created algorithms that we follow in managing these patients (Figure 7).

Figure 1. The natural history of hemangiomas in children follows a pattern of proliferation and involution. Proliferation occurs either before or shortly after birth and stops at approximately age 12 months. The involution phase appears to follow 1 of 2 patterns. A rapid and more visible reduction in size occurs between ages 18 and 24 months. These hemangiomas are considered “early involuters,” with maximum involution occurring by approximately age 4 to 5 years. A slow, gradual, almost imperceptible reduction in size occurs in those hemangiomas considered “late involuters,” with maximum involution occurring between ages 10 and 12 years.

To confuse matters further, treatment options for the management of infants and children with hemangiomas continue to change. These changes are based on a better understanding of the diagnosis, histopathology, and natural history of the vascular lesions in children, the appropriate use of systemic steroids, safer pediatric anesthesia, advances in laser technology and surgical technique, and a clearer understanding of the psychological trauma suffered by children as a consequence of the readily visible hemangioma.

However, despite the medical advances and a clearer understanding of the natural history of hemangiomas, many physicians currently consider intervention for non-functional problems controversial and contraindicated. This perspective is evidenced by a strong dissatisfaction with the medical care initially provided in greater than 50% of the cases eventually referred to a regional hemangioma clinic.17

For this study we reviewed our experience from the Albany Medical Center Vascular Malformation Clinic, Albany, NY, over a 26-month period. Based on the literature, the natural history of hemangiomas, and our experience, we advocate the early evaluation of all vascular birthmarks in infants and children. In patients with multiple hemangiomas, a potentially disfiguring hemangioma, or associated functional problems, we recommend early evaluation and possible treatment with a multidisciplinary approach. Finally, we have created an algorithm outlining our recommendations for the management of infants and children with hemangiomas.

Over a 26-month period from the inception of the Vascular Malformation Clinic at Albany Medical Center, 209 new patient evaluations were performed. Our patient population age ranged from newborn to 51 years. After evaluation, we diagnosed hemangioma in 168 patients
(80%), vascular malformation in 34 (16%), and nonvascular birthmark in 7 (3%). Of those patients with hemangioma, 136 (81%) presented with hemangiomas in the head and neck region. Multiple hemangiomas were noted in 41 patients (24%).

Intralesional steroid injection therapy was performed in 8 patients (4.5%) and systemic steroids were used to treat 7 (3.3%). All the infants treated with steroids showed response as determined by shrinkage or stabilization of proliferation.

All patients experienced adverse effects to varying degrees during steroid therapy, including moon facies, growth delay, insomnia, decrease in appetite, and weight gain. No permanent sequelae occurred in our patient population. In growth-delayed patients a “rebound phenomenon” occurred, and all patients seemed to return...
to their pretreatment rate of growth. Normal sleeping and eating patterns were resumed shortly after systemic steroid treatments were discontinued.

Recommendations for pulse-dye laser therapy alone occurred in 61 patients (36%). Patients received between 1 and 3 treatments. Photodocumentation as well as clinical evaluation confirmed improvement after treatment in all patients; however, the response varied from patient to patient and from hemangioma to hemangioma.

Three patients who were diagnosed very shortly after birth with a proliferating superficial hemangioma and were treated at 4- to 6-week intervals experienced complete resolution within 4 months and before the patient reached age 1 year. There were no hypertrophic scars or other clinically significant complications following pulse-dye laser treatment. Mild temporary postinflammatory hyperpigmentation occurred in 16 patients (26.2%).

Recommendations for surgical intervention occurred in 41 patients (24%). With few exceptions, those patients undergoing surgical intervention additionally underwent 1 or 2 treatments with the pulse-dye laser 4 to 6 weeks after surgery to address the remaining dermal ectasias. Surgery was successful in all patients, and there were no associated complications, including hematoma, postoperative bleeding, infection, wound dehiscence, or hypertrophic scar formation.

Figure 5. A, Pretreatment appearance of a 3½-year-old boy with a massive “late involuter” hemangioma of the right upper lip. B, Appearance of the same boy after surgical resection and 2 treatments with the pulse-dye laser. C, A 4-year-old girl with a late involuter hemangioma of the lower lip that has not demonstrated involution (ie, a substantial reduction in size over the past year). D, The same girl after surgical resection and 1 treatment with the pulse-dye laser. E, A 3½-year-old girl with a late involuter nasal hemangioma and concomitant substantial deformity. F, The same girl, following surgical resection and treatment with a pulse-dye laser.
COMMENT

Nineteenth-century anatomic labels and older descriptive terminology, without regard to biological behavior, continue to confound the diagnosis and management of hemangiomas in clinical practice. However, with a better understanding of the biological behavior, as described in 1982 by Mulliken and Glowacki,19 one can take a more scientific and systematic approach to the management of hemangiomas. In this classic article, the authors clearly defined the difference between hemangiomas and vascular malformations in infants and children based on the physical findings, clinical behavior, and cellular kinetics. Histologically, a hemangioma is a true neoplasm characterized by an increased cell turnover of endothelium, mast cells, fibroblasts, and macrophages.

Although a hemangioma may be present at birth, it usually becomes apparent within a few weeks of life as a small erythematous macular patch or localized telangiectasia, with growth occurring over the following few months (Figure 1). This rapid phase of growth is referred to as the proliferative phase and continues through ages 8 to 12 months, with the most rapid growth usually occurring during the first 3 to 6 months. It is during this rapid proliferation that functional problems (ie, visual impairment, airway obstruction, and/or ulceration) and cosmetic deformities first become apparent. While some hemangiomas increase only slightly in size, others rapidly enlarge, resulting in a very disfiguring lesion. Predicting which lesions will rapidly proliferate is best done by performing serial examinations and/or determining a history of rapid expansion over weeks or months. The proliferative phase is followed by the involuting phase, which begins between ages 8 and 12 months, but can begin as late as ages 18 to 20 months in some patients. During the involuting phase, the tumor rate of growth is proportionately less than the growth rate of the child. Involution is characterized by a reduction in firmness of the hemangioma and a change from a shiny, bright red appearance to a grayish mottled appearance as the vascularity of the lesion becomes replaced with fibrofatty tissue. Involution occurs over the next 1 to 12 years of childhood, and the rate of involution is highly variable, as is the resulting cosmetic deformity. The difficulty and challenge in managing these lesions arises from trying to predict which children will have a substantial deformity at the time they enter school. Equally challenging is determining at what point one should intervene, and with what treatment modality.

Vascular malformations, on the other hand, are by definition present at birth.19,27 They are not neoplasms, but instead exhibit normal endothelial turnover and are errors of vascular morphogenesis manifesting as various vascular channel abnormalities. They usually present in infancy or childhood, although subclinical vascular malformations may be imperceptible or apparent only as a “fullness” until later in childhood or adulthood. Because of the continual intraluminal hydrostatic pressure, malformations increase in size throughout life. During puberty some vascular malformations rapidly expand while others do not. They are subcategorized as capillary, venous, arterial, lymphatic, or a combination of 2 or more of these. According to this classification system, a port-wine stain is considered a venule malformation. Vascular malformations do not involute, and the rate of growth and expansion may depend on several factors, the most important probably being the intraluminal hydrostatic pressure; ie, arterial malformations tend to expand at a much greater rate than venous or lymphatic malformations. The recommended management of patients with vascular malformations depends on several factors. The decision processes are complex and cannot be discussed in full detail in this article. However, an accurate diagnosis and a clear understanding of the differences between vascular malformations and hemangiomas are important because the natural history and the treatment recommendations for these 2 conditions are very different.

The use of systemic corticosteroids in the treatment of rapidly proliferating hemangiomas was a serendipitous discovery first reported in 1967 by Edgerton21 at the Johns Hopkins Hospital in a patient with a large facial hemangioma. The patient was treated with systemic steroids for life-threatening thrombocytopenia associated with a large hemangioma and experienced apparently coincidental shrinkage of the facial hemangioma. Subsequent reports and series have confirmed that steroid therapy is associated with hemangioma shrinkage, demonstrating a
Figure 7. Algorithms developed and used by the Albany Medical Center and Vascular Malformation Clinic to manage and make recommendations for treatment of infants and children with hemangiomas in both the proliferation (A) and involution (B) phases.
response rate of 30% to 90% of all hemangiomas to systemic or intralesional steroid injection, with a more substantial response during the proliferative phase and little or no response during involution.15,22 In our patient population intralesional or systemic steroids were recommended only during the proliferation phase when the attending staff thought a favorable risk-benefit ratio existed, eg, to treat enlarging, disfiguring facial hemangiomas or those causing visual impairment.

Exactly how corticosteroids exert their effects on the pathophysiology of proliferating hemangiomas is poorly understood. Rat studies have shown that steroids induce vascular hypersensitivity, which produces vasoconstriction. This vasoconstriction is believed to be due to arteriolar constriction and narrowing of the precapillary sphincters. It is hypothesized that rapidly proliferating vessels such as those in hemangiomas are very sensitive to this steroid action.

More recent studies investigating cellular markers show that rapidly growing hemangiomas show increased levels of angiogenic peptides, primarily vascular endothelial growth factor and basic fibroblast growth factor.23 These peptides may stimulate proliferation cells to differentiate into hemangiomas. The actions of steroids on these angiogenic peptides open up the possibility of using newer antiangiogenic drugs for the treatment of rapidly proliferating hemangiomas.

Treatment with lasers of different wavelengths has been tried for cutaneous vascular lesions.23-26 However, nonspecific thermal injury resulted in a high and unacceptable rate of scarring, particularly in the pediatric population. In 1990, the tunable dye laser was first introduced for the treatment of vascular lesions. This laser at a wavelength of 577 nm corresponds to the second absorption peak of hemoglobin, the use of which results in selective photothermolysis of vascular lesions in the skin, sparing the adjacent and surrounding cutaneous structures and chromophores. The pulse width of 450 microseconds in this laser is of shorter duration than the thermal relaxation time of skin (700-900 microseconds), making the theoretical risk of thermal injury and subsequent scarring negligible. Several clinical studies have substantiated this theoretical application, and the literature currently supports the safe and effective use of the pulse-dye laser in children and infants for the treatment of vascular lesions with an extremely low risk of scarring.27-29

In our patient population, pulse-dye laser treatment was used as a primary modality only in patients who had superficial or dermal hemangiomas with vascular proliferation, since the depth of penetration is limited to 1 mm. In addition, preliminary reports as well as our anecdotal experience have demonstrated that early pulse-dye laser treatment of superficial proliferating hemangiomas in neonates and infants is effective in selectively destroying the exaction and proliferating dermal ectasia tissue with complete resolution within 3 months (Figure 2).

Advances in surgical technique have resulted in a lower threshold for surgical intervention. As first described by Gonzalez-Ulloa et al in 1954, soft tissue facial reconstruction with attention given to the concept of aesthetic units continues to be emphasized along with techniques of scar camouflage and implementation of laser technology (Figure 5).

The final key issue regarding earlier intervention concerns the psychosocial trauma suffered by children as a consequence of the readily visible hemangioma. While children under age 3 years do not have a well-developed body image (body image beginning to develop shortly thereafter), by age 7 years, children are able to differentiate between “pretty” and “ugly” images. More recently it has been demonstrated that the families of children afflicted with hemangiomas are adversely affected, and the associated adaptive patterns have been characterized.31-33 It is for these reasons that we and others now advocate earlier intervention in children where appropriate surgical correction and/or laser treatment results in a favorable risk-benefit ratio.29,30,34

In this article, we wish to emphasize the importance of a high degree of vigilance and early referral of infants presenting with a small macular blush that may be the initial presentation for a potentially disfiguring or functionally problematic hemangioma. Furthermore, we advocate an early, accurate diagnosis and a clear understanding of the natural history and histopathology of hemangiomas, since it seems that some lesions follow a pattern of early involution while others will involute more slowly and later in childhood, as illustrated in Figure 1. Most hemangiomas do not require close follow-up examinations or treatment. However, the management of patients with potentially problematic hemangiomas should involve a multidisciplinary approach. With contemporary anesthetic techniques, safer and more selective laser therapy, and a conservative tissue-sparing surgical approach, we recommend intervention when appropriate. Finally, we have presented an algorithm to assist in managing infants and children with hemangiomas, as outlined in Figure 7. This algorithm was based on the natural history of this benign neoplasm, the literature, and our experiences in evaluating, observing, and treating patients with hemangioma at The Albany Medical Center Vascular Malformation Clinic.

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REFERENCES


