

# ORIGINAL ARTICLE

# Infantile Hemangioma of the Breast: Long-Term Assessment of Outcomes

Brian I. Labow, MD, FACS, FAAP\*† Shomoukh A. Alshamekh, MD\*‡§ Valerie M. Carlberg, MD\*‡¶ Jennifer L. Zacur, MD, PhD\*‡1 Lily C. Uihlein, MD, JD\*‡\*\* John B. Mulliken, MD\*† Marilyn G. Liang, MD\*‡

**Background:** The literature is meager regarding the natural history and outcomes of infantile hemangiomas (IHs) in the breast. Treatment in childhood may be considered due to psychosocial and physical concerns with breast development. Early surgical intervention may cause iatrogenic breast asymmetry and possibly impair lactation later in life. This study characterizes the clinical presentation, management, and long-term outcomes of IHs arising in the breast.

**Methods:** Female patients aged 11 years or older at presentation were included in a retrospective review of the Vascular Anomalies Center database for patients with IHs of the breast seen at our institution between 1980 and 2020. Breast development was ascertained by a structured telephone interview, physical examination, or photographs.

**Results:** A total of 10 patients met criteria for inclusion in this study. The median age at enrollment was 14 years (11–36 years). Breast asymmetry was noted in 60% of patients (n = 6). Of the four patients who underwent subtotal excision of breast IH, three developed ipsilateral breast hypoplasia. Breast asymmetry was also noted in three of five patients who did not receive medical treatment: two with hypoplasia and one with hyperplasia. No asymmetry was noted in the single patient who received corticosteroid.

**Conclusions:** IHs involving the nipple–areola complex can be associated with breast asymmetry. Hypoplasia was noted in patients not treated with corticosteroid or resection in childhood. These findings suggest that systemic treatment should be considered. Longitudinal follow-up on patients treated with propranolol will elucidate its possible benefits in minimizing breast asymmetry. (*Plast Reconstr Surg Glob Open 2024; 11:e5506; doi: 10.1097/GOX.000000000005506; Published online 8 January 2024.*)

# **INTRODUCTION**

Treatment of infantile hemangioma (IH) in critical areas such as the face and neck is typically recommended to avoid cosmetic or functional defects<sup>1</sup>; however, there is a paucity of literature regarding the management and clinical course

From the \*Harvard Medical School, Boston, Mass.; †Department of Plastic and Oral Surgery, Boston Children's Hospital, Boston, Mass.; ‡Dermatology Program, Boston Children's Hospital, Boston, Mass.; \$Department of Dermatology, King Saud University, Riyadh, Saudi Arabia; ¶Dermatology Program, Children's Hospital Wisconsin, Milwaukee, Wis.; ||St Joseph Mercy Chelsea Hospital, Chelsea, Mich.; and \*\*Department of Dermatology, Kaiser Permanente, Petaluma, Calif.

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Copyright © 2024 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of The American Society of Plastic Surgeons. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal. DOI: 10.1097/GOX.00000000005506 of IH involving the breast.<sup>2,3</sup> The tumor in the proliferative phase could damage the nipple–areolar breast, leading to hypoplasia.<sup>2–4</sup> Surgical intervention could also injure the breast bud causing defective growth.<sup>5</sup> Due to the delayed nature of female breast development, the outcome of untreated or treated hemangiomas may not become apparent until puberty.<sup>2–4,6</sup> Because of psychosocial issues related to breast asymmetry, it is important to foresee these complications and anticipate them in management of breast IH.<sup>4,5,7</sup>

In this study, we characterized the clinical presentation, management options, and long-term outcomes in a small series of breast IHs.

## **METHODS**

Our institutional review board approved a retrospective review and follow-up of patients with IH of the breast.

Disclosure statements are at the end of this article, following the correspondence information.

Related Digital Media are available in the full-text version of the article on www.PRSGlobalOpen.com.

Using our institution's Vascular Anomalies Center database, we identified patients who were diagnosed with IH of the breast and evaluated at Boston Children's Hospital between 1980 and 2020.

We excluded male patients and patients younger than 11 years of age. This cut-off was based on the estimate of mean age of the larche at 10.2 years in the United States general population.<sup>8</sup> Eligible patients who no longer received care at our Vascular Anomalies Center were invited to participate. After written informed consent and assent (if applicable) were obtained, breast development was ascertained by chart review, photographs, physical examination, and a structured telephone interview (Figs. 1-3). (See figure, Supplemental Digital Content 1, which displays patient 5 at 7 years of age. No surgical procedures or other treatments. Right breast is larger at age 14 years. http://links.lww.com/ PRSGO/C966.) [See figure, Supplemental Digital Content 2, which displays patient 6 at (A) age 13 years, and age 17 years before (B), and after (C) breast reduction surgery. Two staged excisions of involuted hemangioma were done at age 13 and 14 years. Corrected asymmetry reported at age 24 years. http://links.lww.com/PRSGO/C967.] [See figure, Supplemental Digital Content 3, which displays patient 8 at age 4 years, before (A) and post (B) subtotal excision of infantile hemangioma on left breast. Patient reports left breast hypoplasia after puberty. http://links.lww.com/ PRSGO/C968.] [See figure, Supplemental Digital Content 4, which displays patient 9 at age (A) 2 weeks, (B) 3 months, and (C, D) 8 years. No surgical procedures or other treatment. Hypotrophy of right breast noted at age 14 years. Patient is planning for right breast implant placement in the future. http://links.lww.com/PRSGO/C969.]

Patients/parents were asked a series of questions, including the appearance and location of the IH, number of IH, medical and birth history, any diagnostic tests performed since diagnosis, the impact of the IH on breast development, the timing of any treatments and/or procedures, and the outcome or complications. Patient photographs and outside records relevant to treatment of IH were obtained.

#### **Takeaways**

**Question:** How does infantile hemangioma (IH) of the breast present and develop, and what are the long-term outcomes with/without treatment?

**Findings:** A retrospective review of female patients aged 11 years or older seen at our institution from 1980 to 2020 was performed to assess the natural history and outcomes of breast IHs. Ten patients with a median age of 14 years were included, and 60% of patients (n = 10) developed breast asymmetry. Patients were untreated, or received surgical (subtotal excision) or nonsurgical (corticosteroid) treatment.

**Meaning:** IH of the breast may result in breast asymmetry, and further investigation is needed to determine if treatment can prevent it.

# RESULTS

We identified 41 patients with breast IH. After applying exclusion criteria, 30 patients were eligible, and only three had follow-up data available in our medical record. Of the remaining 27 patients, seven agreed to participate in the study. A total of 10 patients were included for analysis (Table 1 and Fig. 1).

The average follow-up time was 19.2 years. A total of four of 10 patients were Tanner stage V and had completed breast development at the time of our analysis. The median age of patients at most recent follow-up in the study was 14 years (11-36 years). All breast IH in our cohort appeared between birth and age 4 months and exhibited a normal IH growth pattern. Four patients had at least one other cutaneous IH. All tumors were focal except a single patient who had a regional IH extending onto the ipsilateral chest wall and arm (Fig. 2). All 10 patients had combined superficial and deep IH of the breast involving the nipple–areola. None of the patients had bilateral breast involvement. Ulceration of the skin occurred in one patient (Fig. 3).

Regarding management, five of the 10 patients did not receive medical or surgical treatment of IH of the breast

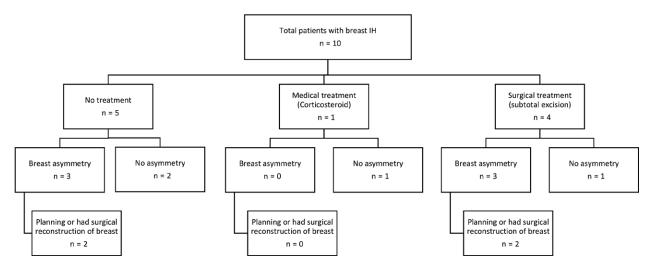


Fig. 1. Treatment and outcomes of patients with breast IH.

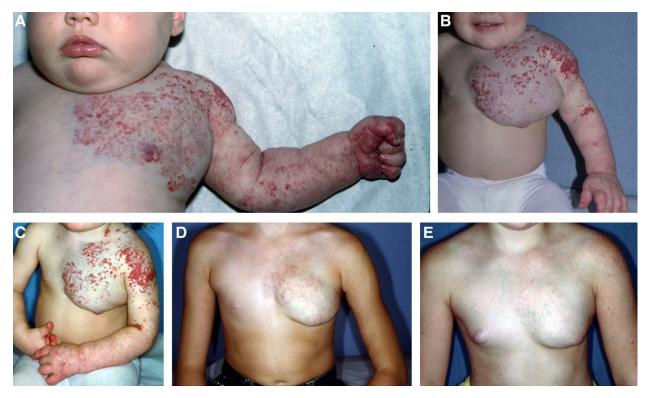
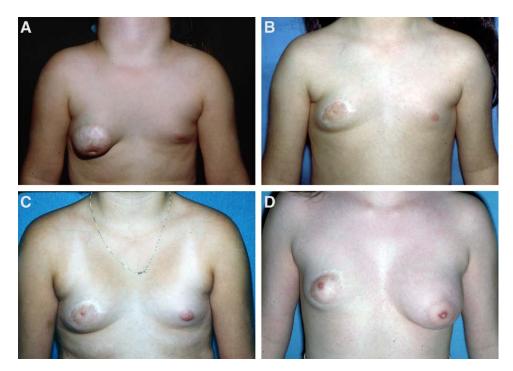


Fig. 2. Patient 4 at (A) 3 months, (B) 14 months, (C) 3.5 years, (D) 7 years, and (E) 11 years of age. The patient received systemic corticosteroid at ages 2–8 months and multiple treatments with pulsed dye laser at 6–10 years. At 17 years, evaluated by plastic surgery: left nipple ptosis (1 cm), but breast volume within normal range of symmetry.



**Fig. 3.** Patient 7 at (A) 4 years, (B) 5 years, (C), 7 years, and (D) 14 years of age. Patient received subtotal excision of involuted hemangioma at age 5 years. Right breast implant placed at age 14 years, persistent hypoplasia of right breast at 36 years.

Patient	Age at Last Follow- up, Years	IH Features						
		Location	Largest Diameter, cm	Ulceration	Concomitant IH	- Nonsurgical Treatment	Surgical Treatment	Breast Outcomes
1	11	Right breast	3	Ν	Right cheek (1)	Ν	Subtotal excision at age 4 and 5	No asymmetry
2	13	Right breast	3	Ν	N	Ν	N	No asymmetry
3	13	Left breast	1	Ν	Right ear (1)	Ν	N	No asymmetry
4	24	Left chest, back, arm and entire left breast	NA	N	N	Systemic cor- ticosteroid at ages 2–8 months	N	Left nipple ptosis (1 cm); otherwise, symmetric
5	14	Right breast	5	N	N	N	N	Right breast hypertrophy and fibrofatty tissue
6	24	Left breast	7	N	Neck (1), back (2)	N	Subtotal excision at ages 13 & 14; bilateral reduc- tion mammo- plasty at age 17	Left breast hypopla- sia at age 17, cor- rected after third breast reconstruc- tion procedure
7	36	Right breast	7	N	N	N	Subtotal excision at age 4; implant placed at age 14	Right breast hypo- plasia at age 14, persisting after two breast reconstruc- tion surgeries
8	16	Left breast	7	Y, involving nipple	Scalp (1), Neck (1)	N	Subtotal excision at age 4	Left breast hypo- plasia
9	13	Right breast	3	N	N	N	N	Right breast hypo- plasia, planning reconstruction
10	14	Right breast	2.5	N	N	N	N	Right breast hypo- plasia, planning reconstruction

#### Table 1. Characteristics of Patients with Breast IH

CM, capillary malformation; IH, infantile hemangioma; IL, intralesional.

(patients 2, 3, 5, 9, 10). Patient 4 received systemic corticosteroid as an infant. Four patients (1, 6–8) underwent IH resection of involuted breast IH between the age of 4 and 13 years.

Breast asymmetry was noted in 60% of patients (n = 6, patients 5-10). Subtotal excision of breast IH was done between age 4 and 5 in three patients and at 13–14 years in one patient; breast asymmetry was noted in both groups. Of the four patients who underwent subtotal excision of breast IH, three developed ipsilateral hypoplasia in the operated breast (6–8). Breast asymmetry was also noted in three of five patients who did not receive any treatment: two with breast hypoplasia (patients 9, 10) and one with breast hyperplasia (patient 5).

Of the six patients with asymmetry, four underwent or were planning to undergo corrective surgery. Patients 6 and 7 underwent breast reconstructive procedures between 14 and 17 years to correct asymmetry: one had a reduction of the larger breast and the other had an implant placed in the hypoplastic breast. Patients 9 and 10 did not have prepubertal excision and are planning to undergo unilateral breast augmentation.

Four of 10 patients reported symmetric breasts: two did not receive any medical or surgical treatment (patients 2 and 3), one had staged excisions of involuted IH between 4 and 5 years of age (patient 1), and one received systemic corticosteroid as an infant and developed ipsilateral nipple ptosis but without asymmetry (patient 4). None of the patients attempted to breastfeed at the time of interview.

#### DISCUSSION

Although IH are benign and have a predictable growth pattern, secondary distortion and destruction of anatomic areas such as the nose, lip, and ear have been described.9-11 To diminish complications and relieve later psychosocial distress, medical or surgical intervention is often advocated early in life.1 Current treatment for IH includes observation, medical treatment with beta-blockers or corticosteroid, and excision; beta-blockers are the current gold standard (ie, propranolol). However, the US Food and Drug Administration did not approve the use of an oral formulation of propranolol until 2014, and in 2015, a large controlled trial demonstrated the effective dosage of propranolol for treating IH.<sup>11</sup> Given that we conducted our retrospective review from 1980 to 2020 and only included patients aged older than 11 years, no patients who may have received beta-blocker treatment for breast hemangioma after 2015 would have been eligible for inclusion in our study, despite beta-blocker treatment now being referred to as the gold standard.

The female breast exists as a bud beneath the nipple– areola complex until thelarche, typically early in the second decade of life.<sup>12</sup> Little is known about the long-term outcome of breast development after subareolar hemangiomatous eruption during infancy.<sup>2,3</sup> The present study evaluated 10 patients, half of whom did not receive treatment and four who underwent excision before breast development. Asymmetry with ipsilateral hypoplasia was reported in both groups. Only one patient was treated medically without surgical intervention and reported satisfactory breast symmetry.

Few case reports describe that untreated involuted breast IH may give rise to unfavorable aesthetic outcome, such as persistent telangiectasias or fibrofatty residuum in childhood, as well as ipsilateral breast hypoplasia or hyperplasia after puberty.<sup>2,3</sup> In our study, three of five patients with untreated breast IH developed breast asymmetry.

Concerns for iatrogenic injury after resection around the breast bud in childhood are published.<sup>5</sup> This occurred in three of our four patients who underwent early resection and developed breast hypoplasia in puberty. The outcome did not differ in the age at which subtotal excision was performed. Both patients who had the procedure at age 4–5 years and 13–14 years exhibited breast asymmetry.

Radiation is no longer used to treat IH; however, radiation was once commonly used. Fuerst et al evaluated 129 women with history of irradiated IHs of the breast.<sup>13</sup> They reported that 57% developed ipsilateral breast hypoplasia, and 8% developed contralateral hypoplasia. Other studies report similar findings after radiation exposure.<sup>14–16</sup>

Breast asymmetry is common, particularly early in breast development during puberty.<sup>8,17</sup> The physical and psychosocial impact can be considerable. A cohort study evaluating 59 adolescent women with breast asymmetry found that those patients had diminished quality of life, lower self-esteem, and disordered eating patterns when compared with unaffected peers.<sup>7</sup> Breast asymmetry can also lead to difficulty finding appropriately fitting bras and clothing, leading to decreased participation in sports and social activities.<sup>18</sup>

Selecting treatment for patients with breast IH remains a challenge, as it is unknown how and when IH affects breast development. Mechanisms that have been suggested to explain hypoplasia include loss of critical adnexal structures during the proliferative phase, primary ulceration and scarring, damage during involution, and early resection.<sup>12,17-22</sup> For small lesions, or in cases in which the patient and parents are not bothered by the IH, observation may be a reasonable approach.<sup>23,24</sup> In girls with localized skin irritation or a large, cumbersome lesion, medical treatment or excision may be considered. Surgical intervention is probably best delayed until the IH has undergone involution when the bulk and vascularity have diminished, and the nipple-areola complex is distinct. For the rare problematic early IH, medical therapy is likely useful. Regardless of management, patients and parents should be counseled on the potential for breast

asymmetry and the possibility for correcting asymmetry in mid-teenage years either nonoperatively with a temporary prosthesis, or surgically once breast and skeletal growth are complete.<sup>18</sup>

Our study is not without limitations. The retrospective nature of this single-institution study and time lag between onset of IH and breast development made it difficult to locate all eligible participants, thereby limiting the sample size. There is also a likely referral bias, given IHs occurring on the trunk are usually perceived as low risk and, therefore, not referred for evaluation.<sup>24</sup> Treatment was variable throughout the period of the study and only included nonintervention, corticosteroid, and resection. Propranolol is now widely used as a first-line therapy for IH; most infants with IH of the breast receiving beta-blockers have yet to reach thelarche. Another confounding factor is that many adolescents have some breast asymmetry, although symmetry is achieved in 75% by late teens.<sup>21,25-27</sup> Future research to quantify and compare the asymmetry experienced by patients with hemangioma of the breast and the general population of adult women is needed to determine if hemangioma results in significantly more extreme breast asymmetry. In addition, though a thorough review of family history of breast asymmetry or other deformity is outside the scope of the current study, these data may help elucidate potential associations between the asymmetry resulting from IH and that of other conditions in future studies. Documenting Tanner stage based on average reported patient age is a further limiting factor affecting accuracy.<sup>27</sup> Three of the four patients with symmetric breasts were 11 and 13 years of age at the time of the study and may develop minor asymmetry as they mature. None of the participants in our study attempted to breastfeed; thus, we cannot draw conclusions regarding the potential impact of IHs of the breast on breastfeeding.

In conclusion, IH of the breast may result in breast asymmetry. Larger multi-institutional studies with longer follow-up are needed to better evaluate treatment options and determine whether medical therapy early in life reduces the risk of breast asymmetry.

> Brian I. Labow, MD, FACS, FAAP Department of Plastic and Oral Surgery Boston Children's Hospital and Harvard Medical School 300 Longwood Avenue Hunnewell 1 Boston, MA 02115 E-mail: brian.labow@childrens.harvard.edu

### DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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