

# Rapidly Growing Ulcerating Infantile Hemangioma Characterized by Leukocytosis and Thrombocytosis in an Infant

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## Abstract:

Infantile hemangiomas are the most common benign soft tissue tumors in childhood, with a multifactorial pathogenesis that remains not fully understood. The diagnosis is primarily clinical, and while most IHs resolve spontaneously, life-threatening cases may require intervention. There are no specific laboratory findings for IHs, though Kasabach-Merritt phenomenon is a rare complication characterized by giant hemangiomas and severe thrombocytopenia, which may lead to life-threatening hemorrhage.

In this case report, a patient with IHs demonstrated leukocytosis and thrombocytosis, which could not be explained by any other factors. Despite two months of propranolol treatment starting at 1 month and 27 days, the hemangioma did not shrink and ulcerated, leading to surgical removal at 4 months and 10 days. Notably, leukocytosis and thrombocytosis persisted for up to 20 months.

We found it appropriate to publish this case because we did not encounter a case of infantile hemangioma presenting with persistent leukocytosis and thrombocytosis in the literature.

**Key words:** infantile hemangiomas; leukocytosis; thrombocytosis

## Introduction

IHs are the most prevalent benign vascular tumors observed in infants, affecting approximately 4-5% of newborns [1]. They follow a distinctive clinical trajectory, characterized by an initial proliferative phase that is subsequently followed by spontaneous involution. While the majority of cases are self-limiting, some necessitate medical intervention due to complications or aesthetic considerations [2].

IHs demonstrate a notable prevalence in pediatric populations, particularly among females [3], premature infants [4], and those with low birth weight [5]. Additional risk factors include multiple gestations, advanced maternal age, and placental anomalies such as preeclampsia [6].

The exact etiology of IHs is not fully understood; however, their pathogenesis appears to be multifactorial, incorporating genetic [7], molecular [8], and environmental [9] influences. A prominent hypothesis suggests that aberrant vasculogenesis and angiogenesis, likely triggered by hypoxia during fetal development, lead to the upregulation of vascular endothelial growth factor (VEGF) and other pro-angiogenic mediators [10]. Recent research has emphasized the significance of glucose

transporter 1 (GLUT1), which is consistently expressed in the endothelial cells of IHs, serving as a reliable diagnostic marker [11].

Typically, IHs present as red, raised lesions within the first few weeks of life, predominantly located on the head and neck, which accounts for nearly 60% of cases [12]. Complications can arise, including ulceration, functional impairments (e.g., visual obstruction), or airway involvement [13]. The diagnosis of IHs is primarily based on clinical evaluation, informed by history and physical examination [14]. A hallmark feature is the GLUT1 positivity observed in endothelial cells, which effectively distinguishes IHs from other vascular anomalies [11]. In rare cases, IHs may lead to the Kasabach-Merritt phenomenon, characterized by thrombocytopenia, microangiopathic hemolytic anemia, and hypofibrinogenemia, which reflects a consumptive coagulopathy [15].

The management of IHs is influenced by several factors, including the size and location of the lesion, its growth phase, and any associated complications [16]. Propranolol, a non-selective beta-blocker, is the primary treatment for complicated IHs [17]. Prior to the introduction of propranolol, systemic corticosteroids were the predominant therapeutic

option [18]. Surgical intervention is infrequently necessary but may be considered in cases of residual lesions after involution or for those that do not respond to medical treatment [19].

### Case Presentation

A three-day-old female infant presented to our clinic on September 14, 2018. Routine measurements showed no abnormalities. There was no history of chronic disease in the infant's family, and the parents were not related.

The infant's general condition was good, with a length of 50 cm, a head circumference of 35 cm, and a weight of 3 kg. A hemangioma measuring 5 x 3.5 cm was observed in the left hypochondriac-lumbar region of her back. Following a thorough evaluation, the infant was discharged with recommendations for regular follow-up visits.

The next examination took place when the infant was one month and 18 days old. Her general condition remained stable, and urinalysis results

were within normal limits. An ultrasound of the left hypochondriac region revealed a subcutaneous hemangioma that had increased in size to 66 x 40 x 17 mm. The externally measurable dimensions of the lesion had grown to 8.5 x 4 cm, indicating rapid growth.

When the baby was one month and 21 days old, propranolol therapy was initiated during hospitalization, starting with an oral dose of 1 mg/kg/day in the first week and increasing to 2 mg/kg/day from the second week onward. However, after 2 months and 13 days of propranolol therapy, there was no significant reduction in the hemangioma's size. By the time she was 3 months and 22 days old, the hemangioma had ulcerated, causing severe discomfort and incessant crying. Although oral analgesics were administered, there was no improvement in her severe discomfort.

At 4 months and 10 days, surgical intervention was deemed necessary because propranolol therapy failed to reduce the size of the ulcerated hemangioma or promote healing. The infant continued to have regular follow-ups until she was 4 years and 9 months old (Figure 1).



**Figure 1:** A. Measured from the skin surface, the hemangioma became 8.5 cm x 4 cm. It is growing very fast. B & C. Baby was 3 months and 22 days old, the hemangioma ulcerated. D. 24 days after the operation, when the baby was 5 months old. E. Baby was 4 years and 9 months old.

Postoperative evaluations indicated a complete resolution of pain and discomfort. However, persistent leukocytosis and thrombocytosis were observed from the second to the twentieth month of life. Notably, even 2 months and 26 days after the hemangioma surgery, leukocytosis and thrombocytosis were still present and could not be attributed to any other cause.

Additionally, the infant experienced nasopharyngitis at 1 year and 4 months of age, with leukocyte and platelet counts of  $33.0 \times 10^9/L$  and

$407.0 \times 10^9/L$ , respectively. These findings pointed to an exaggerated inflammatory response, with no identifiable underlying cause for the leukocytosis or thrombocytosis. C-reactive protein (CRP) values were within expected ranges throughout the entire follow-up period.

By 1 year and 8 months of age, complete blood count results returned to normal. The patient continued to be monitored until 4 years and 9 months of age, during which normal growth and developmental milestones were observed (Table 1).

| Age                 | WBC ( $\times 10^9/L$ ) | Neutrophils (%) | Monocytes % + lymphocytes % | Platelets ( $\times 10^9/L$ ) | CRP (mg/L) (N 0-5 mg/L) | Size of hemangioma (cm) other situations   |
|---------------------|-------------------------|-----------------|-----------------------------|-------------------------------|-------------------------|--|
| 3 days (14.09.2018) |                         |                 |                             |                               |                         | 5 x 3.5  |
| 1 month 21 days     | 16.7                    | 25.8            | 74.2                        | 752                           |                         | 8.5 x 4, Oral propranolol treatment was discussed with her family.                   |
| 1 month 27 days     | 16.4                    | 18.9            | 80.1                        | 733                           | 0.8                     | 8.5 x 4, All analysis results are normal. Oral Propranolol was started, hospitalized |
| 2 months 13 days    | 21.2                    | 25.8            | 74.2                        | 630                           | 1.2                     | 8.5 x 4 routine control for propranolol  |

|                                  |      |      |      |     |     |   |
|----------------------------------|------|------|------|-----|-----|---|
| 2 months<br>18 days              | 24.8 | 56.8 | 43.2 | 508 | 3.2 | 8.5 x 4<br>routine control for propranolol                              |
| 3 months<br>22 days              | 27.2 | 56.2 | 43.8 | 576 |     | 8.5 x 4<br>The hemangioma was ulcerated.                                |
| 4 months<br>10 days              | 19.7 | 20.7 | 79.3 | 617 | 0.6 | She had a hemangioma operation<br>(Her family requested the operation.) |
| 7 months<br>4 days               | 21.4 | 38.8 | 61.2 | 607 | 1.4 | 2 months and 26 days after the<br>operation                             |
| 1 year<br>4 months               | 33.0 | 81.9 | 18.1 | 407 | 1.6 | She has nasopharyngitis<br>All analysis results are normal.             |
| 1 year<br>8 months               | 6.6  | 44   | 56   | 267 |     | Routine control   |
| 2 years<br>7 months              | 21.0 | 78.8 | 21.2 | 423 | 1.3 | She has nasopharyngitis.<br>All analysis results are normal.            |
| 3 years<br>1 month               | 11.4 | 21.9 | 78.1 | 484 | 2.1 | Routine analysis results are normal.                                    |
| 4 years<br>9 months (27.06.2023) | 9.4  | 78.2 | 21.2 | 340 |     | Routine control   |

**Table 1:** Course of leukocytosis and thrombocytosis and other findings during the follow-up period.

## Ethical Considerations

The authors confirm that they obtained all necessary patient consent forms. The patient's parent gave written informed consent to publish this case report and accompanying images. The Golden Life American Hospital Ethics Committee approved this study.

## Discussion

IHs are the most common vascular tumors of infancy, affecting up to 12% of infants by the first year of life. They grow rapidly in the first 3 to 6 months of life [20]. Big IHs, complicated by ulceration, usually require hospitalization [21]. Oral propranolol is now the first-line treatment, and it should be administered as early as possible to avoid potential complications [8].

IHs typically exhibit a rapid proliferative phase, followed by a period of spontaneous involution. Although clinical examination and imaging studies are fundamental to diagnosis, laboratory findings provide important insights, especially in cases of atypical presentation, systemic complications, or during treatment monitoring [2].

Recent research has clarified the role of angiogenic pathways in the pathogenesis of IHs. Consistently elevated levels of VEGF [10] and basic fibroblast growth factor (bFGF) [22] have been observed during the proliferative phase of IH. These findings correspond with the hypervascularity noted histologically, highlighting the dysregulated angiogenesis that contributes to tumor growth. Elevated VEGF levels may serve as a useful biomarker for assessing tumor activity and guiding therapeutic interventions, especially in patients receiving treatment with beta-blockers such as propranolol [10,22].

Laboratory analyses frequently show elevated levels of endothelial progenitor cells (EPCs) in the peripheral blood of infants with IHs [23]. EPCs are thought to play a crucial role in the neovascularization process, and a decrease in their levels is associated with the tumor's transition from a phase of proliferation to involution. Furthermore, studies examining the expression of GLUT1, which serves as a specific marker for IH, provide diagnostic confirmation when the nature of the lesion is uncertain [11].

Instances of IH rarely lead to complications such as the Kasabach-Merritt phenomenon, which is a consumptive coagulopathy associated with large or atypical vascular lesions. Laboratory findings in Kasabach-Merritt phenomenon typically reveal thrombocytopenia, hypofibrinogenemia, and elevated D-dimer levels, indicating ongoing intravascular coagulation. These laboratory results require prompt therapeutic intervention to avert life-threatening hemorrhage [15].

Anemia can sometimes be seen in large or ulcerated IHs due to ongoing blood loss or local inflammation [24]. In these situations, laboratory assessments such as hemoglobin levels and iron studies are essential for accurate diagnosis and management [6]. Additionally, serum cortisol levels should be monitored in patients undergoing treatment with systemic corticosteroids to facilitate the early detection of adrenal suppression [25].

Monitoring laboratory parameters during treatment is essential for assessing both the efficacy and safety of therapy [16]. For example, propranolol, a cornerstone in the management of IHs, requires baseline and follow-up evaluations of blood glucose levels and cardiac function due to potential side effects associated with the medication [17]. Consequently, laboratory results play a crucial role in weighing the therapeutic benefits against the associated risks.

In this case, oral propranolol was started as early as possible. However, the hemangioma was ulcerated quickly, and propranolol did not reduce the size of the hemangioma in 2 months and 13 days. The ulcerated hemangioma caused severe pain in the baby. The baby's comfort improved rapidly after the operation. Leukocytosis and thrombocytosis started in the second month and continued after the operation. However, permanent normal leukocyte and platelet counts were achieved when the baby was 20 months old.

## Conclusion

This case highlights that IHs can induce isolated inflammatory markers, such as leukocytosis and thrombocytosis, even when other inflammatory markers, like CRP, remain normal.

Furthermore, leukocytosis and thrombocytosis may persist for up to 1 year and 8 months, even after surgical intervention. Understanding this phenomenon is crucial to prevent unnecessary antibiotic use and to alleviate concerns among physicians and families. It ensures that these transient hematologic changes are not misinterpreted as indicators of infection or malignancy. Further research is needed to explore the underlying mechanisms of these inflammatory responses and their relationship to the pathogenesis of IHs.

Our study presents what may be the first documented case of IH associated with leukocytosis and thrombocytosis. A review of the literature found no other recorded instances of IH linked to these blood conditions.

In cases of IH, prolonged leukocytosis and thrombocytosis without any identifiable cause can cause significant concern for both healthcare

providers and the patient's family. These findings may lead to unnecessary antibiotic treatments and considerable anxiety. The aim of publishing this case is to increase awareness among clinicians and families, highlighting that in the presence of leukocytosis and thrombocytosis in IH cases, it is important to avoid unnecessary panic, as long as other potential causes have been ruled out.

### Author Disclosure Statement

No competing financial interests exist.

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