

CASE REPORT

Klebsiella pneumoniae-infected hemorrhagic ulcerative infantile hemangioma: A rare complication

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Key Clinical Message

Infections in infantile hemangiomas (IHs) are generally limited, and only few cases have been reported. The rapid expansion of an ulcerated IH should raise concern for possible complications to monitor and provide immediate therapeutic interventions. This case highlights the importance of prompt treatment in large segmental IHs to prevent ulceration and related complications, including bleeding and superinfection.

Abstract

IH is a benign tumor proliferating during early infancy. While many IHs spontaneously resolve, complications like ulceration, bleeding, and potential damage to vital organs can occur, leading to pain, infection, and scarring. A 6-month-old girl with a previously treated IH on her left leg developed a *Klebsiella*-infected ulcer at the site. The ulcer resulted from non-standard treatments used before admission. Upon hospitalization, she was initially treated with cefepime and propranolol, but a week later, the wound culture revealed *Klebsiella pneumoniae*, prompting a switch to piperacillin/tazobactam. After successfully managing the infection and bleeding, the child was discharged in good condition with orders to continue treatment with propranolol for at least a year. This case highlights the potential of IHs to become infected even with uncommon germs such as *Klebsiella* and the importance of receiving appropriate medical care to prevent further complications.

KEYWORDS

bleeding, hemangioma, infection, pediatrics, ulceration

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1 | INTRODUCTION

Infantile hemangiomas (IHs) are a common type of vascular tumor in infancy that typically follow a predictable and distinct growth pattern.¹ IHs usually start to grow within the first two to four weeks after birth, complete their growth phase by 9–12 months, and gradually involute and turn into adipose and fibrous tissue by 4–5 years.²

Although IH complications are uncommon, ulceration is among the most critical ones.³ Other adverse events include disfigurement, scarring, functional impairment, and infection.⁴ There are limited reports of infection in the setting of IHs, of which *Staphylococcal* and *Streptococcal* species are among the most common causes.⁵

Hence, we presented a 6-month-old infant with a large segmental ulcerative IH on her left leg, which was infected with *Klebsiella pneumoniae*. To our knowledge, infection of IHs with *K. pneumoniae* has not been reported in previous literature.

2 | CASE HISTORY/EXAMINATION

A 6-month-old girl presented with fever, irritability, and a necrotic ulcer on her left lower leg. At the age of 2 weeks,

a flat red patch appeared on the lateral side of her left leg, which has gradually increased in thickness and size over a month without the use of any medications. Upon 2 months of age, two small grayish discoloration areas gradually developed into hemangioma, which spontaneously progressed towards ulceration.

At the age of 2 months, a family physician prescribed her triamcinolone acetonide 0.1% ointment and silver spray three times daily, additionally with local wound care with no clinical improvement. At 4 months of age, she was taken to a wound care specialist lacking proper expertise, who carried out wound debridement every other day for 15 days and applied an unidentified topical ointment under occlusion and oral cephalixin daily. Gradually, small ulcers progressed to a large necrotic ulcer.

Upon admission, she had an ulcer with several necrotic areas measuring 6 × 5 cm on the lateral side of her shin, which bled occasionally and contained purulent, green-colored discharge (Figure 1A). In her physical examination, she was febrile (39°C), started 7 days before the admission, irritable, and had local wound tenderness. She was a previously healthy infant born as a full-term neonate with an unremarkable familial medical history.



FIGURE 1 Ulcerated infantile hemangioma. 6-month-old girl with an Infantile Hemangioma infected with *klebsiella pneumoniae* which was treated with propranolol and piperacillin-tazobactam: (A) Initial presentation with bleeding and ulceration; (B) Two weeks after the treatment with significant size reduction; (C) Four weeks after the treatment and granulation tissue formation; (D) Six weeks after the treatment and significant ulcer improvement.

3 | METHODS (DIFFERENTIAL DIAGNOSIS, INVESTIGATIONS AND TREATMENT)

The laboratory findings demonstrated an elevated white blood cell count (WBC) of $18.2 \times 10^9/l$ with a lymphocyte of 53/1% and a neutrophil of 39/1%, an elevated erythrocyte sedimentation rate (ESR) of 42 mm, an increased (greater than 3 mg/L) C-reactive protein (CRP) level, and hemoglobin of 10.2 g/dL. Her serum sodium was also elevated to 147 mmol/L. The rest of her laboratory data were unremarkable.

Soft tissue ultrasonography showed a heterogeneous hypoechoic area with dimensions of $33 \times 5.8 \times 23$ mm and an approximate volume of 5.3 cc at a depth of 7.7 mm from the skin surface, suggesting collection formation. Magnetic resonance imaging (MRI) of the left leg revealed subcutaneous edema and myositis in the posterior fibular muscles without any evidence of osteomyelitis. Abdominal ultrasonography findings were unremarkable. The patient was hospitalized for 2 weeks, suspected to have an infected ulcerated hemangioma. Empirical antimicrobial treatment with intravenous infusion of Cefepime 150 mg/kg/day was initiated. Blood culture test using BACTEC method was obtained but the result showed absence of bacterial growth. Concurrently, a wound culture sample was taken. When the wound culture resulted in *K. pneumoniae* growth, cefepime was changed to intravenous piperacillin/tazobactam 50 mg/kg/day three times daily according to the antimicrobial sensitivity test and continued for 10 days. The results of the antimicrobial sensitivity test are presented in the following table (Table 1). Also, propranolol was started with an initial dose of 0.5 mg/kg/day, which was subsequently raised to 2 mg/kg/day over 3 weeks. Additionally, topical timolol 0.5% twice daily, Burow's solution, fibrinolysin ointment, and wet-to-dry compress were used as localized treatments.

TABLE 1 Antimicrobial sensitivity test results of isolated pathogens.

No.	Antimicrobial drug	Interpretation
1	Amikacin	S
2	Cefepime	R
3	Ceftazidime	R
4	Ciprofloxacin	R
5	Meropenem	S
6	Piperacillin/Tazobactam (Tazocin)	S
7	Trimethoprim/Sulfamethoxazole (Co-trimoxazole)	R

Abbreviations: R, resistance; S, sensitive.

4 | CONCLUSION AND RESULTS (OUTCOME AND FOLLOW-UP)

On the sixth day of admission, the bleeding ceased entirely. After 10 days of antibiotic course therapy, the patient was afebrile, and the size of the ulcer decreased to 2×1.5 cm. Three weeks after discharge, her ulcer had considerably improved. Over the 7 months of follow-up, two additional lesions under 1 cm in size also developed but fully resolved with local wound care and persisting systemic propranolol. The prior ulcerated area entirely resolved into a fibrofatty tissue in follow-ups (Figure 1).

5 | DISCUSSION

Here, we described an infant with large segmental ulcerative IH infected with *K. pneumoniae*. The reported rate of ulceration in IHs ranges from 10% to 30%. The large size, mixed morphology type, segmental pattern, rapidly expanding, and located in bending areas increase the risk of ulceration.⁶ In our case, the first ulceration was detected around the peak growth period.

Infection is an uncommon complication of IHs. The infection may represent a hematogenous spread to the IH or a primary infection within the lesion itself.⁶ Infections predominantly develop at ulcerated hemangioma sites.⁷ The mechanism of infection onset in hemangiomas is not well understood but often follows soon after ulcer formation, likely due to poor perfusion and immunity in the lesion.⁵

K. pneumoniae is a leading cause of difficult-to-treat wound and ulcer infections. It predominates in wounds with ischemia and vascular insufficiency. The anaerobic conditions in ischemic, low-perfusion wounds facilitate its proliferation.⁸ Underlying conditions such as diabetes, pressure ulcers, and venous stasis can make wounds more susceptible to infection with *K. pneumoniae*. Necrotic

TABLE 2 Reported cases of infected infantile hemangiomas.

Author, year	Sex, age at presentation (weeks)	Clinical presentations	Hemangioma location	Diagnostic test for infection, result	Treatments	Outcome
Yagupsky et al., ¹⁰ 1987	Girl, 120	Fever, wound induration and erythema	Left buttock	Blood culture, group A beta-hemolytic <i>Streptococcus</i>	Systemic: intravenous penicillin 100,000 U/kg/day Local: none Surgical: none	Completely resected without any complications within 1 year
	Girl, 10	Fever, pallor, and diarrhea	Left hand	CSF & blood culture, group A beta-hemolytic <i>Streptococcus</i>	Systemic: intravenous penicillin 300,000 U/kg/day Local: none Surgical: none	Completely healed within 6 months
Armstrong et al., ¹¹ 1993	Girl, 156	Pyrexia, tachycardia and lethargy	Lower lip	Blood culture, <i>Streptococcus pyogenes</i>	Systemic: intravenous benzylpenicillin 600 mg, intravenous flucloxacillin 125 mg, oral penicillin 250 mg Local: none Surgical: none	Completely healed within 12 days
	Girl, 8	Well on the admission	Upper lip	Culture of the pus, <i>Streptococcus pyogenes</i>	Systemic: intravenous cephadrine, intravenous benzylpenicillin, oral penicillin 250 mg Local: none Surgical: none	Completely healed within 6 weeks
Lacour et al., ¹² 1996	NA	NA	Neck	Swab culture, NA	Systemic: intravenous and oral antibiotics Local: Mupirocin ointment pulsed dye laser Surgical: none	Completely healed within 4 weeks
Ward et al., ¹³ 1998	Boy, 4	Irritability, but no fever	Left hemiscrotum	Wound culture, <i>Pseudomonas aeruginosa</i>	Systemic: none Local: Pulsed dye laser, mupirocin ointment, hydrocolloid dressing Surgical: none	Completely healed within 8 weeks
Horie et al., ¹⁴ 1999	Boy, 16	NA	Left parotid gland region	Immunohistochemistry, cytomegalovirus	NA	Completely resected at 4 months of age
Rezvani et al., ¹⁵ 2004	Boy, 10	Lethargy and irritability	Right forearm	CSF culture, group A streptococcus	Systemic: Intravenous penicillin G Local: none Surgical: none	The case was discharged on day 26, however, on follow-up at age 14 months, profound neurological sequelae remained due to GAS meningitis
Bard et al., ¹⁶ 2010	Girl, 3	NA	Nose and upper lip	NA, respiratory syncytial virus	Systemic: none Local: Topical and intralesional corticosteroids, pulsed-dye laser Surgical: reconstructive surgery	NA

TABLE 2 (Continued)

Author, year	Sex, age at presentation (weeks)	Clinical presentations	Hemangioma location	Diagnostic test for infection, result	Treatments	Outcome
Maguiness et al., ¹⁷ 2010	Girl, 14	NA	Back	NA, Methicillin-sensitive <i>Staphylococcus aureus</i>	Systemic: Prednisolone 1 mg/kg/day, low dose aspirin Local: Becaplermin gel Surgical: surgical resection	Still not completely healed on the follow up at age 14 months
Annagür et al., ⁷ 2012	Girl, 28	Frequent bleedings	Lower lip	NA	Systemic: none Local: Ankaferd blood stopper spray Surgical: none	Lesion bleeding was readily controlled with ABS application on 18 months follow up
Bacik et al., ¹⁸ 2018	Girl, 40	NA	Lower face and neck	Tissue culture, NA	Systemic: propranolol 2.5 mg/kg/day Local: Dehydrated human amnion/chorion membrane allograft surgical: none	Completely healed within 5 weeks
Gardner et al., ¹⁹ 2021	Boy, 16	Fever, swelling in the right posterior neck, erythema, pain on palpation, and poor oral intake	Right posterior neck	Blood culture, group A Streptococcus	Systemic: Clindamycin Local: none Surgical: Surgical excision	Completely resected without any complications at age 15 months
Leung et al., ²⁰ 2021	Boy, 16	Well on the admission	Left elbow	Swab culture, mixed growth of <i>Staphylococcus aureus</i> and <i>Streptococcus pyogenes</i>	Systemic: Oral cefuroxime 2 mg/kg/day, Oral propranolol 15 mg/kg/dose twice daily Local: Zinc oxide cream, petrolatum-impregnated gauze, mupirocin ointment Surgical: none	Healed within 1 month, contracture and restriction of elbow movement was remained at 2 years old follow up
Nagoba et al., ³ 2021	NA, 24	NA	Left groin	Tissue culture and antimicrobial susceptibility test, <i>P. aeruginosa</i>	Systemic: none Local: 3% citric acid ointment once daily Surgical: none	Completely healed after 24 days
Okorie et al., ⁶ 2023	Girl, 104	Runny nose, malaise, cough, and fever	Right neck	Rapid home test, SARS-CoV2	Systemic: none Local: Topical timolol 0.5% gel Surgical: none	Completely healed within 4 weeks
Our case	Girl, 24	Fever and Irritability	Left leg	Tissue culture, <i>Klebsiella pneumoniae</i>	Systemic: Propranolol syrup 2 mg/kg/day, intravenous cefepime 1125 mg daily, intravenous piperacillin-tazobactam 385 mg daily, intravenous methylprednisolone 1 mg/kg/day Local: Metronidazole gel twice daily, topical timolol 0.5% twice daily, burrow's solution twice daily Surgical: none	The ulceration had considerably reduced in size and she was discharged with orders to continue therapy for at least 1 year

wounds are especially vulnerable to colonization by *K. pneumoniae*.⁹ In our case, the superinfection seemed to occur in the setting of occult dressing, leading to an anaerobic condition and finally causing necrosis formation in the wound.

Antibiotic therapy guided by antimicrobial susceptibilities and debridement of necrotic tissue and biofilms should be considered in all infected ones. Beta-lactams were essential therapeutic options against invasive *K. pneumoniae* wound infections. However, in recent years, they have yet to seem inefficient, considering antibiotic resistance raised in many infecting pathogens with multiple mechanisms, including beta-lactamase production.⁸ For our case, we initiated antibiotic therapy with a broad spectrum, cefepime, which was later changed to piperacillin/tazobactam (which is a beta-lactam/beta-lactamase inhibitor), along with the culture and antibiogram sensitivity results.

Limited cases of infected IHs have been described in the literature (Table 2).^{3,6,7,10–20} To provide a comprehensive overview of the various aspects of IHs, 14 relevant publications were summarized, considering their clinical presentations, demographic characteristics, location, diagnostic tests, and their results, treatments, and outcomes.

According to the table, the most common organisms responsible for the superinfection of IHs are streptococcus and staphylococcus. Most infected IH cases are girls with ages between 3 to 120 weeks old and an average age of 37 weeks. The head and neck regions are the most prevalent sites of infection in IHs. Complications due to infection of the IH were observed in three cases. Two of them developed meningitis,^{10,15} and in one case,²⁰ elbow movement was restricted due to contracture of the elbow.

AUTHOR CONTRIBUTIONS

Bahareh Abtahi-Naeini: Conceptualization; data curation; methodology; supervision; writing – review and editing. **Mahsa Pourmahdi-Boroujeni:** Formal analysis; investigation; writing – original draft; writing – review and editing. **Narjes Alipour:** Data curation; writing – review and editing. **Hossein Sattari:** Formal analysis; investigation; project administration; writing – original draft; writing – review and editing. **Zahra Pourmoghaddas:** Conceptualization; data curation; methodology; supervision; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interests regarding the publication of this paper.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are not publicly available due to containing information that could compromise the privacy of our research participant but are available as requested.

ETHICS STATEMENT

The protocol for this study was approved by the Ethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran (IR.ARI.MUI.REC.1402.189).

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

DECLARATION OF INDEPENDENCY TO GOVERNMENT

We declare that none of the authors are employed by a government agency that has a primary function other than research and/or education. None of the authors have an official representative on behalf of the government.


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