



# Worsening Otitis Media Despite Correct Treatment: A Case Report of Pediatric Leukemia

**Urgent Message:** Clinical worsening of typically treatable infections should trigger clinicians to dig deeper for possible underlying, undiagnosed conditions.

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**Key Words:** Pediatric Leukemia; Otitis-Conjunctivitis Syndrome; Persistent Infection; Urgent Care Diagnosis

## Abstract

**Introduction:** Clinical worsening of typically treatable infections is a common initial presentation for pediatric patients with developing underlying oncologic conditions such as leukemia. Due to the gradual development of these conditions, patients may come to urgent care (UC) with varied and multiple presentations, which can often appear unrelated.

**Clinical Presentation:** An 18-month-old female with no known past medical history presented to urgent care UC with left eyelid swelling, drainage, and left ear pain for 4 days. The patient was seen in UC 2 days prior and was currently on day 2 of amoxicillin-clavulanate for otitis-conjunctivitis. She presented now with worsening symptoms including neck swelling and shortness of breath. Recent history included several months of frequent UC and primary care provider (PCP) visits for nonspecific symptoms including reduced appetite and fatigue. In the UC, the patient was febrile with borderline-low oxygen saturation of 92% with tachycardia and intermittent tachypnea. Initial lab workup included a complete blood count (CBC) with a white blood cell count of  $56.1 \times 10^3/\mu\text{L}$  and the presence of blasts (28.2%).



**Case Resolution:** The patient was transferred to the emergency department by ambulance for suspected sepsis. She was started on intravenous antibiotics and fluids. The patient was admitted to oncology due to the presence of blasts on her CBC. A bone marrow biopsy was consistent with the diagnosis of pre-B acute lymphoid leukemia. Chemotherapy was initiated with eventual improvement in symptoms.

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**Conclusion:** When a patient worsens on typically adequate treatment for a prior diagnosis, consider further workup for underlying conditions. For patients with multiple PCP or UC visits in previous months, consider a deeper chart review. This review can provide further context to current symptoms and can help determine the patients for whom further workup is necessary.

### Introduction

**A**cute lymphoid leukemia (ALL) is an oncologic condition involving rapid proliferation of immature white blood cells (WBCs) called blasts. These non-functioning blasts proliferate rapidly and eventually crowd out normal bone marrow, increasing susceptibility to common and opportunistic infections. For ALL, peak incidence occurs at ages 1-4 years.<sup>1</sup> This presents a diagnostic challenge as many well children at this age will also have multiple viral infections, especially over the winter. Typical, more unique presenting symptoms of ALL include easy bruising or bleeding, petechiae, pallor, joint pain, or unexplained fevers. Fatigue, loss of appetite, or weight loss can also occur. On exam, nontender lymphadenopathy or enlarged liver and/or spleen should increase diagnostic suspicion for an oncologic etiology.<sup>2</sup> Due to the non-specific and gradually developing nature of symptoms, these patients often present to the urgent care (UC). Preliminary work up should include a complete blood count (CBC) with differential for which blasts can often be observed.

### Case Presentation

An 18-month-old female with no known past medical history presented to UC with left eyelid swelling, drainage, and left ear pain for 4 days. The patient was seen in UC 2 days prior and was currently on day 2 of amoxicillin-clavulanate for otitis-conjunctivitis. She presented now with worsening symptoms, including neck swelling and shortness of breath. Her recent history included several months of frequent UC and primary care provider (PCP) visits for nonspecific symptoms including reduced appetite and fatigue.

Her previous UC visits included:

- **3 months prior:** Right lower extremity limping due to fall. X-ray was negative for fracture. Symptomatic management was suggested.
- **1 month prior:** Nausea and loss of appetite for several weeks, prescribed ondansetron. Patient also presented with left eye stye; warm compresses were recommended.
- **2 days prior:** Persistent decreased appetite and fatigue, left eye drainage, left ear pain. Exam dem-

onstrated left-sided lymphadenitis. Patient was started on amoxicillin-clavulanate for conjunctivitis-otitis.

### Physical Exam Findings

The patient presented ill-appearing with significant fatigue but was responsive to stimulation. Vitals included: a temperature of 38.3°C; heart rate of 120 beats per minute; respiratory rate of 48 breaths per minute; and an oxygen saturation of 92% on room air. The left eyelid appeared swollen with associated conjunctival injection and drainage. The left tympanic membrane was erythematous and bulging with loss of landmarks. Left submandibular lymph nodes were palpable. Chest exam was significant for diminished sounds bilaterally at the bases. Bilateral capillary refill was measured at 3 seconds.

### Medical Decision Making

Due to the patient's ill appearance with clinical worsening on standard therapy of amoxicillin-clavulanate for otitis-conjunctivitis, initial blood work was drawn. Lab results included:

- **CBC:** WBC 56.1 x 10<sup>3</sup>/uL, blasts 28.2%; absolute neutrophil count 9.2 x 10<sup>3</sup>/mm<sup>3</sup>; hemoglobin 14.2 g/dL; platelets 194 x 10<sup>3</sup>/uL.
- **Chemistry:** sodium 133 mmol/L; potassium 5.1 mmol/L; chloride 108 mmol/L; bicarbonate 20 mmol/L; blood urea nitrogen 14 mg/dL; creatinine 0.15 mg/dL; glucose 78 mg/dL

An ambulance was called to transfer the patient to the emergency department (ED) for suspected sepsis. An intravenous (IV) catheter was placed prior to transfer, and maintenance fluids were provided on route to the hospital. Based on initial workup, an underlying oncologic etiology was strongly suspected as the primary cause for the patient's clinical worsening on standard therapy for otitis-conjunctivitis. As such, the on-call oncologist was consulted. Due to the high prevalence of *haemophilus influenzae* (*H. flu*) in otitis-conjunctivitis,<sup>3</sup> development of antibiotic resistance was also considered in the differential but was thought to be a less likely given the blast findings on the patient's CBC.

### Case Conclusion

On arrival to the ED, the patient was started on IV antibiotics and continued maintenance fluids. A chest x-ray in the ED demonstrated pneumonia with bibasilar consolidation. The patient was admitted to oncology following stabilization of vital signs including improved heart rate. During the hospital admission, a bone marrow biopsy was performed, which was diagnostic for

pre-B ALL. Based on the diagnosis, chemotherapy was initiated with eventual improvement in symptoms. The patient is currently in remission for ALL, and she is growing and developing normally.

### Discussion

The often fast-paced urgent care setting is at risk for biases that may result in delayed diagnosis. Framing bias, where a provider's decisions are influenced by how information is presented or "framed,"<sup>4</sup> may have played a role in this case of delayed diagnosis of leukemia. As a thought experiment, if the patient had presented with the symptoms of fatigue, poor appetite, and limping simultaneously, an oncologic etiology may have been considered sooner, prompting earlier lab evaluation. However, this patient presented with these symptoms as separate visits to different UC clinicians. Potential methods to overcome framing bias include chart review, checking on resolution of symptoms from prior recent clinic presentations, and a thorough history and physical exam. Of note, in pediatric patients with a complaint of limping, it is important to clarify if limping occurred prior to a fall or due to a fall. Normal x-rays, while often reassuring in the urgent care setting, can sometimes obscure the underlying diagnosis. Therefore, at a minimum, ensure adequate patient follow-up for persistent limping.

ALL is an oncologic condition involving rapid proliferation of immature WBCs called blasts. These non-functioning blasts proliferate rapidly to eventually crowd out bone marrow and increase susceptibility to common and opportunistic infections. Oncologic diagnoses such as ALL can frequently be found after patients have common infections that do not resolve or worsen while on antibiotics.<sup>5</sup> Patients will often have multiple UC and/or PCP visits for nonspecific symptoms before the diagnosis is made. Preceding non-specific symptoms include fatigue, lack of appetite, or easy bruising. Multiple visits over a few months with these types of concerns may indicate a need for further work-up. Additionally, an oncologic etiology such as leukemia, can be identified by obtaining a CBC with a differential. This course of action could make sense for patients who are not improving on antibiotics or who have multiple presentations for nonspecific symptoms.

For cases of suspected or confirmed oncologic diagnoses such as ALL, urgent consultation with a hematology-oncology specialist is essential. For newly diagnosed ALL, patients typically require admission to the hospital to initiate chemotherapy. With early diagnosis and proper treatment, the 5-year survival rate for ALL is approximately 90%.<sup>6</sup>

### Ethics Statement and Guardian Perspective

Informed consent for publication was obtained from the patient's father. He said he hoped his daughter's condition would be a good opportunity for other doctors to learn from.

### Takeaway Points

- Symptoms of new onset ALL include fatigue, loss of appetite, weight loss, easy bruising or bleeding, pallor, or joint pain/limping. Exam findings include non-tender lymphadenopathy and an enlarged liver or spleen.
- CBC findings which would require further oncologic diagnostic workup include the presence of blasts, extremely elevated WBC count, low hemoglobin, or low platelets.
- With worsening symptoms on typically adequate treatment for a prior diagnosis, consider workup for underlying causes. Brief chart reviews, especially for patients with multiple presentations, can provide further context to current symptoms and indicate when further workup is necessary. ■

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