

Revisiting the History: Hypereosinophilia in a 4-Year-Old With Purpura

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CASE

A 4-year-old boy with developmental delay was admitted for evaluation of a new rash in the setting of leukocytosis and eosinophilia. The patient was healthy until 1 week before admission when he developed cough, congestion, and malaise. Upon presentation, he was on day 5 of amoxicillin, prescribed by an outside provider for unclear indications, but he took no other medications on a regular basis. The day before presentation, his mother noted “red, flat, pimple-like” lesions on his upper thighs that progressively spread down his legs and resembled “bruises.” At a local hospital, a complete blood count (CBC) demonstrated a white blood cell (WBC) count of 66 600/mm³. Although the patient was afebrile and non-toxic appearing, a blood culture was obtained, and he received intramuscular ceftriaxone due to the profound leukocytosis and concerns for possible infection. He was subsequently transferred to the emergency department of our hospital for further evaluation.

In the emergency department, vitals were notable for a pulse of 100 beats per minute, temperature of 35.2°C, respiratory rate of 32 breaths per minute, and oxygen saturation of 98% on room air and normal BMI for age. Physical examination was notable for a nontender, nonpruritic rash consisting of purpuric papules and macules of various stages of development on the bilateral lower extremities (Fig 1). He was otherwise well appearing with no joint or abdominal tenderness and no hepatosplenomegaly. Initial laboratories were notable for WBC count of 56 100/mm³ with 59% eosinophils and an absolute eosinophil count (AEC) of 33 100/mm³, a normal hematocrit of 37.2%, normal platelet count of 300 K/mcL, and normal coagulation markers. The patient was noted to have an elevated lactate dehydrogenase of 555 unit/L but normal uric acid level. A urinalysis obtained via a catheterized specimen was notable for trace protein and moderate blood; no urinary eosinophils were detected. He had a normal chest radiograph. He was subsequently admitted to the hospital medicine service.

During the hospitalization, additional history revealed that the patient’s mother was taking several medications including paroxetine, lamotrigine, ziprasidone, alprazolam, hydrochlorothiazide, and oral contraceptive pills. The possibility of accidental ingestion of these medications by the patient was a consideration because he had done this previously. The patient’s mother later reported he occasionally ate dirt and sand when outside. The patient lived in a rural area and had several insect bites over the course of the summer, but no known tick or animal exposures, including livestock or pets. He had no recent travel and no new exposures including household products. The patient was afebrile with no gross hematuria and had only 1 loose, nonbloody stool since starting amoxicillin, which he had received previously without adverse reaction.

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Question *What Are the Etiologic Considerations in This Case?*

Etiologic considerations in this case included the patient's preceding upper respiratory infection, drug reaction due to amoxicillin use and potential exposure to other medications, parasitic infection secondary to history of pica of dirt and sand, and malignancy. His presentation had elements spanning hematologic, allergic, immunologic, and infectious etiologies, adding to the complexity of this case.

Hypereosinophilia can be classified in several ways including severity, primary versus secondary and infectious versus noninfectious etiology. The World Health Organization divides eosinophilia into categories of severity: mild (AEC from upper limit of normal to $1500/\text{mm}^3$), moderate ($1500\text{--}5000/\text{mm}^3$), and severe ($\text{AEC} > 5000/\text{mm}^3$). Our patient had severe eosinophilia with an AEC of $33\,100/\text{mm}^3$,

which is important to consider when narrowing the differential. Primary causes of eosinophilia include clonal bone marrow disorders or idiopathic eosinophilia, with the latter representing a diagnosis of exclusion. Hypereosinophilic syndrome is defined as $\text{AEC} > 1500/\text{mm}^3$ for > 6 months, leading to end-organ damage compared with idiopathic eosinophilia that does not result in end-organ damage.¹ The major secondary or reactive causes of eosinophilia are due to allergic disorders, hypersensitivity and medication reactions, collagen vascular disease, neoplasms, Addison disease, or response to an infection.¹ Secondary eosinophilia is classically associated with parasitic infections but can also result from bacterial or viral infections, which tend to cause only mild eosinophilia.

In considering this case, the patient's exposures include medications, including

potential ingestion of his mother's prescriptions, and pica of sand and dirt. Allergic and drug reactions typically result in only mild to moderate eosinophilia and not the marked elevation seen in this case.² Although secondary causes of eosinophilia must be excluded before diagnosing primary causes, secondary causes, with the exception of parasites, rarely cause $\text{AEC} > 1500\text{ cells}/\text{mm}^3$. Helminths are 1 of the few secondary causes of eosinophilia associated with the severe levels observed in this case. Most helminths, including *Toxocara canis*, typically cause moderate eosinophilia. The level is usually proportional to the extent of tissue invasion and depends on the life cycle of the parasite. Few parasitic infections are known to cause our patient's level of eosinophilia; those include *Ascaris lumbricoides*, *Trichinella spiralis* (typically moderate), *Strongyloides stercoralis* (usually mild),



FIGURE 1 Rash at presentation consisting of nonblanching papules and macules of various coloration ~ 0.5 cm in diameter on all surfaces of bilateral legs with concurrent ecchymotic lesions diffusely throughout. The rash was not pruritic or painful.

filarial worms, *Schistosoma* species (usually mild-moderate), and liver and lung flukes (usually moderate). Parasites are the most common cause of eosinophilia worldwide, but prevalence is lower in the United States.¹⁻³ The patient's history of pica, although not initially known, was supportive of potential helminth infection, but the severe level of eosinophilia, marked leukocytosis, and the rash complicated diagnosis.

Case Continuation

Several consulting services were involved in the care of the patient including hematology-oncology, allergy-immunology, and infectious disease. Over the next 36 hours of hospitalization, the patient's rash spread to include the bilateral upper extremities with few macules on the lower back and face. He remained otherwise well. On hospital day 3, the rash began to spontaneously regress. Peripheral smear demonstrated increased eosinophils without clonal expansion of any other cell lines. Oncology evaluated the patient and thought malignancy was unlikely. Troponin and transaminases were normal. Repeat urinalysis was negative for blood, protein, and eosinophilia. Screening tests for neoplastic hypereosinophilic syndrome were drawn including soluble interleukin 2 receptor, lymphocyte subpopulations, vitamin B₁₂, tryptase, and immunoglobulins (Ig). These tests were within normal limits except for an elevated IgE at 6948 IU/mL, IgA at 207 mg/dL, and IgM at 458 mg/dL, all nonspecific. On the basis of this information, diagnostic considerations remained directed toward secondary causes of eosinophilia.

Stool ova and parasite testing was performed; 3 samples were collected and were negative. Serology for *Strongyloides* and *Toxocara* was obtained and pending at the time of discharge. Given the patient's well appearance and reassuring examination and workup, no further studies were obtained, and he was discharged with the plan for close follow up by his pediatrician and trending of a weekly CBC and differential. Three days after discharge, the patient's mother reported that he was continuing to do well, and the rash was nearly resolved. One week after discharge,

results of serologic testing for *Strongyloides* returned negative, but *Toxocara* serology was positive: titer 3.468 optical density, greater than the upper limit of normal of 0.299. He was treated as an outpatient with albendazole per Red Book guidelines.⁴ His rash resolved, and repeat CBC showed WBC count of 16 100/mm³ with 37% eosinophils (AEC 6000/mm³) 7 days after treatment. Additional trending of serial CBCs and serologies were recommended to monitor complete resolution of eosinophilia; however, the patient's primary care provider elected to not obtain further CBCs given his improved clinical appearance.

Question Is Purpura Usually Seen With Helminth Infections?

The patient's rash added to the diagnostic complexity of this case. A palpable, purpuric rash in a child classically evokes Henoch-Schonlein purpura (HSP); however, the differential for purpura is broad and includes vasculitides, trauma, sequelae from hemostasis, and infections with organisms such as *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, nontuberculous mycobacteria, *Rickettsia*, *Mycoplasma*, viral hepatitis, HIV, and parvovirus.¹ Furthermore, acute bacterial purpura fulminans must be considered in any patient who presents with a characteristic rash, fever, and/or signs of acute illness as prompt administration of antibiotics and correction of coagulopathy are essential to reducing morbidity and mortality. Our patient's rash and initial proteinuria and hematuria was concerning for HSP or another vasculitic disorder; however, repeat urinalysis was unremarkable, there was no joint or abdominal pain or diarrhea, and the lesions were of different stages of development.

Although helminth infections can lead to a rash, they do not typically present with palpable purpura.⁵ In a review of the literature, we identified 4 case reports of vasculitis related to *Toxocara canis* infection including HSP caused by toxocariasis, although the incidence is thought to be underestimated.⁶⁻⁹ The skin manifestations of toxocariasis are pleomorphic, depending

on the number and location of the larvae and the immune system of the host, with a chronic pruritic rash being the most common skin manifestation; forms of eczema and chronic urticaria are also seen.^{5,6} Our patient's rash was purpuric and inconsistent with the often pruritic rash of cutaneous larva migrans. The rash was not biopsied given its spontaneous regression but was suggestive of a leukocytoclastic vasculitis.

Question How Is *Toxocara canis* Infection Diagnosed and Treated? What Are the Potential Complications?

Toxocara canis was eventually determined to be the most likely etiology in this case given the positive titer and response to therapy. *Toxocara canis* is a nematode with its primary hosts consisting of cats and dogs, and the human acting as a dead-end host. Risk factors for infection include owning a cat or dog, young age, living in poverty, or living in a hot, humid region where eggs are kept viable in soil.³ Up to 14% of the US population has been infected with *Toxocara canis* compared with 40% worldwide. Therefore, detection of antibodies alone is not diagnostic. Inoculation in our patient likely occurred as a consequence of ingestion of dirt and sand. Pica is defined as the persistent eating of nonnutritive substances and has a high incidence among children with developmental delay.^{10,11} In this case, the history of pica was key to diagnosis. *Toxocara* infections are usually negative on stool testing, but ova and parasite stool testing helps evaluate for other parasites. Diagnosis of toxocariasis is confirmed by direct detection of larva on tissue biopsy, which was not clinically indicated in our patient; however, the presence of eosinophilia in conjunction with compatible signs and symptoms were strongly suggestive of the diagnosis.¹²

Complications of *Toxocara canis* result if there is visceral or ocular involvement. Severe eosinophilia from any cause can lead to organ infiltration. Visceral larva migrans, which is most often asymptomatic, results from direct organ involvement by larva and can manifest in a variety of ways including fever, hepatomegaly, cough, or neurologic

impairment. Eosinophilia and leukocytosis in conjunction with an appropriate exposure history and symptoms were highly suggestive of visceral larva migrans in our patient. However, our patient did not have the aforementioned clinical manifestations of organ involvement and had normal transaminases, troponins, electrocardiogram, and chest x-ray. Given his well appearance, improvement, lack of infiltrative symptoms, and normal studies, skin or liver biopsy was not thought to be clinically indicated, especially because most patients with visceral larva migrans recover even without therapy.¹⁷ Ocular larva migrans is typically a localized infection that presents with unilateral vision loss without systemic signs or symptoms and is less often accompanied by eosinophilia.¹³ Ocular involvement was not suspected in this case based on normal fundoscopic exam, degree of eosinophilia, and skin involvement.

After diagnosis, *Toxocara canis* treatment consists of 400 mg albendazole by mouth twice daily for 5 days, as our patient received.⁴ Corticosteroids can be added in severe cases or if ocular involvement is present. Preventative measures include veterinary care for pets, hand-washing, and keeping pets out of public playgrounds.³

CONCLUSIONS

This illustrative case describes hypereosinophilia and a vasculitic rash in a 4-year-old boy with pica as a unique presentation of toxocariasis. Additionally, the case highlights diagnostic considerations for eosinophilia and purpura and how to treat *Toxocara canis* infections. Finally, the case reinforces the importance of good history taking. The exposure history was pivotal to the refinement of the differential diagnosis and workup. The pica history was not initially elicited until hospital day 2 and reminds the clinician that revisiting the history can be essential.

Ultimately, when faced with a pediatric patient with eosinophilia and purpura, a broad and systemic approach is needed.

LEARNING POINTS

- The history of presenting illness is instrumental to the development of a differential diagnosis in cases of eosinophilia and may need to be revisited if initial workup is indeterminate.
- Any patient with severe leukocytosis, fever, purpura, and septic appearance should raise concern for acute infectious purpura fulminans and warrants prompt antibiotic treatment and correction of coagulopathies.
- Clinical appearance should help guide workup and limit invasive procedures.
- Parasite infections are the most common cause of eosinophilia worldwide and should not be ignored even in places such as the United States where they are less common.

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