Bacillary angiomatosis (BA), a manifestation of *Bartonella*-mediated disease seen most commonly in immunocompromised hosts, was first described in patients infected with human immunodeficiency virus (HIV) [1]. It is also rarely seen as a consequence of immunosuppression related to solid organ transplantation [2]. We report a case of BA in a patient with pediatric cancer and summarize the literature for all cases of BA in patients with cancer.

The patient was a 5-year-old white girl diagnosed with B-cell acute lymphoblastic leukemia (ALL) in July 2009. Prior to her cancer diagnosis, she was healthy and without medical problems. At diagnosis, her initial white blood cell count was 45,000 cells/mm$^3$, and she had negative minimal residual disease by flow cytometry at the end of a 3-drug chemotherapeutic induction regimen. She had favorable-risk cytogenetics with t(12;21). She was treated on a Children’s Oncology Group clinical trial for children with standard-risk B-ALL. During the maintenance phase of her chemotherapy, she presented with fever to 102°F and left eye swelling accompanied by watery discharge. Laboratory values on admission were significant for a white blood cell count of 45,000 cells/mm$^3$, hemoglobin of 8.7 g/dL, and platelet count of 139,000/mm$^3$ with an absolute neutrophil count (ANC) of 1340. A computed tomography scan demonstrated a soft-tissue mass near the left epicanthal fold (Figure 1A). A biopsy of this mass was reported to have pathologic findings consistent with a hemangioma. The patient was discharged to home without any additional interventions after spontaneous resolution of her fevers. Several weeks later she was readmitted with fever to 102°F accompanied by clear yellowish drainage from the biopsy incision and a new enlarged left cervical lymph node. Early recurrence of B-ALL was suspected at that time based on clinical findings that included persistent pancytopenia (ANC 740, hemoglobin 7.5 g/dL, and platelets 132,000/mm$^3$), fever, and lymphadenopathy. Repeat imaging demonstrated persistence of the original mass and an enlarged left cervical lymph node. Lymph node biopsy demonstrated mild vascular proliferation with histiocytic infiltrate (Figure 1B). Warthin-Starry stain of lymph node tissue showed rare organisms (Figure 1C). The tissue from the original biopsy of the ocular mass was reexamined, and extensive vascular proliferation with histiocytic infiltrate was noted (Figure 1D). Numerous bacilli were seen on Warthin-Starry stain of the ocular mass (Figure 1E). Polymerase chain reaction for *Bartonella* was positive from both the ocular mass and the lymph node. Testing was performed by ARUP laboratories and would recognize both *B. henselae* and *B. quintana*. *B. henselae* serologies were sent to ARUP and resulted as immunoglobulin G (IgG) of 1:128 (negative <1:64) and IgM of <1:16 (negative <1:16). HIV serology was negative. She was started on azithromycin 10 mg/kg on day 1 and 5 mg/kg daily thereafter, and demonstrated rapid improvement over a 3-month treatment course. The patient and her family resided in rural Georgia. They owned 2 cats, a dog, and a horse. The patient frequently played with the cats, which were both less than 2 years of age. She had been bitten and scratched by the cats but the family did not recall a specific event prior to the onset of her ocular symptoms.
A review of the literature identified 7 previously reported cases of BA in patients with cancer (Table I) [3–10]. Ours is the second pediatric case to be reported in the literature. The first case also affected a child with ALL [8]. Among the adult cases, chronic lymphocytic leukemia was the most common diagnosis, occurring in 4 of 6 patients. Only 1 patient with BA had a solid tumor, making hematologic malignancy the most common type of cancer associated with BA. Five of the patients had absolute neutrophil counts (ANC) <1500 near the time of presentation. Our patient presented with a soft-tissue mass, 5 patients presented with only skin lesions, 1 had skin lesions with subsequent dissemination to the bone, and 1 had splenic lesions. We are not able to make any distinct associations between the severity or location of BA and a particular chemotherapeutic regimen. One exception may be patient 7, who had a prolonged course that was poorly responsive to antibiotic therapy, resulting in dissemination from skin lesions to the bone. In that case report, the authors hypothesize that the profound immunosuppression induced by fludarabine contributed to the severity of her case [3]. However, of the reported cases of BA in patients with cancer, only this patient had confirmed infection with *B. quintana*. Interestingly, *B. quintana*, but not *B. henselae*, has been epidemiologically associated with lytic bone lesions, which this patient developed [11]. Therefore, it is unclear if patient 7’s prolonged course was secondary to her chemotherapeutic regimen or to the species of *Bartonella* with which she was infected. Four of the 8 patients had speciation confirmed, and of those, 3 were *Bartonella henselae*.

Serological testing for *Bartonella* was not developed until the mid-1990s [12], and therefore was not commercially available for patients 1—4. Serological testing was performed and was found to be negative for 3 of the remaining 4 patients. Our patient was the only one with positive serology; however, tests were drawn on the second presentation, approximately 1 month after her initial presentation, and this could have permitted time for antibodies to develop. Alternatively, our patient developed disease while in remission from her cancer, so her immunosuppressive regimen was not as intense as the other patients, and this may explain why she was able to mount a detectable antibody response. Additionally, 3 of the patients were reported to have hypogammaglobulinemia, which may have affected serological testing.

All of the patients who had BA associated with cancer had full resolution of disease with treatment. Treatment regimens were mainly focused on macrolides or tetracyclines, except for patient 5, whose response was likely related to the aminoglycoside component of his regimen. Of note, several patients developed disease while on trimethoprim-sulfamethoxazole prophylaxis. Additionally, patients 4 and 6 were receiving treatment with a fluoroquinolone (ciprofloxacin and levofloxacin) for other indications (*H parainfluenza* pneumonia and sinusitis respectively), but their BA lesions did not respond to this therapy. The initial reported
Table I. Summary of All Reported Cases of Bacillary Angiomatosis in Patients With Cancer

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Cancer Type</th>
<th>Clinical Presentation</th>
<th>Absolute Neutrophil Count</th>
<th>Treatment</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>M</td>
<td>ALL</td>
<td>Skin lesion</td>
<td>Prednisone, vincristine, 6-MP, cytarabine, methotrexate, 16s rRNA sequencing</td>
<td>820</td>
<td>Erythromycin x 6 weeks</td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>F</td>
<td>Ovarian carcinoma</td>
<td>Noted on routine scan</td>
<td>Cyclophosphamide, carboxamin</td>
<td>NR</td>
<td>Doxycycline x 4 weeks</td>
</tr>
<tr>
<td>3</td>
<td>78</td>
<td>M</td>
<td>CLL</td>
<td>Skin lesions, fever, skin lesion</td>
<td>Chlorambucil, prednisone, vincristine</td>
<td>2430</td>
<td>Histology, PCR</td>
</tr>
<tr>
<td>4</td>
<td>55</td>
<td>M</td>
<td>CLL</td>
<td>Skin lesions, fever, headache</td>
<td>Clarithromycin x 4 weeks</td>
<td>3476</td>
<td>Erythromycin x 6 weeks, Clarithromycin x 4 weeks</td>
</tr>
<tr>
<td>5</td>
<td>61</td>
<td>M</td>
<td>CML to AML</td>
<td>Skin lesions, fever, cervical lymphadenopathy, splenomegaly</td>
<td>Chlorambucil, prednisone, methotrexate, idarubicin</td>
<td>&lt;100</td>
<td>Histology, PCR</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
<td>M</td>
<td>CLL</td>
<td>Fever, skin lesion</td>
<td>Clarithromycin + doxycycline + fusidic acid x 10 days</td>
<td>650</td>
<td>Piperacillin + amikacin x 4 weeks and teicoplanin + fusidic acid x 10 days</td>
</tr>
<tr>
<td>7</td>
<td>66</td>
<td>F</td>
<td>CLL, pure red cell aplasia</td>
<td>Skin lesions, foot swelling</td>
<td>Chlorambucil, fludarabine, cyclophosphamide, rituximab, etoposide</td>
<td>520</td>
<td>Histology, PCR</td>
</tr>
<tr>
<td>8</td>
<td>5</td>
<td>F</td>
<td>ALL</td>
<td>Soft-tissue mass, lymphadenopathy</td>
<td>Vincristine, dexamethasone, 6-MP, cytarabine, methotrexate, methotrexate</td>
<td>1340</td>
<td>Azithromycin x 3 months</td>
</tr>
</tbody>
</table>

Abbreviations: ALL, acute lymphoblastic leukemia; WSS, Warthin-Starry stain; EM, electron microscopy; NR, not reported; CLL, chronic lymphocytic leukemia; GMS, Gomori-Grocott methenamine silver stain; CML, chronic myelogenous leukemia; AML, acute myelogenous leukemia; PCR, polymerase chain reaction.
case of bacillary angiomatosis in an HIV-infected patient demonstrated complete resolution of lesions on erythromycin [1], therefore, macrolides have become the treatment of choice for BA. Doxycycline has also been consistently successful in case reports, both as monotherapy and in combination with rifampin [13]. Based on these reports and the currently available literature, a reasonable therapy recommendation for treatment of bacillary angiomatosis in patients with underlying cancer would include a prolonged course of a macrolide antibiotic, either alone, or in combination with another potentially efficacious agent (eg, rifampin or an aminoglycoside). If rifampin is used in the regimen, drug-drug interactions must be considered and managed accordingly.

In summary, while most cases of bacillary angiomatosis occur in patients with HIV, clinicians must remain aware that any immunocompromised patient could develop this form of Bartonella-mediated disease. Our case was unique among those that were previously reported in that our patient’s disease did not manifest as a skin lesion, but rather as a soft tissue mass and later as an enlarged lymph node. Although our patient had positive serologies, other reported cases of BA in patients with cancer did not. Serology should not be relied upon for ruling out the diagnosis and tissue should be obtained for histological analysis from any suspicious lesion. Finally, given the high incidence of HIV in conjunction with BA, all patients diagnosed with BA should have appropriate HIV testing performed.

Acknowledgments

Potential conflicts of interest: All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References