



BACILLARY

ANGIOMATOSIS

Epidemiology

BA is most commonly seen in patients with acquired immunodeficiency syndrome (AIDS) and a CD4 count less than 50 cells/mm³, with an incidence of 1.2 cases per 1000 at-risk patients. Patients with other forms of immunosuppression, including patients with leukemia and recipients of organ transplants, have been reported. Uncommonly, human immunodeficiency virus-negative and nonimmunosuppressed persons develop BA. In the cases of BA in immunocompetent persons, however, although the lesions were proliferative vascular papules, they were limited in number, the affected persons had limited or no systemic involvement and a benign course. There is no predisposition in terms of race, sex, or age.

BACILLARY ANGIOMATOSIS AT

AGLANCE

- Etiology: Bartonella henselae and B. quintana
- Acquired from infected cats
- Most commonly in patients with acquired immunodeficiency syndrome but also in other forms of immunosuppression
 - Pyogenic granuloma-like and subcutaneous nodules
 - Hyperpigmented plaques in African Americans
 - May be associated with hepatic and systemic lesions
 - Treatment: erythromycin or doxycycline

Etiology and Pathogenesis

Both *B. henselae* (the CSD bacillus) and *B. quintana* (the agent of trench fever) have been identified as causative agents of BA. At one end of the clinical spectrum, classic CSD is seen in young, immunocompetent hosts as a limited infection. At the other end, BA is seen in patients who are severely immunocompromised as a systemic disease. Thus, it is the immunocompetence of the host and the bacterial load that dictates the clinical manifestations of the disease. Moreover, immunocompromised patients with BA develop an angioproliferative response in response to intracellular hypoxia. The presence of intracellular bacilli induces hypoxia-inducible factor-1 that in turn induces vascular endothelial cell growth factor, leading to vascular proliferation.²⁹ BA caused by *B. henselae* is acquired from infected cats and is a manifestation of CSD in the immunocompromised host. Peliosis hepatitis is exclusively associated with *B. henselae* infection.³³ In contrast, patients with BA caused by *B. quintana* develop subcutaneous masses and lytic bone lesions.

Clinical Manifestations

CUTANEOUS LESIONS

The incubation period for BA is unknown. In AIDS patients, the clinical constellation includes fever, cutaneous or subcutaneous vascular lesions, lymphadenopathy, and/or abdominal symptoms. The most common cutaneous morphologies of BA are (1) pyogenic granuloma-like lesions, (2) subcutaneous nodules, and (3) hyperpigmented indurated plaques. The same patient may have several morphologies. Lesions resembling pyogenic granuloma can range in size from 1 mm to many centimeters and are dusky-red in color with a collarette of scale and peripheral satellite lesions. The lesions are firm, bleed easily, and are often tender. They occur on skin and mucosa. Subcutaneous nodules can range from distinct nodules to diffuse swellings

with or without induration and are also often tender. Hyperpigmented plaques are most commonly seen in African Americans with BA and are oval in shape; they are several centimeters in diameter with indistinct borders. Large, fungating masses rarely occur. Patients with BA may have few to thousands of lesions with the number of lesions gradually increasing over time. Additional immunosuppression with chemotherapeutic agents may be followed by a shower of miliary skin lesions.

Box 182-2 Differential Diagnosis of Bacillary Angiomatosis

Most Likely

- Pyogenic granuloma
- Kaposi sarcoma
- Angioma

Consider

- Chronic herpes simplex
- Hypertrophic scars
- Nocardiosis

Always Rule Out

- Amelanotic melanoma
- Squamous cell carcinoma
- Basal cell carcinoma
- Dermatofibroma protuberans
- Merkel cell carcinoma

RELATED PHYSICAL FINDINGS

In addition to cutaneous lesions, other organ systems may be affected. Hepatic and splenic vascular lesions can occur concomitantly with or independently of cutaneous lesions and can be a cause of significant blood loss and anemia. Bartonella infection, especially that caused by *B. quintana*, can affect bone and soft tissues. Lesions of the central nervous system have been reported and can result in neurologic and psychiatric disorders. Bacteremia, chronic fevers, and pulmonary and gastrointestinal lesions have also been reported. Radiologic studies usually identify areas of systemic involvement. Ocular vascular proliferative lesions can produce loss of vision.³⁴

There are several reports of patients with other cutaneous diseases concomitant with BA, as well as the simultaneous existence of BA and another infection within the same lesion. Several patients have been reported with both BA and Kaposi sarcoma. Cytomegalovirus, Epstein-Barr virus, *Cryptococcus neoformans*, and *Mycobacterium avium-intracellulare* have been found within lesions of BA.

Differential Diagnosis

Laboratory Findings

Patients with AIDS and BA are anemic and may have elevated liver function tests (characteristically, lactic acid dehydrogenase and alkaline phosphatase are more elevated than

hepatocellular enzymes). Blood cultures are positive for Bartonella sp. in approximately one-half of BA patients. B. henselae and B. quintana can be cultured from skin lesions. The organisms grow slowly and may not be detected without prolonged culture (more than 1 month). PCR of affected tissue is virtually always positive if lesions are histologically characteristic. The vast majority of cases are diagnosed histologically, with identification of the causative bacteria by Warthin-Starry staining.

Histopathology

Lesions of BA have the general features of a lobular capillary hemangioma (pyogenic granuloma) , but in contrast to a pyogenic granuloma, the endothelial cells are often larger and polygonal; they may have marked atypia. There is a prominent inflammatory

infiltrate, with significant numbers of neutrophils as well as leukocytoclastic debris . Polymorphonuclear leukocytes (PMNs) are scattered throughout the lesion, as opposed to classic pyogenic granuloma lesions in which the PMNs are at or near the surface, even if the pyogenic granuloma is eroded and impetiginized. There is usually a finely granular pink to purple material in areas of PMN infiltration adjacent to blood vessels. This represents large clumps of bacteria, best visualized with a modified Warthin-Starry stain. Standard tissue Gram stain and the Warthin-Starry stain used for syphilis do not stain the organisms. If the diagnosis cannot be confirmed with special stains, electron microscopy may be used. The lack of spindle cells, atypically shaped vascular channels, and hyaline globules distinguish BA from Kaposi sarcoma. Lesions of BA in tissues other than liver show similar histologic features.

Clinical Course

In the immunocompromised host, the natural history of untreated BA is gradually progressive disease, with increasing numbers of skin lesions and involvement of many visceral organs. Untreated, severely immunocompromised patients might die of their infection.

Treatment

Erythromycin, 500 mg four times a day, or doxycycline, 100 mg twice a day for 3 months, is the treatment of choice for BA. Other antibiotics thought to be effective are minocycline, tetracycline, chloramphenicol, azithromycin, and roxithromycin. For peliosis hepatis, 4 months of treatment is recommended. Some patients require life-long suppressive therapy. Relapses have been reported, especially with shorter treatment courses. A Jarisch-Herxheimer reaction not uncommonly occurs after initiation of therapy. Most patients respond rapidly to antibiotic therapy. The rapid disappearance of the vascular lesions may relate to the effects of the macrolides and tetracyclines on protein synthesis, stopping the production of vascular growth factors. If patients are not treated for a sufficient period, they are likely to relapse, despite the fact that their skin lesions vanish after a few weeks of treatment. The additional treatment is required to sterilize visceral or hematologic reservoirs of bacteria.