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# INFECTIOUS DISEASE ROUNDS

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## Unusual Presentation of Cat Scratch Disease in a Patient Positive for Antibody to the Human Immunodeficiency Virus

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DR. WAYNE MARASCO. The patient is a 26-year-old man who was well until late November of 1988, when he removed a hangnail from his right index finger. One week after removing the nail, he developed redness and tenderness of his finger with an accompanying red streak up his arm. He was seen at Harvard Community Health Plan (HCHP), Boston, and treated with dicloxacillin for 5 days, without response. Subsequently, he developed high fevers in the range of 102°F and right axillary adenopathy.

On 16 December 1988 the patient returned to his physician and was treated with cephalexin for 7 days, with little improvement. He was also found to have a large pedunculated left thigh lesion measuring ~1.5 cm that was believed to be a large molluscum. He remembered scratching his left upper thigh; a growth resulted that looked like a "mushroom" and was treated with liquid nitrogen. On 20 December 1988 he was seen in a local emergency room, where he had the nail of his right index finger wedged and was placed on a regimen of dicloxacillin. Two days later he again presented to HCHP complaining of a more painful right axillary lymph node. A new 5-mm by 5-mm nodule that appeared to be granulation tissue was noted on the tip of his index finger, with an adjacent structure that looked like a hemangioma. On 27 December 1988 a diagnosis of pyogenic granuloma of the finger was made, and silver nitrate therapy was initiated. On examination the patient was noted to have a markedly enlarged right axillary lymph node measuring 5 cm, as well as left inguinal and femoral lymphadenopathy on the side of the large polypoid molluscum on the inner aspect of his thigh. The inguinal adenopathy was thought to be secondary to the liquid nitrogen treatment.

On 30 December 1988 the patient presented to another hospital because of continued fevers in the range of 102°F–102.5°F; he was weak and fatigued. On 2 January 1989 he underwent surgical removal of the lesions on his right index finger and left thigh. Therapy was begun with oral ciprofloxacin, with marked improvement of his constitutional symptoms. A gallium scan on 6 January revealed increased uptake of radionuclide only in the right axilla and right index finger. By 11 January his right axillary adenopathy had decreased to 3 cm, and he was afebrile. He continued to improve until 19 January, when the growth on his index finger recurred. Over the subsequent 3 days he developed fever. On the day before admission, his finger became markedly swollen, erythematous, and painful. On the day of admission a red streak 23 cm up the lateral aspect of his finger, wrist, and distal forearm was noted. He was seen by a hand surgeon at HCHP and referred to the Brigham and Women's Hospital (Boston) emergency room for further evaluation.

The patient had an unremarkable past medical history. He was a florist and worked mostly with cut flowers but occasionally with exotic orchids. His hands did come into contact with dirt and Spanish

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moss. He did not remember cutting himself. He had a cat at home that was declawed, and he did not remember being scratched. He had traveled to California in June 1988 for 10 days. He had had homosexual contact with several partners 5 years earlier but none recently, and he was engaged to be married.

Physical findings on examination included a temperature of 99.3°F and normal head, eyes, ears, nose, throat, pulmonary, cardiac, and abdominal examinations. He had a 2-cm right axillary lymph node, large epitrochlear nodes on the right, and two 1.0-cm left inguinal nodes. His right index finger was edematous, erythematous, and warm and appeared cellulitic. His arm was in a splint obscuring the red streaking that had been confirmed by the emergency room physician. On the medial aspect of the nailbed of his finger was a 1.0-cm brown, crusted exophytic growth.

Laboratory findings included a hematocrit of 30.5% and a white blood cell count of 6.5/mm$^3$. An X-ray film of his finger and hand showed no bony involvement. Review of his HCHP record showed negative purified protein derivative (PPD) and candida skin tests in December 1988. Cultures of sputum samples taken in December for *Pneumocystis carinii* and acid-fast bacilli were both negative to date. Antibody testing for human immunodeficiency virus (HIV) was pending. We obtained the pathology report from the other hospital where the lesions had been removed surgically. The right index finger lesion was reported as ulcerated skin with inflamed granulation tissue, and the left thigh lesion, as consistent with granuloma pyogenicum.

DR. JEFFREY PARSONNET. The infectious diseases service of the Brigham and Women's Hospital was asked to see the patient in the emergency room. In summary, the patient was a young man with a history of fever, adenopathy, and malaise of several months' duration, with a recurrent growth on his right index finger and a history of an exophytic growth on a lower extremity. He presented to our hospital with fever and what appeared to be cellulitis of his hand.

PHYSICIAN. Do you know what prompted the sputum evaluation? Did he have respiratory symptoms or hypoxemia?

DR. MARASCO. It is not clear, but the HCHP records from probably a dozen visits over a short period showed that he had had a cough on one visit, and this prompted the sputum examination and gallium scan. He had no respiratory complaints when we saw him.

DR. ROBERT FINBERG. Do we know if he had ever had pus or a culture of material from the finger performed?

DR. MARASCO. He had had a superficial culture done that yielded some *Staphylococcus* species and *Pseudomonas aeruginosa*. He presented to HCHP on one occasion, demanding that pus from his finger be drained. The physician, however, did not find pus on examination.

DR. FINBERG. I gather he did not work with roses?

DR. MARASCO. He did work with cut flowers, but he did not remember being pricked by thorns.

DR. LEO LIU. Did he have any contact with seawater or raw shellfish at any time? I ask because there are a few unusual cutaneous processes caused by bacteria such as *Erysipelothrix* that can be acquired from contact with raw shellfish.

DR. LAWRENCE MADOFF. I would think of *Mycobacterium marinum* or a fungal infection such as histoplasmosis.

DR. JOYCE FINGEROTH. One would have to include sporotrichosis, especially since the patient is a florist. Since he did travel some, blastomycosis also would have to be included as a fungal disease with cutaneous manifestations.

DR. PARSONNET. Which of these infections could account for both the recurrent lesion on the finger and the exophytic growth on his thigh?

DR. FINGEROTH. Sporotrichosis certainly could. Blastomycosis or histoplasmosis also can disseminate, although I am not sure they would readily produce this sort of picture.

DR. MARASCO. Actually, it can look like this. I looked through one of my atlases of dermatology and was amazed at how broad the differential can be. In fact, *Cryptococcus*, *Histoplasma*, and *Coccidioides* can all produce lesions such as these, as can *Trichophyton* and other dermatophytes. Sporotrichosis was raised as a possibility. However, he did not have any other lesions on his arm and did not have any subcutaneous nodules, which you often see in that disease.

DR. EDWARD KASS. The worst case of sporotrichosis I have seen was in a man with an almost unrecognizable lesion on one finger and widely disseminated disease, without other cutaneous lesions.

DR. LIU. I would also consider cat scratch disease, which can involve multiple systems and can

have atypical and more severe presentations in HIV-positive patients.

DR. PARSONNET. His only exposure to animals was to the cat in his household, which had been declawed.

DR. LIU. Many infections can be acquired without a scratch.

DR. FINBERG. In fact, in 50% of patients with cat scratch disease, there will be no history of a scratch.

DR. FINGEROTH. Since he handled soil, protothecosis is another possibility associated with alga-like organisms.

PHYSICIAN. The filamentous fungus *Fusarium* associated with cactus can cause disseminated lesions.

DR. FINBERG. We should not forget in this exotic differential list a common problem such as recurrent bacterial infection in the setting of a foreign body in the finger.

DR. MICHAEL WESSELS. Herpes simplex virus (HSV) should be considered as well. Especially if the patient is HIV-positive, one can see very atypical lesions that can persist.

DR. PARSONNET. HSV would not account for the thigh lesion, but it is important to consider in patients with risk factors for HIV infection and unusual skin lesions. We also should consider noninfectious etiologies in this patient. Kaposi's sarcoma certainly should be on our list of possible diagnoses, given his social setting. We have learned that Kaposi's lesions may have a variety of appearances in patients with AIDS; a biopsy often is required to verify the diagnosis.

DR. DORI ZALEZNIK. I think you would have to say that there was bacterial superinfection if this were a Kaposi's sarcoma lesion. Lymphangitic streaking certainly would be unusual in Kaposi's.

DR. KENNETH MCINTOSH. What about tularemia? It does not produce exophytic lesions, but it still seems as though it should be included.

DR. PARSONNET. Our list of diagnoses to consider now includes infection with a variety of pathogenic fungi, several exotic bacteria, atypical mycobacteria, and HSV, as well as Kaposi's sarcoma. Dr. Marasco, what was done to evaluate and treat this patient?

DR. MARASCO. We placed the patient on cefazolin for his obvious cellulitis while awaiting further diagnostic material. We tried to obtain the tissue blocks from the other hospital. We only received hematoxylin and eosin stains of the finger lesion at that point with the pathology report, as I previously described. Low-grade fevers persisted for the first 5 days of the hospitalization, although his cellulitis had improved. We did not have a diagnosis for the fingertip lesion, however. Several days before discharge, the patient was taken to the operating room for removal of the 1-cm exophytic growth from his fingertip.

DR. MCINTOSH. What was the patient's HIV antibody status?

DR. MARASCO. The day that he left the hospital, the patient's HIV antibody test returned positive. After resection of the lesion, he was given oral ciprofloxacin for 2 weeks. The finger lesion resolved completely, as did his constitutional symptoms. Now, 7 weeks after completing antibiotic therapy, he remains well. The diagnosis of the lesions was established after discharge. Dr. Susan Lester from the pathology department worked on the case and will present the findings.

DR. SUSAN LESTER. We first received consultation slides of the patient's thigh lesion, which was biopsied approximately 3 weeks before admission. The lesion was a poorly circumscribed exophytic nodule and consisted of an intradermal vascular proliferation in an edematous stroma (figure 1, *left* and *right*). The lumina were rounded and lined by flattened, mature endothelial cells. The overlying epidermis focally was thinned and ulcerated. The cellular infiltrate surrounding the vessels consisted of abundant neutrophils, with scattered lymphocytes and macrophages. The original diagnosis by the pathologists at the other hospital was pyogenic granuloma, and the lesion does have features of that entity. Large branching vessels were present centrally, suggesting the so-called vascular lobule characteristic of pyogenic granuloma. However, the typical collarette of surrounding thickened epidermis was not clearly present.

The term *pyogenic granuloma* is somewhat of a misnomer. Granulomas are not present, and the lesion is thought to arise from a neoplastic vascular proliferation. An equivalent, more appropriate name is lobular capillary hemangioma.

DR. FINBERG. What is this lesion thought to be associated with?

DR. LESTER. As a clinical entity, it is usually a solitary raised polypoid mass on the hands or face, which may ulcerate centrally. Excision usually is curative; however, satellite lesions may occur. Al-

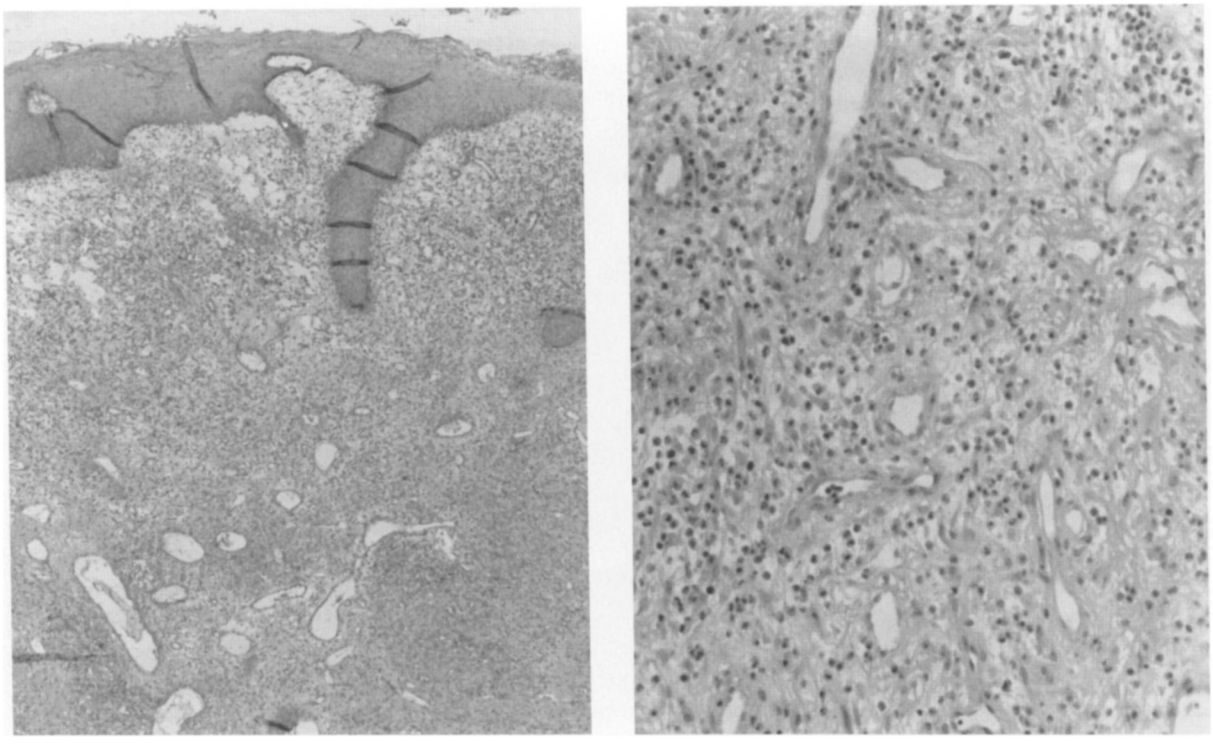

**Figure 1.** Biopsy of the patient's thigh lesion: (*left*) skin showing intradermal vascular proliferation with superficial ulceration (hematoxylin and eosin stain; original magnification, ×5); (*right*) mature blood vessels of variable sizes surrounded by an inflammatory infiltrate, consisting predominantly of neutrophils (hematoxylin and eosin stain; original magnification, ×13).

though pyogenic granulomas originally were thought to be infectious in nature because of the exuberant inflammatory infiltrate, an etiologic agent has never been established.

DR. KASS. I think of these lesions as usually being bright red in appearance.

DR. LESTER. Because pyogenic granulomas are vascular lesions, the appearance is that of red to purple raised papules.

Consultation slides of the original biopsy of the finger lesion were not received, but the lesion was described in the outside surgical pathology report as "ulcerated skin with inflamed granulation tissue."

The patient underwent debridement of the index finger lesion during his admission at the Brigham. The specimen consisted of multiple fragments of skin and soft tissue, with a microscopic appearance similar to that of the thigh lesion (figure 2, *left*). A proliferation of small vessels in a stroma infiltrated predominantly by neutrophils was present, with focal areas of leukocytoclastic debris. The appearance was histologically consistent with granulation tissue and acute inflammation.

Organisms were not seen with use of Goodpasture's gram, methenamine silver, Dieterle silver, or Ziehl-Neelsen stain. However, staining with the Warthin-Starry silver impregnation technique revealed numerous small coccobacillary forms, with occasional branched forms in clusters in the stroma and surrounding blood vessels in both the thigh and finger lesions (figure 2, *right*). The bacilli were gram-negative as determined by the Brown-Hopps gram technique.

The finding of Warthin-Starry-positive bacilli suggested that both of the lesions in this patient were caused by infection with the cat scratch bacillus, which has been described to produce similar lesions in HIV antibody-positive patients [1–4]. The characteristic lesions have been described as vascular proliferations with a surrounding inflammatory infiltrate consisting predominantly of neutrophils. The lesions may occur as superficial skin papules or subdermal nodules or may be present in lymph nodes. The endothelial cells may appear mature and flattened, such as in this patient, or plump and cuboidal with moderate to marked atypia. The atypia and

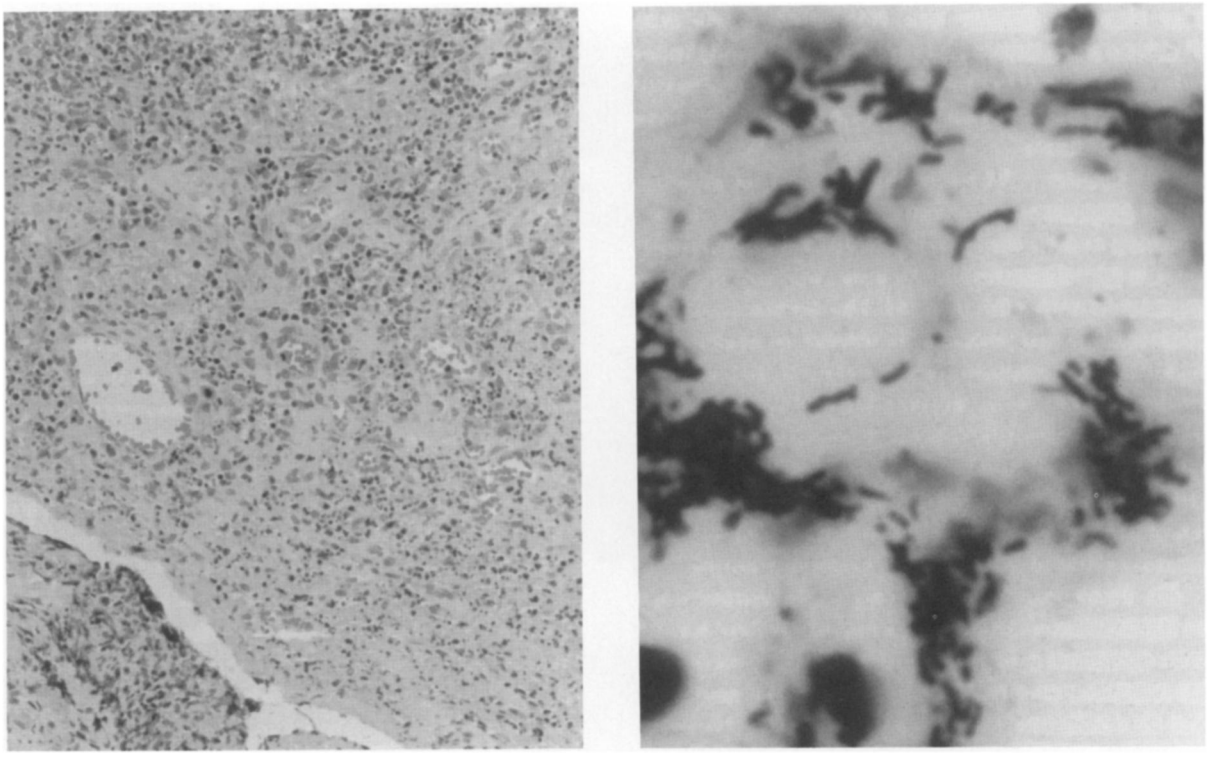

**Figure 2.** Biopsy of the patient's finger lesion: (*left*) vascular proliferation with surrounding inflammatory infiltrate (hematoxylin and eosin stain; original magnification, ×20); (*right*) clusters of small bacilli surrounding blood vessels (Warthin-Starry stain; original magnification, ×400).

the presence of numerous mitoses may suggest the diagnosis of angiosarcoma in a few patients. In some cases a vascular lobule is present together with a well-formed collarette, and the lesions are morphologically indistinguishable from pyogenic granulomas. The general term *epithelioid angiomatosis* has been used to describe these lesions. The name *epthelioid hemangioma* has been suggested for this type of lesion in HIV antibody-positive patients [5].

An inflammatory infiltrate is always present and consists predominantly of neutrophils, but it may also include eosinophils, lymphocytes, and macrophages. Small areas of necrosis and karyorrhexis may be present, but large, necrotic areas are not seen. In five HIV antibody-positive patients with epithelioid hemangiomas but without an inflammatory infiltrate, staining with the Warthin-Starry silver impregnation technique failed to reveal bacilli, a situation suggesting that inflammation is a diagnostic feature of this entity [2, 5].

These lesions may grossly resemble Kaposi's sarcoma, but they are hisotologically distinct. A spindle cell proliferation with slitlike channels is not present and extravasated blood cells are not a feature here, but they would be found in Kaposi's sarcoma. An inflammatory infiltrate, however, is not characteristic of Kaposi's sarcoma.

Epithelioid hemangiomas also lack the features of the cutaneous, conjunctival, and lymph node lesions found in normal hosts infected by the cat scratch bacillus [6]. Characteristically, large zones of necrosis are present, surrounded by palisading histiocytes and a mantle of lymphocytes. Numerous eosinophils and multinucleated giant cells may be present. In the setting of these changes, a proliferation of capillary-sized vessels and dilation of lumina have been observed in conjunctival lesions [7]. However, endothelial atypia is not seen, and the proliferation is not a predominant feature of the lesion. The extent of necrosis and vascular proliferation may be related to the host's ability to mount an immune response and may be responsible for the variability of the lesions seen in cat scratch disease.

DR. LIU. I think the impressive numbers of organisms seen on the slides from this case in the absence of any granulomatous response was a strong

clue that the patient was HIV-positive. As with *P. carinii* pneumonia and tuberculosis, among other infections in AIDS, it may be that the pathology of cat scratch disease is different in AIDS patients than in normal hosts.

DR. LESTER. There certainly were a large number of organisms present in these specimens. It is interesting to note that Carrion's disease, or bartonellosis, is also characterized by a vascular proliferation associated with a bacillus [8]. The dermal lesion, or nodular verruga peruana, is similar in appearance to a pyogenic granuloma. However, it differs from the lesions seen with cat scratch bacillus in that solid aggregates of histiocytoid cells or spindle cells are seen commonly, and the surrounding infiltrate consists predominantly of plasma cells and eosinophils. The bacilli may be seen within the stroma and surrounding blood vessels after Giemsa staining.

DR. FRANZ VON LICHTENBERG. The second stage of bartonellosis consists of a mushroomlike lesion, with epithelial proliferation at the base. One would see a marked proliferation of venules and capillaries and also a chronic inflammatory infiltrate. Huge accumulations of histiocytes, which one would find in bartonellosis, are lacking in the specimens from this case. The endothelium in bartonellosis is very prominent, and one can see the bartonellae at very high power in the endothelial cells as well as in the red blood cells. One can see these organisms only with Giemsa or other polychrome stains. The *Bartonella* organisms are even smaller than cat scratch bacilli. The cat scratch organism is small enough ($\sim$3 μm), but the *Bartonella* organism is <0.5 μm. Daniel Alcides Carrion was the heroic medical student from Lima, Peru, who infected himself with *Bartonella* and proved, by dying of the disease, that the verrucous form of the disease was identical to what was called Oroya fever, which is seen mostly in the mountain slopes of Peru. Oroya fever is the more acute systemic form of the disease. I think the lesions in the case today are incompatible with a diagnosis of bartonellosis because one can see numerous silver-stained extracellular organisms in these specimens, especially in a subendothelial position. Whether these are cat scratch bacilli, I will leave for you to discuss.

DR. PARSONNET. Sporotrichosis was the most popular diagnosis when the case was first presented, but I have been convinced that cat scratch disease is the most likely diagnosis. Dr. Marasco will now review the recent literature on cat scratch disease.

DR. MARASCO. I would like to talk briefly about cat scratch disease, as well as typical and atypical features in AIDS patients who develop cat scratch disease. Cat contact does not have to be an actual scratch. The diagnosis of cat scratch disease, at least traditionally, has been made by the meeting of three of these four criteria: (*1*) cat contact, with the presence of a scratch or a primary dermal or eye lesion; (*2*) a positive cat scratch disease skin test; (*3*) regional lymphadenopathy, with normal results of laboratory studies for other causes of lymphadenopathy; and (*4*) characteristic histopathologic changes in a lymph node or skin lesion [9, 10]. The demonstration of small pleomorphic bacilli in collagen fibers, in abscesses, or in granulomas stained by the Warthin-Starry silver impregnation method (or Brown-Hopps stains) confirms the diagnosis [9, 11, 12].

At the primary inoculation site, the patient usually develops a papule or nodule. While a positive skin test is listed as one of the four diagnostic criteria, it is not in widespread clinical use because the cat scratch antigen is difficult to obtain and has not been standardized.

The lesions in this disease are quite interesting because they can vary tremendously. The typical papules are 0.5–1 cm, red, and raised and often bleed. They can occur as several lesions or hundreds disseminated widely over the body. They can be as large as 4 cm in diameter [12, 13] and can be exophytic; some will display an area of necrosis and ulceration.

DR. VON LICHTENBERG. The reddening around the base of each lesion is atypical for an ordinary pyogenic granuloma. You seldom see any reaction around the base of those lesions, although most of the putative cat scratch lesions seem to show erythema in the surrounding skin.

DR. MCINTOSH. How are you defining cat scratch disease in this case?

DR. MARASCO. We are making the diagnosis from the positive Warthin-Starry stain. The patient did own a cat and had systemic symptoms consistent with cat scratch disease. I called Dr. Douglas Wear at the Armed Forces Institute of Pathology (AFIP), who has been credited with discovering the bacillus, culturing it, and raising the antisera to it [9]. By his account, the Warthin-Starry stain is diagnostic. No other organisms, in his opinion, look like the cat scratch bacillus by Warthin-Starry stain, except *Bartonella*, which does not fit the clinical course here. Dr. Wear has performed retrospective studies using rabbit antibody raised to the vegeta-

tive form of the bacillus that he grew in culture, and all of those cases have been Warthin-Starry-positive and immunoperoxidase-positive. Stains for a number of infectious agents, including many we discussed in the differential diagnosis of this patient, have all been negative. We have sent specimens from our patient to the AFIP for immunoperoxidase staining.

DR. KASS. Was any of the material saved outside of the fixative? In the past, some laboratories have used specimens such as this as a source of antigen for skin testing.

PHYSICIAN. This patient is HIV-positive. In the AIDS era untested patient materials are risky to use.

DR. MARASCO. According to the literature, the prevalence of skin test positivity to this antigen is up to 20% in the general population, which does not make the test very helpful.

DR. LIU. The sources of skin test antigen are unknown and, therefore, a potential problem. When one obtains antigen from Dr. Margileth, one must complete a very long consent form that is difficult for patients to comprehend.

DR. FINGEROTH. Is there any realistic possibility of acquiring bartonella infection in this country?

DR. MARASCO. I do not believe so. I raised with Dr. Wear the remote possibility that this patient could have contracted bartonellosis though his contact with South American orchids and soil. It seems unlikely, however, that he really was exposed. Dr. Wear then did agree to perform the immunoperoxidase stains, recently reported in the *Annals of Internal Medicine* [12], to confirm positive Warthin-Starry staining of lesions in four AIDS patients with cat scratch disease.

DR. VON LICHTENBERG. Transmission of *Bartonella* depends on a sandfly vector and must occur at an appropriate altitude. However, there are sporadic hemobartonella infections in humans from animal contacts—with guinea pigs, for example—that cause an acute febrile illness without skin lesions.

DR. MARASCO. In most normal hosts, the typical presentation of cat scratch disease is as a benign illness. It is interesting that 74% of cases occur in the fall or winter [10]. At the inoculation site a papule develops, accompanied by regional lymphadenopathy that usually persists for several weeks to months, although persistence for as long as 2 years has been reported [14]. In 59% of cases in one series, the inoculation lesion was on the skin, eye, or mucous membrane [10]. Table 1 summarizes the data of Margileth et al. on the signs and symptoms in 832 patients seen over a 20-year period [10]. Regional lymphadenitis is the only manifestation of the disease in 50% of the cases. Another 30% developed fever and malaise, while ~12% of patients developed a more systemic illness, with constitutional symptoms of headache, anorexia, emesis, weight loss, and splenomegaly. One to two percent of patients have prolonged morbidity, with persistent high fever, suppurative lymphadenitis, and severe systemic symptoms.

**Table 1.** Clinical features in 832 patients with cat scratch disease.

| Sign or symptom | Percentage of patients with indicated sign or symptom | Mean duration in d (range) |
|---|---|---|
| Adenopathy only | 51 | 105 (14-365) |
| Fever (38.3°C-41.1°C) | 31 | 6 (1-30) |
| Malaise and/or fatigue | 28 | 13 (1-21) |
| Headache | 13 | 4 (1-7) |
| Anorexia, emesis, weight loss | 13 | 5 (3-30) |
| Splenomegaly | 12 | 11 (7-21) |
| Sore throat | 9 | NA (1-5) |
| Exanthem | 4.4 | 8.5 (5-14) |
| Conjunctivitis | 4.3 | NA (1-11) |
| Swelling of the parotid gland | 2.0 | NA (7-28) |

NOTE. All patients had a positive skin test for cat scratch disease. Data are adapted from [10]. NA = data not available.

In a series of 1,174 patients with cat scratch disease collected by Margileth et al., 88.4% had a typical presentation [10]. Unusual presentations found in 11.6% of patients included Parinaud's oculoglandular syndrome, a granulomatous conjunctivitis with unilateral periauricular lymphadenopathy (6.3%), encephalopathy (2.3%), and chronic, severe, systemic disease (2%). Other reports have described granulomatous or anicteric hepatitis [15], splenitis [15, 16], osteomyelitis [17], pleurisy [10], splenic abscesses [10], and central nervous system involvement—usually encephalopathy [18] and neuroretinitis [10].

Table 2 summarizes some clinical features of the severe presentation of cat scratch disease compared with the typical manifestations [10]. The severe form of the disease is characterized by persistence (≥2 weeks) of major symptoms and signs and/or systemic involvement (one or more organ systems). For example, fever is found in ~31% of patients with typical disease compared with 70% with severe disease, and in the severe form, fever may persist for several

**Table 2.** Clinical presentation in severe vs. typical cat scratch disease.

| Characteristic | Percentage of patients with indicated characteristic | |
|---|---|---|
| | Severe ($n$ = 23) | Typical ($n$ = 832) |
| Cat contact | 70 | 73 |
| Male | 70 | 57 |
| Age >21 y | 78 | 17 |
| Skin or mucous membrane as primary inoculation site | 78 | 61 |
| Increased frequency and duration of fever | 70 | 31 |
| Prolonged malaise and fatigue of 10 d to 7 mo | 83 | 28 |
| Anorexia and/or weight loss (5–40 lb) | 52 | 13 |
| Duration of splenomegaly of 1–3 mo | 30 | 12 |
| Skin eruptions | 4χ* | χ |
| Myalgias, synovitis, arthritis | 39 | NA |
| Multiple sites of adenopathy | 43 | 35 |
| Axillary adenopathy | 57 | 25 |
| Mean lymph node size | 5.5 cm | <5 cm |
| Lymph node fluctuance | 52 | 12–16 |

NOTE. All patients had a positive skin test for cat scratch disease. NA = data not available.

* Four times more frequent in severe disease.

months. Weight loss of 5–40 lb is seen in patients with severe disease. Splenomegaly lasting 2 weeks to 10 months is also seen in a number of these cases, as well as myalgias, arthritis, and synovitis, which persists for 2–4 weeks. Skin eruptions (urticaria, vesiculopapular lesions, and erythema nodosum) occurred four times more often in severe cases. There is a predominance of men among patients with severe cases, and older patients tend to get the more severe form of the disease. Multiple sites of adenopathy are more common; axillary adenopathy is also more common than adenopathy in other sites. Fluctuance in the lymph nodes is about twice as common in the severe form of the disease as in the typical form and lymph nodes are larger.

The patient presented here is HIV-positive. I thought it would be useful to review the spectrum of cutaneous diseases one finds in AIDS patients [19, 20]. The skin manifestations include diseases caused by infection, neoplasm, and miscellaneous other causes. Neoplastic diseases include Kaposi's sarcoma, Burkitt's lymphoma, basal cell epithelioma, and anorectal squamous cell carcinoma. Skin diseases for which a clear etiology has not been established include seborrheic dermatitis, papular eruption of AIDS, yellow-nail syndrome, xerosis, ichthyosis, psoriasis, thrombocytopenic purpura, and miscellaneous nutritional deficiences. Table 3 summarizes the work of Goodman et al. [19], who studied 90 adult patients with AIDS and 27 with AIDS-related complex seen consecutively in three New York hospitals, and provides prevalence data on the frequency of skin manifestations seen in HIV disease. The most common cutaneous findings were candidiasis in 47% of cases, dermatophytosis in 30%, HSV infections in 22%, molluscum contagiosum in 9%, seborrheic dermatitis in 32%, and acquired ichthyosis or xerosis in 30%.

Among the viral diseases of the skin seen in AIDS patients, HSV was associated with severe disseminated disease in 12% of the cases. Verrucae were seen in 8%, disseminated varicella in 3%, and herpes zoster in 1% of the patients. Of the fungal diseases, only candidiasis and dermatophytosis were seen in this study, although cutaneous histoplasmosis and cryptococcosis have been reported in other studies. Bacterial diseases are actually relatively uncommon, with acne being the most common (7%). Abscesses, cellulitis, and folliculitis occur but are not common. Proliferative disease, such as Kaposi's sarcoma, is found in about 7% of patients. Papular eruptions, found in <2% of patients, are not well characterized. I believe that our patient may fit into this last category.

**Table 3.** Prevalence of cutaneous disease in patients with AIDS.

| Disease | Percentage of patients |
|---|---|
| Viral | |
| Herpes simplex | 22 |
| Herpes zoster and disseminated varicella | 1, 3 |
| Molluscum contagiosum | 9 |
| Fungal | |
| Candidiasis | 47 |
| Dermatophytosis | 30 |
| Bacterial | |
| Acne | 7 |
| Abscess, cellulitis, folliculitis, hidradenitis suppurativa | <2 |
| Seborrheic dermatitis | 32 |
| Proliferative disease | |
| Kaposi's sarcoma | 7 |
| Miscellaneous | |
| Acquired ichthyosis or xerosis | 30 |
| Papular eruption | <2 |

NOTE. Data are adapted from [19].

**Table 4.** Cat scratch disease in patients with AIDS.

| Sign or symptom | Percentage of patients with indicated sign or symptom | |
|---|---|---|
| | [2–4, 13] ($n$ = 14) | [21]* ($n$ = 7) |
| Fever | 71 | 0 |
| Malaise/fatigue | 36 | NA |
| Anorexia/weight loss | 36 | NA |
| Severe systemic disease | 93 | NA |
| Bone lesions | 21 | NA |
| Recurrence | 14 | NA |
| Multiple skin sites | 93 | 86 |
| Duration of illness | 3–6 mo | NA |

* NA = data not available.

In table 4, I have compiled a summary of the signs and symptoms of cat scratch disease from five reports involving 14 patients with AIDS. Severe disease is common, with prominent constitutional symptoms including fever in 71% of the patients, malaise and fatigue in 36%, anorexia and weight loss in 36%, and severe systemic disease (as previously defined) in 93% of the cases. Disseminated cutaneous lesions also are very common. Osteolytic lesions were found in three patients and were located underneath cutaneous nodules [3, 12]. Prolonged duration of illness, 3–6 months, was seen frequently. While AIDS patients may present with a number of concurrent infections, which makes categorizing the manifestations of the disease difficult, most of these 14 patients were thought to have signs and symptoms referable to cat scratch disease alone.

In contrast, in a study published by LeBoit et al. [21], seven patients with AIDS and cat scratch disease were reported in whom cutaneous nodules but no systemic manifestations of the disease were found. Antibody to the cat scratch bacillus also was evaluated. In three of seven patients there was a fourfold rise in antibody titer directed to the bacillus. Four of those seven patients had maximum titers of 1:32–1:128. LeBoit's information was acquired retrospectively after biopsy material was examined and may in part explain the discrepancy between the clinical course of the disease described in this study and those of the five other studies and the case that we have presented. I would summarize this small number of studies by suggesting that systemic symptoms and a more severe form of the disease are probably more common in cat scratch disease in AIDS patients.

The issue of treatment is somewhat complicated, and the literature is not entirely clear. In a typical presentation in a normal host, Wear and his group at AFIP suggest that no treatment is needed, since this is a self-limited disease, despite lingering regional lymphadenopathy. If there is abscess formation, they recommend symptomatic treatment with warm moist compresses, and if the node becomes painful and fluctuant, they aspirate but do not administer antibiotics. One could argue with that approach. In the more severe systemic disease, antibiotics are clearly indicated, and I believe some dramatic responses to antibiotics have been observed in some patients. In immunocompromised hosts, cat scratch disease can be life threatening. There is at least one report in the literature in which a renal transplant recipient presented with sepsis from the cat scratch bacillus and responded immediately to antibiotics [21].

In terms of antibitoic susceptibility, there are some differences between the in vitro antibiotic susceptibility testing reported by Wear and his colleagues at the AFIP after they isolated the bacillus [9] and the observed clinical responses of treated patients. The bacillus is sensitive in vitro to cefoxitin, cefotaxime, aminoglycosides, including netilmicin, and mezlocillin, with intermediate susceptibility to trimethoprim-sulfamethoxazole, vancomycin, ticarcillin, and piperacillin. The organism is resistant to penicillin, ampicillin, erythromycin, tetracycline, cephalothin, chloramphenicol, clindamycin, cefazolin, cefamandole, cefoperazone, and nitrofurantoin. After reviewing the literature, I think it is fair to summarize that there is a poor clinical response to penicillin, dicloxacillin, and cefazolin, to all of which the bacillus is resistant in vitro. There is, in fact, a good clinical response to erythromycin and doxycycline [4, 12, 22], both of which are also in the resistant category by susceptibility testing. The most dramatic responses, however, which may have come in part from use in sicker patients, were found with the antituberculous drugs. There are cases described where patients had widely disseminated cutaneous lesions that were treated with isoniazid, rifampin, and ethambutol, with resolution of the lesions in a matter of days [3, 12, 13, 21].

DR. LIU. Are there in vitro data to accompany the clinical case report?

DR. MARASCO. I could find no in vitro data on the use of antituberculous drugs.

DR. JEFFREY BERGELSON. The data published on in vitro susceptibilities, though, derive from the organism isolated from a single patient and really have not been standardized in any way.

DR. MARASCO. That is true. Wear's group published the susceptibility data from one patient [9]. I would say that in vitro data have to be questioned, and one would make antibiotic selections on the basis of clinical data generated to date. I think that erythromycin, doxycycline, and rifampin are the three antibiotics one might choose from. In our patient it appeared that there was a clear clinical response to ciprofloxacin.

DR. ZALEZNIK. Given the in vitro and clinical data you have presented thus far, how was ciprofloxacin chosen?

DR. MARASCO. The choice was based on the patient's report that 5 days of ciprofloxacin as an outpatient had led to disappearance of symptoms. We gave him a trial of ciprofloxacin, and he did well.

DR. RICHARD PLATT. In fact, the surface growth of *P. aeruginosa* is what initially triggered the choice of ciprofloxacin, and he even received ticarcillin and tobramycin for a few days when he had a fever spike. I think people were focusing on *Pseudomonas* to determine antibiotic selections.

DR. MARASCO. Following his discharge, the patient completed 2 weeks of ciprofloxacin therapy, and at present, 7 weeks later, he has had no recurrence of fever or other constitutional symptoms.

DR. KASS. There seems to be a paradox here. The cat scratch bacillus does not seem to be an intracellular organism, and yet the antibiotics that appear most effective are ones that get inside the cell. Are we missing something here?

DR. MARASCO. It seems that the antibiotics that are ineffective against the cat scratch bacillus are agents involved in cell wall synthesis [9, 12]. One finds both in vivo and in vitro cell wall-deficient and vegetative forms of the organisms [9]. The cell wall-deficient forms are found in patients who have not been treated with antibiotics. It may be that antibiotics that are involved in blocking protein and RNA synthesis are more active against this bacillus than cell wall-active agents.

I would like to summarize the Brigham and Women's Hospital's recent experience with cat scratch disease from 1987 to date. By using the hospital's computer, I was able to find nine patients in the last 2 years in whom the diagnosis of cat scratch disease was included in the differential diagnosis based on histopathologic findings. In none of these cases were Warthin-Starry stains performed. Eight of the nine patient specimens were from lymph nodes. The distribution of the nodes is shown in table 5: five of nine were inguinal, one of nine cervical, and one of nine retroperitoneal. I also reviewed charts of patients in whom the diagnosis of pyogenic granuloma was made. These diagnoses were typically made from skin lesions, whereas the cat scratch diagnoses came from lymph node specimens. There were 42 cases of pyogenic granuloma at the Brigham in the last 2 years. The distribution of the lesions is shown in table 5; 63% of the lesions were in exposed areas of head, neck, arms, and hands. The histopathologic features are similar to those already described by Dr. Lester. It seems possible that a number of these skin lesions actually were caused by the cat scratch bacillus. I think we might make the diagnosis of cat scratch disease more often if we requested Warthin-Starry stains on nodular lesions. There is also a short note from Hong Kong [23] looking at seven pyogenic granulomas and other vascular lesions, with failure to find bacilli. However, these may not be representative of the lesions that are seen in other hospitals.

**Table 5.** Summary of cases of cat scratch disease and pyogenic granuloma in pathologic specimens from Brigham and Women's Hospital, Boston, 1987–1989.

| Features of | No. of cases (%) |
|---|---|
| Cat scratch disease* ($n$ = 9) | |
| Exposure to cat | 1 (11) |
| Suppurative lymphadenitis | |
| Inguinal | 5 (55) |
| Neck | 1 (11) |
| Retroperitoneal | 1 (11) |
| Pyogenic granuloma ($n$ = 42) | |
| Head and/or neck | 15 (36) |
| Arm | 4 (9.5) |
| Hand | 7 (17) |
| Leg | 2 (4.7) |
| Foot | 4 (9.5) |
| Trunk | 8 (19) |

* Pathologic findings included follicular hyperplasia, histiocytic aggregates, and stellate microabscesses.

In summary, we describe an HIV antibody-positive patient with systemic cat scratch disease. His illness was characterized by several months of fevers, malaise, and two anatomically separated cutaneous lesions. One of his cutaneous lesions recurred, despite surgical removal and a short course of ciprofloxacin. In the end, his illness appeared to respond to a combination of surgical intervention and a 2-week course of oral ciprofloxacin. This case emphasizes that a more severe and systemic illness from

the cat scratch bacillus may be seen in HIV-positive patients than in the normal host.

*Addendum.* While this paper was in proof, Schlossberg et al. [24] reported a case of culture-proven disseminated cat scratch disease in a patient with AIDS.

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