Bacillary angiomatosis in renal transplant recipient and the helpful investigation by PCR to identified *Bartonella spp*

Nutthamon Bowornsathitchai MD,

Ratchathorn Panchaprateep MD PhD.

ABSTRACT:

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DIVISION OF DERMATOLOGY, DEPARTMENT OF MEDICINE, KING CHULALONGKORN MEMORIAL HOSPITAL, BANGKOK, THAILAND.

A 37-year-old Thai man, with end stage renal disease, who underwent renal transplantation, presented with a 1-month history of solitary, asymptomatic, rapidly-growing fragile erythematous-violaceous nodule on the dorsum of right hand. He also had subacute fever, fatigue and weight loss of 3 kilograms in 2 weeks. Skin excisional biopsy was performed and revealed pyogenic granuloma like lesion. Bacterial identification by PCR technique showed *Bartonella henselae.* He also had a history of contact with many cats near his home.

Bacillary angiomatosis (BA) is angioproliferative disease caused by *Bartonella henselae* or *Bartonella quintana* infection found in immunocompromised host especially HIV infection and organ transplant patients. The disease has potentially life-threatening course yet easily treatable. PCR has higher sensitivity, specificity and need shorter time than other methods to identify *Bartonella spp*. Treatment of choice is macrolide or doxycycline.

Key words: bacillary angiomatosis, renal transplant recipient, PCR.

From : Division of Dermatology, Department of Medicine, King Chulalongkorn Memorial Hospital, Bangkok, Thailand

Corresponding author : Ratchathorn Panchaprateep MD PhD., e-mail: rpanchaprateep@gmail.com

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A 37-year-old Thai man was diagnosed with end stage renal disease from congenital renal artery stenosis in 2002 and had undergone renal transplantation 11 years ago in December 2007. He had been received many immunosuppressive drugs after transplantation such as tacrolimus, mycophenolate mofetil and prednisolone. No antirejection therapy was given during the post-transplant period. After transplantation, he had stable status (functional class 1) but only asymptomatic mild anemia due to chronic renal failure and Hb E trait. He regularly contacted with many cats in his residency but didn't have history of scratch from cat.

In January 2018, while receiving tacrolimus (1.5g/day), mycophenolate mofetil (1g/day), prednisolone (5mg/day). He presented with solitary, asymptomatic, rapidly growing skin lesion with history of easily contact bleeding on dorsum of the right hand for 1 month.At this time, he was admitted into the hospital with subacute fever for 2 weeks and suspected problem of septic shock. He also had fatigue and weight loss 3 kg in 2 weeks.

Physical examination found a single, well defined, asymptomatic firm hyperkeratotic erythematous-violaceous nodules 2 cm in diameter surrounded by small satellite erythematous papules on dorsum of the right hand (Figure 1). Multiple subcentrimeter cervical lymphadenopathy and a single Rt. axillary lymphadenopathy, sized 2 cm were also noted. Fever were recorded upto 39°c. Hepatomegaly 3 FB below Rt. costal margin were found. No splenomegaly.

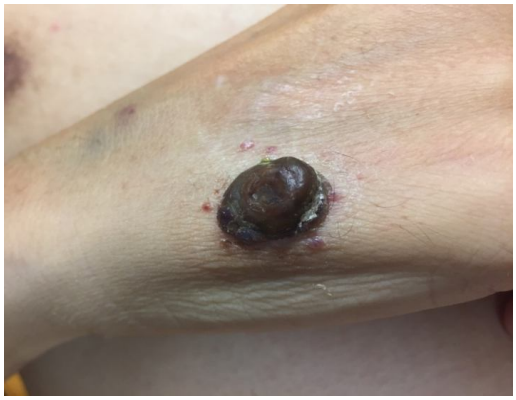

Figure 1 Solitary well defined, firm hyperkeratotic erythematous-violaceous nodules 2 cm surrounded by small satellite erythematous papules on the right dorsal hand

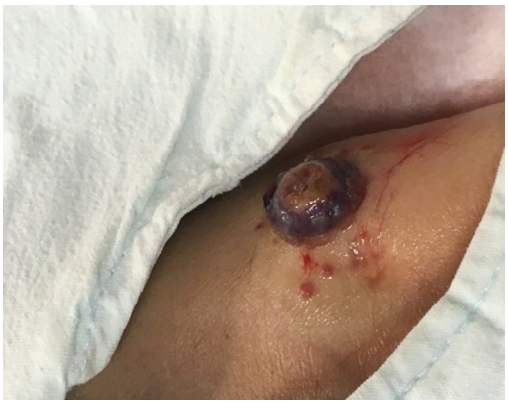

Figure 2 In the operation after keratotic crust was removed the lesional surface was friable and easily bleeding

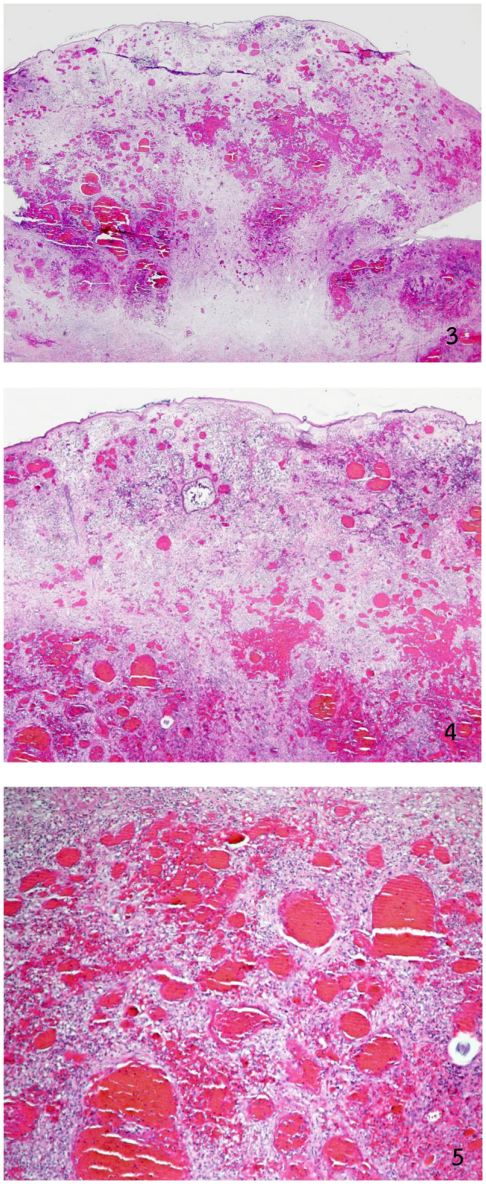

Figure 3-5 H&E, magnification X20, X40, X200
The section shows lobular proliferation of small blood vessels with mixed inflammatory cells infiltration and eroded surface

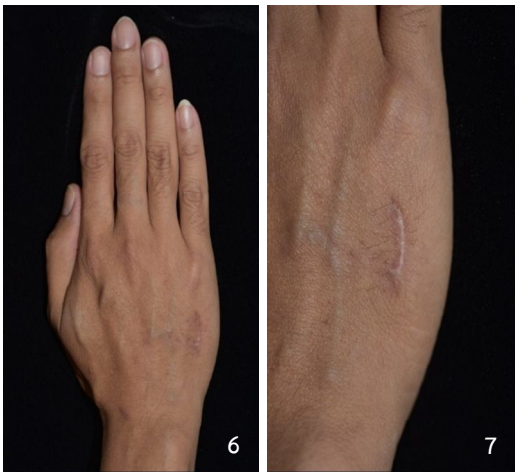

Figure 6,7 After treatment with oral doxycycline, no recurrent after follow up for 8 months

Septic work up was done, the results of search in blood for fungi, CMV, hepatitis B and C virus (HBV, HCV), HIV, *Toxoplasma gondii, Treponema pallidum, Rickettsiae*, mycobacteria and *Bartonella* were negative. Urine and stool cultures couldn't identify any organism. CXR also showed no abnormalities. The cutaneous lesion was totally excised and be sent for histopathology and organism identification. In the operation after hyperkeratotic crust was removed, the lesional surface was friable and easily bleeding (Figure 2).

Skin biopsy revealed lobular proliferation of small blood vessels with mixed inflammatory cells infiltration and eroded surface like features of pyogenic granuloma (Figure 3-5). Bacterial identification from tissue by PCR revealed *Bartonella henselae*. No microorganisms ware

detected on special stains such as Gram, AFB, mAFB, Wright and Grocott Gomorimethenamine silver. Warthin-Starry stain wasn't performed due to lacking of laboratory facilities. Skin tissue cultures for aerobic bacteria, fungus, mycobacterium tuberculosis were negative all. Detection of mycobacteria and fungus by PCR were negative.

Further laboratory investigations including complete blood count found anemia, thrombocytopenia and leukocytosis with neutrophil predominate, mild elevated liver function tests and decreased renal function (serum creatinine level 5.1mg/dl, from baseline 2.8mg/dl). Bone marrow biopsy showed erythroleukoblastic blood picture. Hematologist considered it was reactive process from infection.

The patient was treated with oral doxycycline 100 mg twice daily for 5 months, showed good response with no recurrent after follow up for 8 months (Figure 6-7).

Discussion

Bacillary angiomatosis (BA) is a rare vasculoproliferative infectious disease of the skin and can involve many organs, including lymph nodes, gastrointestinal tract, brain, bone marrow, respiratory system and rare in mucosa[1]. It caused by *Bartonella henselae* (BH) *or Bartonella quintana* (BQ) infection which can promote angiogenesis. *Bartonella* is the only genus that release factors to stimulate endothelial cells to produce angiotensin-2 and epidermis to produce vascular endothelial growth factor (VEGF). BadA protein on the cell surface is also known to promote angiogenesis via inducible hypoxia factor-1 (IHF-1) in BH[2].

Skin is the most affected site of BA.Initial manifestations include fever and lymphadenopathy in association with cutaneous lesions of angiomatous tumors, mimicking pyogenic granuloma or kaposi sarcoma[3]. The common internal organ involvements are liver, spleen, and lung nodules. Clinical spectrum of BA caused by different species differs. Peliosis hepatis and lymph node involvement are associated with BH, while bone and subcutaneous involvement are associated with BQ[3]. Human infection occurs by direct contact with cats or scratching by cats, also can spread by cat flea and human body louse[1,4]. The incubation period varies from 10 to 210 days, with an average of 60 days[4]. BA is frequently reported in HIV-infected patients, occasionally reported in other immunodeficiencies such as organ transplantation, chronic lymphocytic leukemia and rarely reported in immunocompetent host[4-8]. The difference of clinical presentations between organ transplant recipients and HIV-infected patients is the number of the lesions. Organ transplant recipients usually present with few lesions, while HIV-infected patients have multiple

lesions[6]. Fever is the symptom that is mostly found and may coexist with night sweats, chills, anorexia, myalgia and weakness. Skin lesions of BA can located in various areas. They usually manifest as erythematous or violaceous papules or nodules, which may be crusted or ulcerated.

The disease has potentially life-threatening course yet easily treatable. Early recognition, prompt diagnosis and adequate treatment are essential[1]. The diagnosis of BA is based on the identification of BH or BQ, by histopathology with special stain, cultures, serologic tests or molecular biology detection of DNA in tissue by PCR[6]. Histopathology of BA demonstrates lobular proliferation of blood vessels with mixed inflammatory cells infiltration with the presence of small, extracellular bacilli stained with Warthin-Starry. However, Warthin-Starry stainis not available in many laboratories due to difficulty in the preparation process. Causative organisms are fastidious and need a long time to identify in culture. Serology is more sensitive than cultures but the results from serologic tests are variable[2,5-8]. Serology can cross-react and may be falsely negative in an immunocompromised host.Until now, PCR is the best way to identify Bartonella[6-8].

Treatment of choice is macrolide or doxycycline[2,6,10]. Macrolides have a disadvantage of drug interaction with calcineurin inhibitors that are given in most transplant patients[6]. The duration of treatment is difficult to determine but should be prolonged until the lesions disappear[2,10]. In HIV patients, treatment should be continued until CD4 count is above 200cells/mm3 for over 6 months[2]. Our patients have been treated with doxycline for over 5 months with good response.

In summary, we report a case of bacillary angiomatosis in renal transplant recipient

References

1. Eyer-Silva WA, Soares P, Azevedo M, et al. An unusual case of bacillary angiomatosis in the oral cavity of an AIDS patient who had no concomitant tegumentary lesions - case report and review. Rev Inst Med Trop Sao Paulo 2017; 59: e59.
2. Akram SM, Bhimji SS. Mycobacterium Chelonae. StatPearls. Treasure Island (FL): StatPearls Publishing StatPearls Publishing LLC. 2018.
3. Diniz LM, Medeiros KB, Landeiro LG, Lucas EA. Bacillary angiomatosis with bone invasion. An Bras Dermatol 2016; 91: 811-4.
4. Nikam BP, Vijayendran N, Jamale V, Kale M. Bacillary Angiomatosis in an Immunocompetent Individual. Indian Dermatol Online J 2018;9:205-6.
5. Fulchini R, Bloemberg G, Boggian K. Bacillary Angiomatosis and Bacteremia due to Bartonellaquintana in a Patient with Chronic Lymphocytic Leukemia. Case Rep Infect Dis 2013;2013:694765.
6. Orsag J, Flodr P, Melter O, Tkadlec J, Sternbersky J, Hruby M, et al. Cutaneous bacillary angiomatosis due to Bartonellaquintana in a renal transplant recipient. TransplInt 2015;28:626-31.

7. ShamekhiAmiri F. Bartonellosis in Chronic Kidney Disease: An Unrecognized and Unsuspected Diagnosis. TherApher Dial 2017; 21:430-40.
8. C. Moulin JK, B. Ranchin, C. Chauvet, Y. Gillet, E. Morelon, S. Euvrard. Cutaneous bacillary angiomatosis in renal transplant recipients report of three new cases and literature review. transplant infectious disease 2012; 14:403-9.
9. Diddi K CR, Sharma N, Dhawan B. Strategy for identification & characterization of Bartonellahenselae. Indian J Med Res 2013; 137:380-7.
10. Prutsky G, Domecq JP, Mori L, Bebko S, Matzumura M, Sabouni A, et al. Treatment outcomes of human bartonellosis: a systematic review and meta-analysis. Int J Infect Dis 2013;17: e811-9.