Secondary syphilis presenting as leukocytoclastic vasculitis in a 61-year-old man

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Abstract

Cutaneous lesions of secondary syphilis are highly infectious and can mimic many skin disorders, making the diagnosis more difficult. They typically present as generalized, nonpruritic erythematous-to-copper-colored macules and papules, characteristically involving palms and soles. In 80% of patients the rash develops insidiously. However, rare forms of secondary syphilis present as rapidly progressive papulopustular lesions. These forms of syphilis are usually associated with human immunodeficiency virus infection and immunosuppression. We report a case of secondary syphilis presenting with an acute, rapidly progressive purpuric eruption mimicking leukocytoclastic vasculitis. A 61-year-old man presented with a 6-day history of nonpruritic rash on his chest and lower extremities associated with fatigue, sore throat, and night sweats. Examination revealed purpuric papules, extending from the dorsal feet to the hips; mucosal surfaces were not involved. A diagnosis of cutaneous small-vessel vasculitis was favored with possible triggers of IgA vasculitis. Initial work-up showed acute kidney injury and microscopic hematuria. Renal biopsy showed IgA nephropathy with mesangioproliferative glomerulonephritis. The patient's rash progressed to cover almost his entire body sparing palms and soles. Skin biopsy showed heavy perivascular lymphoplasmacytic infiltrate, capillary endothelial cell swelling, and sparse perivascular neutrophilic nuclear dust. Spirochetal stain highlighted scattered epidermal and dermal organisms.

Keywords: leukocytoclastic, palpable purpura, secondary syphilis, treponema pallidum, vasculitis

Introduction

Acquired syphilis is usually described in terms of its four stages: primary, secondary, latent, and tertiary [1]. The incidence of acquired syphilis in the United States has continued to increase almost every year since it reached a historic low in 2000-2001. During 2019–2020, the rate of primary and secondary syphilis increased by 6.8%. In 2020, 133,945 new cases of syphilis (all stages) were reported. Rates increased in both males and females and in three regions of the United States (Midwest, Northeast, and South), [2]. Syphilis is caused by the spirochete *Treponema pallidum*. It typically spreads through contact between infectious lesions and mucous membranes or a disrupted skin barrier. Primary syphilis (chancre) occurs at the site of inoculation and usually appears about 21 days after exposure. Secondary syphilis is caused by hematogenous dissemination of the organism leading to widespread manifestations, usually 4-8 weeks after the chancre. The symptoms of secondary syphilis start insidiously as a macular erythematous eruption and can be accompanied by constitutional symptoms including fever, lymphadenopathy, sore throat, patchy hair loss, headaches, weight loss, muscle aches, and fatigue [3,4].

The cutaneous lesions of secondary syphilis are typically non-pruritic, erythematous or reddish-

brown colored macules, 5-10mm in diameter. The rash is often generalized and may include palms and soles. Mucous membrane lesions such as sores in the mouth, vagina, or anus can also be present [5]. An atypical clinical presentation with accelerated progression may occur in immunocompromised and human immunodeficiency virus (HIV) patients [6,7]. On histopathology, secondary syphilis shows psoriasiform epidermal hyperplasia and parakeratotic scale, often with vacuolar interface changes and spongiosis. Dermal changes include papillary dermal edema and perivascular lymphocytic or lymphohistiocytic infiltrate [8].

Leukocytoclastic vasculitis (LCV) or allergic vasculitis is a reaction pattern of small dermal vessels to the circulating immune complex. Leukocytoclastic vasculitis may be idiopathic in up to 40% of cases, but is often associated with infection, drugs, chemicals, foreign proteins, autoimmune disease, or rarely, underlying malignancy. Clinically, LCV is characterized by palpable purpura usually affecting the lower extremities. Leukocytoclastic vasculitis histology shows perivascular neutrophilic infiltrate with nuclear dust secondary to leukocytoclasia. Perivascular lymphocytes, eosinophils, or histiocytes may be present. The dermal vessels often show endothelial cell swelling with or without fibrinoid necrosis of the vessel wall [9,10]. Cases of syphilis manifesting with LCV are rare, with only a few cases reported in the literature, including congenital, primary, and secondary syphilis in HIV patients [11-15]. We report an interesting case of secondary syphilis in a non-HIV patient presenting with clinical and histopathological features of LCV.

Case Synopsis

A 61-year-old man presented with a 6-day history of nonpruritic rash on his chest and lower extremities that appeared after a hot shower. The rash was associated with fatigue, sore throat, and night sweats. He denied any fever, chills, joint pains, or recent changes to his medications. The patient had a history of hypertension, asthma, and depression. Examination revealed purpuric papules ranging from 1mm-1cm in diameter, extending from the dorsal feet to the hips (**Figure 1A**). Lighter pink

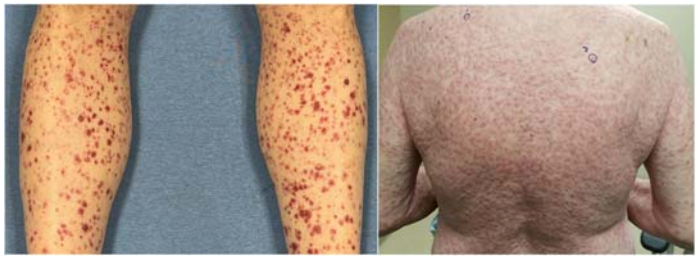

Figure 1. *Palpable purpura on bilateral legs, and erythematous papules and nodules over the trunk.*

papules coalesced into plaques over the trunk. Mucosal surfaces were not involved. The initial workup showed elevated serum creatinine (2.32mg/dl), hematuria, and granular casts in the urine. A diagnosis of cutaneous small-vessel vasculitis was favored with possible triggers of IgA vasculitis, considering the hematuria. Given the history of renal involvement and systemic symptoms, granulomatosis with polyangiitis was considered in the differential diagnosis. Urine culture and drug screen were negative. Screening tests for beta-hemolytic streptococcus, HIV, hepatitis C virus (HCV), and COVID-19 were all negative. Complement levels and antineutrophil cytoplasmic antibodies were normal.

A nephrology consultant raised concerns for an acute kidney injury with rapidly progressive glomerulonephritis and an urgent renal biopsy was recommended. The patient's blood pressure was stabilized with a mean arterial blood pressure of more than 65mm Hg. He was started on a renal diet (reduced diet sodium to less than 2g/24 hours and moderate protein intake at 0.8g/kg body weight) and avoided nephrotoxic drugs. All his medications were adjusted to the kidney function. Within one week of supportive management, serum creatinine dropped to 1.18mg/dl and repeated urine analysis showed resolved hematuria. A renal biopsy showed IgA nephropathy with mesangioproli-ferative glomerulonephritis and mild chronic changes with focal sclerosed glomeruli. The patient started a low dose of an angiotensin-converting enzyme inhibitor and the serum creatinine dropped to the patient's baseline of 0.8mg/dl.

One month later, despite the kidney function improvement, the patient's rash progressed to cover almost his entire body but spared palms, soles, face,

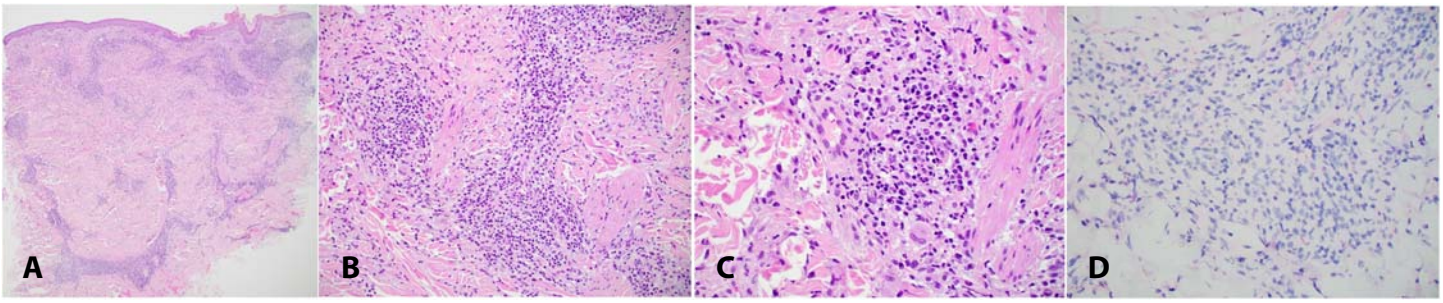

Figure 2. *Leukocytoclastic vasculitis with treponemal infection.* ***A)*** *Heavy perivascular and scattered interstitial dermal infiltrate with unremarkable epidermis. H&E, 20×.* ***B)*** *Inflammatory infiltrate composed of plasma cells, lymphocytes, and scattered neutrophils. H&E, 200×.* ***C)*** *Neutrophilic infiltrate around the vessels with karyorrhexis (nuclear dust). The capillary endothelial cells are edematous. H&E, 400×.* ***D)*** *Treponema pallidum immunostain highlighted scattered epidermal and dermal organisms, 400×.*

and vertex scalp (**Figure 1B**). Punch biopsies from the left and right upper back revealed heavy perivascular and interstitial lymphoplasmacytic infiltrate with scattered neutrophils and rare eosinophils (**Figure 2A, B**). Capillary endothelial cell swelling and sparse perivascular neutrophilic nuclear dust were noted (**Figure 2C**). The epidermis was uninvolved. The spirochete stain highlighted scattered epidermal and dermal organisms (**Figure 2D**). A diagnosis of secondary syphilis was favored. Serum venereal disease research laboratory (VDRL) test was reactive with high titer (1:512), and fluorescent treponemal antibody absorption test (FTA-ABS) was reactive at 3+ confirming the diagnosis. The patient symptoms continued to progress and he developed blurred vision in the left eye. Serum venereal disease research laboratory and FTA-ABS of the cerebrospinal fluid were reactive. The patient was treated by daily intravenous penicillin infusion of 2.4 million units for two weeks. Within one month of treatment the patient reported improvement in his vision and rash resolved from legs and trunk. Six-month follow-up showed stable renal function and complete resolution of the cutaneous eruption.

Case Discussion

The typical cutaneous manifestations of secondary syphilis are localized or generalized well-defined, erythematous to brown colored macules followed by a generalized, non-pruritic papulosquamous eruption involving the trunk and extremities, including the palmar and plantar surfaces. Other well recognized but less common cutaneous manifestations include syphilitic "moth-eaten" alopecia and condyloma lata [16]. However, secondary syphilis can present with a broad spectrum of atypical clinical manifestations that may mimic other dermatoses. Atypical presentations of secondary syphilis include lues maligna and a variety of nodular, ulcerative, annular, pustular, corymbose, and granulomatous lesions. These may be particularly impressive in immunocompromised patients, such as the elderly and those with concurrent HIV infection [16-18]. The atypical manifestations can render the diagnosis of syphilis challenging even for experienced dermatologists, especially in the absence of exposure history or a history of a primary lesion (chancre).

Leukocytoclastic vasculitis is known to be associated with a variety of infectious processes. Streptococcal infection is the most commonly implicated infection, followed by miscellaneous viral infections, *Mycobacterium tuberculosis*, and malaria [19,20]. However, LCV association with syphilis is extremely rare, with five cases reported in the literature (**Table 1**). One case was associated with congenital syphilis [11], another with primary syphilis [14], and three with secondary syphilis [12,13,15]. All patients were males ranging from 45 days to 74 years old. Three cases showed the typical palpable purpuric eruption of LCV and two cases were associated with HIV infection [11-15].

In our patient, besides the atypical cutaneous manifestation, the renal function and biopsy findings were also unusual for syphilis which made the case more challenging. Nephrotic disease with

Table 1. *Reported cases of leukocytoclastic vasculitis associated with syphilitic infection.*

Study	Age	Sex	Type/ Stage	Clinical picture	HIV status
Çam et al [11]	45 days	M	Congenital syphilis	Generalized palpable purpura and hemorrhagic vesicles involving palms and soles	Negative
Chao et al [12]	74 years	M	Secondary syphilis	Large ulcer on the right dorsum foot and palpable purpura over both chins	Negative
Furlan et al [13]	37 years	M	Secondary syphilis	Syphilitic roseola and bilateral panuveitis	Positive
Kim et al [14]	46 years	M	Primary syphilis	Multiple painless erythematous eroded papules on the glans penis	Negative
Li et al [15]	22 years	M	Secondary syphilis	Palpable purpura and petechiae on legs and feet. Nodules and ulcers with eschars on face, trunk, and arms	Positive

membranous nephropathy±mesangial hypercellularity is the most common presentation of congenital and acquired syphilis [21]. IgA-dominant infection-related glomerulonephritis, seen in our case, is uncommon [22]. The typical presentation of LCV (palpable purpura) together with the hematuria and acute renal impairment pointed towards IgA vasculitis, granulomatosis with polyangiitis, or infections known to be associated with LCV. Therefore, serologic tests for syphilis were not initially ordered, which led to delayed diagnosis.

Conclusion

In recent years, the incidence of syphilis has been increasing in the United States [2] and it is important to keep this diagnosis in mind during the work up of LCV cases to make an early diagnosis and start proper treatment.

Potential conflicts of interest

The authors declare no conflicts of interest.

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