

Small-vessel vasculitis: A review and case report

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Small-vessel vasculitis is responsible for a wide variety of diseases that affect vascular structures such as venules, capillaries, arteries, and arterioles with classic inflammation. The inflammation, in turn, can damage the affected organ, which can lead to a wide variety of signs and symptoms. The most commonly affected organ is the skin. There are many causes of vasculitis, and in recent years, diagnosis has substantially progressed due to the discovery of more pertinent labs, as well as the use of biopsy techniques. This review of small-vessel vasculitis will also present a case in the lower extremity with biopsy and treatment.

Keywords Vasculitis, ulcer, small-vessel vasculitis, cutaneous vasculitis, purpura, leg ulcer

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The first historical accounts of vasculitis are of small-vessel vasculitis, especially forms associated with purpura [1]. The Latin term vasculitis may have derived from the Greek *porphyra*, describing the color produced by a mollusk (purpura lapillus) [1]. Small-vessel vasculitis accounts for a wide range of diseases that affect venules, capillaries, arteries, and arterioles with classic inflammation. It is important to note that small-vessel vasculitis may affect arteries, and thus the vascular distribution overlaps with that of the medium-sized-vessel and large-vessel vasculitides [2]. Excess leukocytes within the vessels lead to a loss of structural integrity and possible destruction [3]. Clinical presentation may vary widely, depending on the organs affected. Generally, the only organ involved is the skin, but it is possible for systemic involvement to occur also. Skin lesions may represent the initial sign of a systemic vasculitis [4]. Cutaneous small-vessel vasculitis is characterized by a spectrum of cutaneous lesions, but palpable purpura is most common [4].

The etiology of small-vessel vasculitis is unknown in many cases but may be due to primary diseases such as microscopic polyarteritis and connective tissue disorders. Lotti, et al., reported that systemic lupus erythematosus, Sjogren's syndrome, rheumatoid arthritis, and Behcet's disease are some common primary causes. Secondary causes to an underlying disorder, such as drug reaction, post viral syndromes, infection (bacterial, fungal, protozoan, or helminths), or malignancy, were also reported [1,3]. In addition, patients with hyperglobulinemic states and cryoglobulinemia may have small-vessel vasculitis and, occasionally, it is associated with bowel bypass syndrome, ulcerative colitis, cystic fibrosis, primary biliary cirrhosis, and HIV [4]. Still, as in all forms of vasculitis, most cases of small-vessel vasculitis are idiopathic (45-54%), due to medications (10-45%), or infections (10-36%) [1]. Drug-induced vasculitis usually develops within 7 to 21 days after treatment begins [1].

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Medications most commonly associated with small vessel vasculitis are insulin, penicillins, aminopenicillins, sulfonamides, allopurinol, retinoids, quinolones, hydantoin, propylthiouracil, pyrazolones, and diuretics. Foods, such as gluten and milk proteins, and chemicals such as insecticides, should also be considered as a cause. Lotti, et al., states that small-vessel vasculitis occurs equally in both sexes and at all ages, and approximately 10% of affected patients are children. It is important as a clinician to think outside the box in diagnosing.

Cutaneous vasculitis may present as purpura, erythema, urticaria, nodule, bullae, or skin infarction leading to ulceration [5]. In the beginning stages, all patients have purpura, but the lesions might not be palpable. According to Gamarra, et al., as the process continues, the lesions, which range in size from pinpoint to several centimeters, may become papulonodular, vesicular, bulbous, pustular, or ulcerated as superficial infarctions occur. Occasionally, subcutaneous edema in the area of the vascular lesions can be observed [1]. Lesions occur in stages and while they may appear in other areas, they predominantly appear in the legs and ankles [1]. Lesions may be mildly pruritic or painful and subside within 3 or 4 weeks, leaving residual hyperpigmentation or atrophic scars [1,4]. Patients may describe “flu-like” symptoms, such as fever, malaise, arthralgias, and myalgias, although presentation can vary greatly. Although most cases of vasculitis are self-limiting, 10% of patient are likely to have recurrence of symptoms with new crops of lesions appearing for months or years [1,2,4].

Since cutaneous ulceration is usually caused by small-sized to medium-vessel vasculitis, it is important to obtain a complete list of differential diagnoses for your patient and take a thorough history and clinical exam. Further studies must be performed to diagnose your patient appropriately. Laboratory testing consisting of serum creatinine, liver function test, urinalysis, complete blood count, antibody testing [including antinuclear antibody (ANA) and antineutrophil cytoplasmic antibody (ANCA)], hepatitis B and C serologies, immunoglobulins, as well as radiographs, are helpful in achieving a diagnosis. The current gold standard for diagnosis of vasculitis is biopsy of the affected vessel.



Figure 1 Initial presentation of patient with extremely sensitive, painful lesions of his bilateral lower extremities outstanding for the duration of 4 weeks.



Figure 2 The lesions of his lower extremities were ulcerated with purulent drainage.



Figure 3 Palpable purpura with several non-blanchable, pinpoint, erythematous lesions of the bilateral upper and lower extremities, as well as the abdominal region.

The histopathologic examination of the biopsy will reveal angiocentric segmental inflammation, fibrinoid necrosis, and a neutrophilic infiltrate around the blood vessel walls with erythrocyte extravasations. A positive biopsy supports the diagnosis, while a negative one does not necessarily exclude it [1].

Case Report

A 41-year-old male with an unremarkable past medical history presented to clinic for extremely sensitive, painful lesions of his bilateral lower extremities for 4 weeks (Figure 1). The patient was not currently on any medications, nor were there any noticeable changes to his daily routine.

Physical examination revealed palpable purpura with several non-blanchable, pinpoint, erythematous lesions of the bilateral upper and lower extremities, as well as the abdominal region (Figures 2, 3).



Figure 4 Lower extremity lesions, hemorrhagic vesicles of varying sizes, as well as pustular lesions with various stages of ulceration were present ranging in a plethora of sizes from 0.5 cm to as large as 2.0 cm with areas of necrosis present.

Among the lower extremity lesions were hemorrhagic vesicles of varying sizes, as well as pustular lesions, with various stages of ulceration present ranging from 0.5 cm to as large as 2.0 cm with areas of necrosis (Figure 4).

The patient had initially seen his primary care doctor and the lesions were locally treated with mupirocin 2% ointment and dry sterile dressings. At follow-up, only mild improvement was noted and extensive laboratory work was ordered by the primary care physician. The many tests ordered include; a liver function test, hepatitis panel, rheumatoid factor, antinuclear antibody, and complete blood count with differentials, and the patient was referred to our clinic with the results. In our clinic, radiographs were performed, which were negative for any significant related pathology, and the lab work was reviewed and noted to be unremarkable.

A 3-mm punch biopsy was performed on a non-ulcerative lesion and sent for pathology. Local wound care was continued. The biopsy results revealed “small and medium-sized vessel vasculitis” with sections demonstrating a mixed inflammatory infiltrate with a predominance of neutrophils centered within the deep reticular dermis. Small muscular vessels exhibit neutrophils within their walls in concert with fibrin extravasation. The etiology of his condition was unknown, and the patient was started on oral prednisone 50 mg, twice daily, and tapered accordingly. The patient continued to have local wound care performed and his signs and symptoms greatly improved at each follow-up appointment.

Results

When possible, identification and removal of the causative agent are an effective approach to treatment [4]. This is occasionally followed by rapid clearance of the skin lesions, and no other treatment is necessary [4]. In many patients, small-vessel vasculitis will have a relatively benign, self-limited course, especially if the disease is limited to the skin; however, for the patients with aggressive disease, it is imperative to begin the appropriate treatment quickly [2]. Topical therapy, such as antibiotic ointments and corticosteroid creams, as well as routine debridement and local wound care may prove helpful to the patient. If localized edema is present, gradient support stockings can help with symptoms as well. Systemic treatment can include, but not limited to, systemic corticosteroids, non-steroidal anti-inflammatory medications, colchicines, dapsone, potassium iodide, antihistamines, fibrinolytic agents, aminocaproic acid, immunosuppressive agents, and monoclonal antibodies [4]. In our case, systemic corticosteroids were chosen due to the significant cutaneous ulcerations. Rebound is a serious problem with rapid reduction of the medication dose; therefore, if this therapy is selected, the authors recommend a gradual taper over 3 to 6 weeks [4].

Discussion

Small-vessel vasculitis can present itself in a variety of ways. It is important to obtain a thorough medical history and physical examination, as well as obtain a list of any pre-existing and new medications the patient may have started. Obtaining a thorough family history may help in diagnosing connective tissue disorders that the patient himself may not have been diagnosed with yet. Extensive laboratory testing is an essential key to diagnosing small-vessel vasculitis in addition to a biopsy, which is the gold standard. Biopsies should be performed within 24-48 hours after the appearance of a vasculitic lesion to prevent the pathological characteristics of vasculitis from being lost [3]. Once biopsy results are reviewed, appropriate therapy should be started. Therapeutic approach requires elimination of the cause (drugs, chemicals, infections, food allergens) when possible and in patients where the etiology is unknown, local and systemic therapy is recommended [4]. The goal should be neither to over-treat a mild disease nor to under-treat a severe disease [2].

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