acta medica

INVITED REVIEWS

Single organ vasculitis: Description based on Chapel Hill Conference Consensus 2012 and a case report

Gizem Sevik[1], Haner Direskeneli[1]

[1] Marmara University, Department of Internal Medicine, Division of Rheumatology, İstanbul, Türkiye.

Corresponding Author: Haner Direskeneli • E-mail: hanerdireskeneli@gmail.com
This manuscript was peer-reviewed by Prof. Dr. Cemal Bes

Definition

The term systemic vasculitis denotes the inflammation of blood vessels involving multiple territories or organs. Less often, vascular inflammation is restricted to a single organ, in which lesions may be focal or diffuse.

Single-organ vasculitis (SOV) is defined as vasculitis in arteries or veins of any size in a single organ that has no features that indicate that it is a limited expression of systemic vasculitis. Vasculitis distribution may be unifocal or multifocal (diffuse) within an organ. If the features of vasculitis are confined to one organ indicating that it is a limited presentation of systemic vasculitis, then it should be considered a limited presentation of that vasculitis, rather than SOV [1].

Clinical Features

a. Single-organ vasculitis with diffuse involvement

Diffuse SOV has been reported to affect the skin, central nervous system (CNS), kidneys, and coronary and pulmonary vessels. Diffuse SOV cannot be surgically treated and requires immunosuppressive treatment. Therefore, diffuse forms of SOV have higher relapse rates and a less favorable prognosis than focal SOV.

Primary CNS vasculitis (PCNSV) is one of the most recognized forms of SOV which can affect patients of any age. The symptoms are generally nonspecific, the patients may present with headache, stroke, or cognitive disorders [2]. It is important to rule out the conditions that may mimic PCNSV, including infections (e.g. tuberculosis, varicella-zoster virus), atherosclerosis, reversible cerebral vasoconstriction syndrome, and systemic rheumatological diseases. The diagnosis may be difficult because of the absence of a serological biomarker, the high false-negative rate of brain biopsy, and the angiographic findings that can be observed in other diseases. A complete analysis of cerebrospinal fluid should be done to rule out certain infections. Magnetic resonance imaging is useful in distinguishing PCNSV from reversible cerebral vasoconstriction syndrome [3].

Peripheral nervous system vasculitis, or *non-systemic vasculitic neuropathy (NSVN),* is usually presented clinically as distal axonal asymmetric progressive neuropathy, predominantly affecting the lower limbs. The Peripheral Nerve Society has published guidelines for the classification and treatment of NSVN. Although the sensitivity of the sural nerve and superficial peroneal nerve biopsies is low, it is emphasized that histopathological confirmation is important for diagnosis [4]. Also, ANCA tests should be negative and no histological evidence of vasculitis in a tissue other than nerves (with the exception of muscle involvement) should be present for the diagnosis of NSVC.

Localized vasculitis restricted to calf muscles is usually due to a local non-granulomatous vasculitis with necrosis and leukocytoclasis. The characteristic presenting symptoms are muscle pain, tenderness,

and swelling usually affecting a single calf muscle. Musculoskeletal and constitutional symptoms may also present in up to half of the patients. Concomitant skin lesions like purpura are also reported and this should be considered as a form of systemic vasculitis [5,6].The differential diagnosis includes popliteal cysts, deep vein thrombosis, and myositis.

Renal-limited vasculitis can occur without evidence of systemic disease. Weidner et al. compared the patients with renal-limited vasculitis with ANCA-associated vasculitis (AAV) with renal involvement. They reported that end-stage renal disease (ESRD) only occurred in 1 of 20 patients with renal-limited vasculitis, whereas nearly 30% of AAV patients progressed to ESRD. Despite the limited number of patients, the prognosis of renal-limited vasculitis seems better than AAV with renal involvement [7].

Isolated coronary or pulmonary arteritis is rare and is usually found incidentally after surgery or autopsy examination. Pulmonary artery SOV is also called isolated pulmonary Takayasu arteritis and imaging studies show an occlusive or stenotic pulmonary lesion in the majority of patients with the presence of high acute-phase reactants. It is reported that although some patients have a good outcome after surgery, there is a high risk for pulmonary hypertension postoperatively. A careful follow-up of these patients is mandatory because of the risk of vasculitis that can be seen in other vessels.

b. Focal single-organ vasculitis

Focal SOV may involve the breasts, genitourinary and gastrointestinal structures and is generally incidentally diagnosed after biopsy or surgical resection with the suspicion of cancer, infection or other abnormalities. Focal SOV has a very low risk of progression to systemic vasculitis. Most patients with focal forms of SOV can be cured after surgical resection of the affected tissue

Vasculitis of the breast is a rare condition that is characterized by non-granulomatous medium-sized vessel vasculitis which can occur bilaterally [8]. Granulomatosis with polyangiitis is the most common systemic vasculitis that presents with breast involvement [9]. The systemic vasculitides with breast involvement are generally present with constitutional symptoms, anemia and higher acute phase reactants, which are not present in the localized form [8]. It is also very important to rule out malignancy in a suspected case of vasculitis of the breast.

Vasculitis of urogenital structures is a rare condition that is reported at very low rates in gynecological and testicular surgeries [10,11]. In gynecological organ vasculitis, mostly small and medium-sized vessels are affected with a non-granulomatous vasculitis in contrast to systemic vasculitis with gynecological organ involvement, in which the most common histological finding is arteritis with giant cells. The most common symptoms are vaginal bleeding, pelvic pain, asymptomatic abdominal masses and uterine prolapse. In a review of 163 cases with gynecological organ vasculitis, it was reported that constitutional symptoms, anemia and high ESR are more common in systemic vasculitis when compared to SOV.

Testicular vasculitis typically presents with painful testicular and epididymal masses or swelling, and less commonly as a painless testicular or epididymal mass, which is unilateral in 80% of the cases. A non-granulomatous inflammation in medium-sized vessels is most commonly seen and coexistent malignancy is reported in some cases [11]. It was reported that the patients with systemic vasculitis and testicular involvement had more constitutional and musculoskeletal symptoms, anemia, and higher acute phase reactants when compared to isolated testicular vasculitis [11]. Polyarteritis nodosa is the most common systemic vasculitis with testicular involvement. Testicular involvement may also be seen in IgA vasculitis, Behçet's disease, Hepatitis-associated vasculitis, and ANCA-associated vasculitis, so a patient presenting with testicular vasculitis must be carefully investigated for these diseases.

Vasculitis of the gastrointestinal tract is extremely rare and it is often an incidental pathological finding of a biopsy of an abdominal mass or it may present as unexplained abdominal pain/ gastrointestinal bleeding [12]. Esophagus, stomach, small or large bowel, peritoneum, appendix, gallbladder, and pancreas can be affected. In a case series, 18 patients with vasculitis of the gastrointestinal tract were evaluated and the most common symptom was abdominal pain. The development of systemic vasculitis is most commonly seen in the first 5 months after the diagnosis [13]. In this regard,

because the vasculitis of the gastrointestinal tract may be the initial manifestation of systemic vasculitis, a complete evaluation of the patients for the presence of systemic vasculitis is required. The isolated vasculitis of the appendix and gallbladder can be cured after surgical excision and therefore has a good prognosis [14,15].

Diagnosis

Focal SOV is generally diagnosed incidentally and is a result of a biopsy or surgical resection done with the suspicion of cancer, infection or other abnormalities. Systemic vasculitis may affect all the regions in which SOV has been found to occur and isolated SOV may sometimes progress to systemic vasculitis. The diagnosis of SOV is less certain than any kind of systemic vasculitis given the uncertainty regarding future changes in disease patterns, therefore it is a 'working diagnosis' and may change to a systemic vasculitis in the follow-up.

A detailed questioning of symptoms and signs regarding systemic vasculitides and a careful physical examination should be done on all patients. According to the involved organ, multiple laboratory or imaging tests may be required to rule out infections, underlying malignancies and systemic vasculitis. A diagnosis of SOV can be done when there is no feature indicating systemic vasculitis and the other possible etiologies are excluded.

CASE PRESENTATION

A 32-year-old male presented with malaise, fever, swelling, and pain in the right scrotum in 2015. Ciprofloxacin was prescribed for a preliminary diagnosis of orchitis. Recurrent scrotal swelling and pain complaints without fever continued for four months and intermittent antibiotic therapy was prescribed. Scrotal Doppler ultrasonography was performed due to refractory symptoms. Oedema and increased thickness of the cutaneous and subcutaneous layers in the right scrotum, increased diameter of the right spermatic cord, and oedema in the wall, together with increased vascularity, inflamed, oedematous adipose tissue areas surrounding the vascular structures in the epididymis were detected. Right inguinal orchiectomy was performed with the preliminary diagnosis of chronic epididymo-orchitis. In pathological examination, necrotizing vasculitis in medium and small vessels, eosinophile-rich perivascular inflammation, and patchy involvement in adipose tissue, spermatic cord and testicular parenchyma adjacent to the epididymis were detected. He was referred to our rheumatology clinic for treatment and follow-up with the diagnosis of vasculitis.

The patient's past medical history did not reveal any chronic disease or use of regular medications. He had been smoking for five years. He did not have any systemic or organ-specific complaints other than fatigue and inflammatory arthralgia in the wrist, ankle, and knees for a month. Initial vital signs were fully normal. There was no abnormality in his physical examination. There was no abnormal result in laboratory results except for erythrocyte sedimentation rate (76 mm/hr) and CRP (55 mg/L) elevation. Anti-nuclear antibody, antibodies to extractable nuclear antigens, rheumatoid factor, antineutrophil cytoplasmic antibodies, viral serology, QuantiFERON-TB test and pathergy test were negative. Echocardiographic and electromyographic findings were normal. Computed tomography did not reveal any pathological image except a 4 mm nodule in the lung.

Although there were no signs of systemic vasculitis and the patient was diagnosed with isolated testicular vasculitis, because of the past musculoskeletal complaints and persistently elevated acute phase reactants, methylprednisolone 32 mg per oral daily and azathioprine 100 mg per oral daily treatments were initiated. Methylprednisolone was tapered and discontinued and azathioprine treatment was continued due to the absence of symptoms and normal acute phase reactants in the 6th month of treatment. Azathioprine dose was reduced to 50 mg after 5 years without a relapse, and the patient had no complaints and had normal acute phase reactants at the last visit.

Key messages

- Single-organ vasculitis (SOV) is vasculitis in an organ without the features of systemic vasculitis.
- Surgical excision is usually curative for focal SOV and it has a good prognosis.
- Diffuse SOV has a higher relapse rate and a less favorable prognosis than focal SOV.

– Immunosuppressive (IS) treatment is generally required for diffuse SOV, whereas only some cases of focal SOV may need according to the risk of relapse and damage in the involved organ.

REFERENCES

[1] Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 2013;65(1):1-11.

[2] Hajj-Ali RA, Singhal AB, Benseler S, Molloy E, Calabrese LH. Primary angiitis of the CNS. Lancet Neurol. 2011;10(6):561-72.

[3] Chen SP, Fuh JL, Wang SJ, Chang FC, Lirng JF, Fang YC, et al. Magnetic resonance angiography in reversible cerebral vasoconstriction syndromes. Ann Neurol. 2010;67(5):648-56.

[4] Collins MP, Dyck PJ, Gronseth GS, Guillevin L, Hadden RD, Heuss D, et al. Peripheral Nerve Society Guideline on the classification, diagnosis, investigation, and immunosuppressive therapy of non-systemic vasculitic neuropathy: executive summary. J Peripher Nerv Syst. 2010;15(3):176-84.

[5] Kamimura T, Hatakeyama M, Torigoe K, Nara H, Kaneko N, Satou H, et al. Muscular polyarteritis nodosa as a cause of fever of undetermined origin: a case report and review of the literature. Rheumatol Int. 2005;25(5):394-7.

[6] Khellaf M, Hamidou M, Pagnoux C, Michel M, Brisseau JM, Chevallier X, et al. Vasculitis restricted to the lower limbs: a clinical and histopathological study. Ann Rheum Dis. 2007;66(4):554-6.

[7] Weidner S, Geuss S, Hafezi-Rachti S, Wonka A, Rupprecht HD. ANCA-associated vasculitis with renal involvement: an outcome analysis. Nephrol Dial Transplant. 2004;19(6):1403-11.

[8] Hernández-Rodríguez J, Tan CD, Molloy ES, Khasnis A, Rodríguez ER, Hoffman GS. Vasculitis involving the breast: a clinical and histopathologic analysis of 34 patients. Medicine (Baltimore). 2008;87(2):61-9.

[9] Allende DS, Booth CN. Wegener's granulomatosis of the breast: a rare entity with daily clinical relevance. Ann Diagn Pathol. 2009;13(5):351-7.

[10] Hernández-Rodríguez J, Tan CD, Rodríguez ER, Hoffman GS. Gynecologic vasculitis: an analysis of 163 patients. Medicine (Baltimore). 2009;88(3):169-81.

[11] Hernández-Rodríguez J, Tan CD, Koening CL, Khasnis A, Rodríguez ER, Hoffman GS. Testicular vasculitis: findings differentiating isolated disease from systemic disease in 72 patients. Medicine (Baltimore). 2012;91(2):75-85.

[12] Gonzalez-Gay MA, Vazquez-Rodriguez TR, Miranda-Filloy JA, Pazos-Ferro A, Garcia-Rodeja E. Localized vasculitis of the gastrointestinal tract: a case report and literature review. Clin Exp Rheumatol. 2008;26(3 Suppl 49):S101-4.

[13] Salvarani C, Calamia KT, Crowson CS, Miller DV, Broadwell AW, Hunder GG, et al. Localized vasculitis of the gastrointestinal tract: a case series. Rheumatology (Oxford). 2010;49(7):1326-35.

[14] Hernández-Rodríguez J, Tan CD, Rodríguez ER, Hoffman GS. Single-organ gallbladder vasculitis: characterization and distinction from systemic vasculitis involving the gallbladder. An analysis of 61 patients. Medicine (Baltimore). 2014;93(24):405-13.

[15] Hernández-Rodríguez J, Hoffman GS. Updating single-organ vasculitis. Curr Opin Rheumatol. 2012;24(1):38-45.

