



# Known infectious causes of vasculitis in man

STANLEY J. NAIDES, MD

**A**n array of pathogens is known to cause vasculitis in man.<sup>1,2</sup> For several of these agents, vasculitis is the major manifestation of disease. The majority, however, typically present as infectious processes in which vasculitis is an occasional manifestation of disease. For many, vasculitis may be a component of disease pathogenesis but is not a prominent feature of the clinical presentation. The various agents—viruses, bacteria, and fungi—share a common target, blood vessels. The involvement of vessels may be direct, with vascular structures serving as targets. Many infectious pathogens have tissue tropism that includes endothelium. Other agents may bind to the vessel wall because the vascular endothelium expresses specific receptors for the pathogen or another moiety with which the pathogen travels. Even when the agent does not enter the endothelial cell, the immune response to the agent may be focused at the vessel wall because the pathogen is adherent to the endothelial cell surface, thereby promoting innocent by-stander injury to the vessel. Processes that target the endothelium directly are usually acute in nature. Innocent bystander injury is often chronic and may be insidious in onset.

Demonstration of infectious agents as the cause of some cases of vasculitis fuels interest in searching for infectious etiologies of idiopathic vasculitis. The advent of highly sensitive molecular techniques has encouraged searches for various known pathogens in idiopathic vasculitis. Recognition that infectious agents are dynamic populations of organisms prompts us to search for emerging pathogens as previously unknown causes of vasculitis. Such pathogens “emerge” as new species or strains develop from older species in their traditional host population. Others may emerge due to spread into a new host population. The new, previously non-susceptible population may become infected because the pathogen adapts to the new host species. Alternatively, the agent may spread to a new susceptible host population as a consequence of changes in the physical environment or human or vector behavior that promotes geographical spread. In mirror fashion, changes in the behavior of pathogens, vectors, and hosts,

and our ability to intervene in disease processes, have rendered some causes of vasculitis far less common.

## ■ VIRAL CAUSES OF VASCULITIS

Our knowledge of viral pathogenesis has exploded in the last quarter of the twentieth century, accelerated in large part by epidemics of “emerging” viral diseases. Hepatitis C virus, discovered in 1989, has worldwide prevalence.<sup>3</sup> The 10- to 20-year latent period before hepatic or rheumatic manifestations of disease explains the increasing number of cases of hepatitis C virus-mediated vasculitis currently being seen in the United States following the epidemic of new infections in the 1980s.<sup>4</sup> Prior to the discovery and characterization of hepatitis C virus in the late 1980s, the triad of arthritis, palpable purpura, and type II cryoglobulinemia was given the sobriquet “essential mixed cryoglobulinemia” and considered an idiopathic vasculitis. Availability of diagnostic testing for hepatitis C virus demonstrated that almost all of these cases were associated with hepatitis C virus infection. Immune response to the virus elicits a response to the Fc portion of immunoglobulin with the majority of elicited antibody having the Wa idiotype.<sup>5,6</sup> Immune complexes of anti-Fc Wa idiotype antibody and pre-existing antibody, and virus have the peculiar physical property of precipitating out of solution in the cold (“cryoglobulins”). Presumably, Wa idiotype recognizes a cross-reactive epitope found on hepatitis C virus and immunoglobulin. Extremities and skin are sufficiently cold so as to explain a predilection for small-vessel leukocytoclastic vasculitis of the skin; gravity enhances vascular injury in dependent distal vessels, giving rise to palpable purpura predominantly in the lower extremities. More severe cases may manifest visceral organ involvement including membranoproliferative glomerulonephritis and bowel involvement. Small- and medium-sized arteries may be involved as well, especially in the kidneys.

Hepatitis B virus (HBV) infection provides the classic example of virally mediated immune complex disease. A lymphocytic venulitis or neutrophilic vasculitis of small vessels with leukocytoclastic or fibrinoid changes presents typically as an “urticaria-arthritis syndrome.”<sup>7</sup> Immune complexes of hepatitis B virus surface antigen (HBsAg) and antibodies to hepatitis B virus surface antigen (HBsAb) circulate in the blood and are found deposited in vessels in association with complement.<sup>8,9</sup> The long latency period of HBV allows time for an immune response to occur. Viral replication increases HBsAg load, and is tem-

From the Division of Rheumatology, Penn State Milton S. Hershey Medical Center, Hershey, PA.

Address correspondence to S.J.N., Thomas B. Hallowell Professor of Medicine, Professor of Microbiology and Immunology, Professor of Pharmacology, and Chief, Division of Rheumatology, Penn State Milton S. Hershey Medical Center, Hershey, PA 17033.  
E-mail: snaides@psu.edu.

porally associated with jaundice.<sup>10</sup> The immune complexes eventually no longer form in antigen excess, and the serum sickness-like illness resolves. HBV has also been associated with large-vessel polyarteritis nodosa-like illness.<sup>11</sup> Onset is early in the course of chronic HBV hepatitis. Immune complexes containing HBsAg, HBsAb, and complement are found in the vessel wall.<sup>12</sup> The determinants of small vessel versus larger vessel disease in the two syndromes of HBV infection are unknown.

Human immunodeficiency virus (HIV) patients may present with a variety of vasculitides. However, it is difficult to specifically attribute the various vasculitides seen to HIV because of frequent co-infections with other agents that may cause vasculitis in the absence of HIV infection. Human T lymphotropic virus 1 infection may cause retinal, cutaneous, or central nervous system vasculitis.<sup>13-16</sup>

The herpesviruses (cytomegalovirus, varicella-zoster, herpes simplex viruses 1 and 2, and herpes hominis) may be associated with retinal vasculitis in immunocompromised patients.<sup>17-23</sup> Varicella-zoster may also cause a diffuse central nervous system small arterial granulomatous vasculitis, or a small- and/or large-artery vasculopathy.<sup>24-27</sup> Herpes simplex viruses 1 and 2 have been associated with cutaneous vasculitis and necrotizing arteritis of small and medium vessels.<sup>28-30</sup> Epstein-Barr virus has been suggested as a cause of both small- and large-vessel disease in a number of cases and short series.<sup>31-36</sup> However, the ability to demonstrate causality in many instances is made all the more difficult by the latency of herpesvirus infection.

Parvovirus B19 has been suggested as the causative agent of Wegener's granulomatosis and polyarteritis nodosa in a number of cases and short series.<sup>37-42</sup> However, the issue of latency and the failure to eliminate B19 from pooled blood products provides a cautionary note when considering causality.<sup>43-46</sup> Rare cases of vasculitis have similarly been reported following rubella virus, adenovirus, echovirus, coxsackievirus, parainfluenza virus, herpes simplex viruses, and hepatitis A virus infections.<sup>1,47-57</sup>

## ■ BACTERIAL CAUSES OF VASCULITIS

Bacterial seeding of vessels may lead to necrosis through direct bacterial action. Vessels may be seeded intraluminally at sites of endothelial injury or flow turbulence. Seeding of vasa vasora may cause destruction of vessels from the outside in. An injury of a large vessel by this mechanism is classically termed a "mycotic aneurysm." Contiguous spread from an infected site to a vessel may occur. Vessels may also be seeded from within the lumen, as in subacute bacterial endocarditis in which septic emboli embed within the wall of smaller vessels, causing a "mycotic" process via a luminal route. Immune response to bacteria or to bacterial components may also lead to vasculitis, usually by immune-complex-mediated mechanisms.<sup>2</sup>

In subacute bacterial endocarditis, direct spread via septic emboli and immune complex injury may occur. Patients may present with evidence of elevated acute-phase reactants, fever, malaise, myalgia, arthralgia, Osler's nodes, Janeway lesions, and septic infarcts.<sup>58,59</sup>

Staphylococcus and streptococcus infections are common causes. Gram-negative organisms, other gram-positive cocci, fungi, and parasites may be causative as well, and their occurrence depends on the clinical setting.<sup>60-66</sup> Mycotic aneurysms resulting from septic emboli are common with staphylococcus, streptococcus, and *Salmonella* species.<sup>67-69</sup> Patients with subacute infections may develop cryoglobulins.<sup>70-72</sup> Bacteremia may present as leukocytoclastic vasculitis.<sup>73,74</sup> Small-vessel vasculitis may be associated with post-streptococcal infection, distinct from endocarditis.<sup>75,76</sup> The *Rickettsiae* are a group of obligate intracellular bacteria with tropism for vascular endothelium.<sup>77</sup> Infection results in widespread microvascular leak, local thrombosis, and ultimately multisystem failure if untreated.<sup>78,79</sup>

In the lung, necrosis of vessels may occur from septic emboli or from contiguous spread in primary pneumonias. In the latter setting, *Pseudomonas aeruginosa* and *Legionella pneumophila* often cause direct necrosis via contiguous spread.<sup>80</sup> The presentation, however, is that of pneumonia. Mycobacterial or fungal pulmonary infections may mimic Wegener's granulomatosis or Churg-Strauss vasculitis in eliciting a granulomatous reaction in vessels.<sup>81</sup> Spread of *Mycobacterium tuberculosis* to the aorta may be seen as a cause of tuberculous aortitis, coronary arteritis, and mycotic aneurysm.<sup>82-84</sup> *Aspergillus aeruginosa*, *Aspergillus fumigatus*, and *Mucor* may be characterized by direct vessel invasion and necrosis.<sup>68,85,86</sup>

*Coccidioides immitis* meningitis may be associated with vasculitis that can be confused with central nervous system angiitis.<sup>87,88</sup> *Coccidioides immitis* may also present as an immune-complex-mediated disease with erythema nodosum, periarteritis predominantly of the ankles, and bilateral lymphadenopathy.<sup>89,90</sup> This presentation is often confused with Löfgren's syndrome of sarcoidosis. While sarcoidosis as a cause of Löfgren's syndrome is more prevalent in eastern United States populations, *Coccidioides immitis* is a more likely cause of a Löfgren's-like presentation in the western United States.

*Neisseria* species may be associated with small-vessel vasculitis. In *Neisseria gonorrhea* infection, cutaneous papules vesiculate, then become necrotic.<sup>91</sup> In *N meningitidis* infections, vasculitis may manifest in the skin and gastrointestinal tract with the endothelium showing necrosis and thrombosis.<sup>92-94</sup> In immunocompromised hosts, *Pseudomonas aeruginosa* and other gram-negative organisms can present as a large 1- to 5-cm macular erythema that develops central necrosis and peripheral edema and induration—a condition termed "ecthyma gangrenosum." Vessel thrombosis results from direct bacterial invasion of the vessels. Similar lesions may be seen in immunocompromised patients with disseminated *Pseudomonas*, *Nocardia*, *Aspergillus*, *Mucor*, *Curvularia*, *Pseudallescheria*, *Fusarium*, *Morganella*, *Metarrhizium*, *Xanthomonas*, *Klebsiella*, *E coli*, and *Aeromonas* infections.<sup>95-107</sup>

Before AIDS, syphilis was the infectious agent known as the "great imposter," presenting as large- or medium-size vessel disease (aortitis or coronary arteries) or as the small-vessel rash of secondary lues. Aortic aneurysms

were insidious in clinical presentation. *Treponema pallidum* spirochetes were rarely detected in fibrosed and scarred vessels.<sup>108-110</sup> At least briefly, *Borrelia burgdorferi*, the causative agent of Lyme disease, was known as an "imposter." Vasculitic changes may be seen in the central nervous system, retina, and temporal arteries.<sup>111-124</sup>

Parasites are a rare cause of vasculitis. The local response to a parasite may include vessel changes typical of vasculitis, but these are localized to the offending

pathogen. In a few instances, however, more distant effects have been reported. *Toxocara canis* presented in an adolescent as palpable purpura with additional features suggesting Henoch-Schönlein purpura.<sup>125</sup> *Cysticercus* has caused vasculitis and arachnoiditis as it infects the central nervous system.<sup>126</sup> *Angiostrongylus* nematodes apparently caused a Wegener's granulomatosis-like pulmonary angitis.<sup>127</sup> *Loa loa*, a filarial parasite, presented with cutaneous leukocytoclastic vasculitis.<sup>128</sup>

## ■ REFERENCES

- Vassilopoulos D, Calabrese LH. Virus-associated vasculitides: clinical aspects. In: Hoffman GS, Weyand CM, editors. Inflammatory diseases of blood vessels. New York: Marcel Dekker, Inc., 2001: 565-597.
- Sneller MC. Vasculitis secondary to bacterial, fungal, and parasitic infection. In: Hoffman GS, Weyand CM, editors. Inflammatory Diseases of Blood Vessels. New York: Marcel Dekker, Inc., 2001: 599-608.
- Lavanchy D, McMahon B. Worldwide prevalence and prevention of hepatitis C. In: Liang TJ, Hoofnagle JH, editors. Hepatitis C. San Diego: Academic Press, 2000: 185-201.
- Fillet AM, Reux I, Joberty C, Fournier JG, Hauw JJ, Hoang PL, et al. Detection of human herpes virus 6 in AIDS-associated retinitis by means of in situ hybridization, polymerase chain reaction and immunohistochemistry. J Med Virol 1996; 49:289-295.
- Newkirk M, Chen PP, Carson D, Posnett D, Capra JD. Amino acid sequence of a light chain variable region of a human rheumatoid factor of the Wa idiotype group, in part predicted by its reactivity with anti-peptide antibodies. Mol Immunol 1986; 23:239-244.
- Agnello V. Mixed cryoglobulinaemia after hepatitis C virus: more and less ambiguity. Ann Rheum Dis 1998; 57:701-702.
- Agnello V, Abel G. Localization of hepatitis C virus in cutaneous vasculitic lesions in patients with type II cryoglobulinemia. Arth Rheum 1997; 40:2007-2015.
- Gocke DJ. Extrahepatic manifestations of viral hepatitis. Am J Med Sci 1975; 270:49-52.
- Neumann HA, Beretty PJ, Folmer SC, Cormane RH. Hepatitis B surface antigen deposition in the blood vessel walls of urticarial lesions in acute hepatitis B. Br J Dermatol 1981; 104:383-388.
- Hoofnagle JH DBAM. Serologic diagnosis of acute and chronic viral hepatitis. Semin Liver Dis 1991; 11:73-83.
- Makowski GS, Davis EL, Aslanzadeh J, Hopfer SM. Enhanced direct amplification of Guthrie card DNA following selective elution of PCR inhibitors. Nucleic Acids Res 1995; 23:3788-3789.
- Dienstag JL. Immunopathogenesis of the extrahepatic manifestations of hepatitis B virus infection. Springer Semin Immunopathol 1981; 3:461-472.
- Mochizuki M, Watanabe T, Yamaguchi K, Takatsuki K, Yoshimura K, Shirao M, et al. HTLV-I uveitis: a distinct clinical entity caused by HTLV-I. Jpn J Cancer Res 1992; 83:236-239.
- Mochizuki M, Tajima K, Watanabe T, Yamaguchi K. Human T lymphotropic virus type 1 uveitis. Br J Ophthalmol 1994; 78:149-154.
- Buisson GG, Vernant JC. [Neurologic pathology and HTLV-I virus]. Rev Prat 1990; 40:2124-2126.
- Sasaki K, Morooka I, Inomata H, Kashio N, Akamine T, Osame M. Retinal vasculitis in human T-lymphotropic virus type I associated myelopathy. Br J Ophthalmol 1989; 73:812-815.
- Kuo YH, Yip Y, Chen SN. Retinal vasculitis associated with chickenpox. Am J Ophthalmol 2001; 132:584-585.
- Kashiwase M, Sata T, Yamauchi Y, Minoda H, Usui N, Iwasaki T, et al. Progressive outer retinal necrosis caused by herpes simplex virus type 1 in a patient with acquired immunodeficiency syndrome. Ophthalmology 2000; 107:790-794.
- Adám E, Nász I, Lengyel A. Characterization of adenovirus hexons by their epitope composition. Arch Virol 1996; 141:1891-1907.
- Chatzoulis DM, Theodosiadis PG, Apostolopoulos MN, Drakoulis N, Markomichelakis NN. Retinal perivasculitis in an immunocompetent patient with systemic herpes simplex infection. Am J Ophthalmol 1997; 123:699-702.
- Nasir MA, Jaffe GJ. Cytomegalovirus retinitis associated with Hodgkin's disease. Retina 1996; 16:324-327.
- Margolis TP, Lowder CY, Holland GN, Spaide RF, Logan AG, Weissman SS, et al. Varicella-zoster virus retinitis in patients with the acquired immunodeficiency syndrome. Am J Ophthalmol 1991; 112:119-131.
- Savir H, Grosswasser Z, Mendelson L. Herpes virus hominis encephalomyelitis and retinal vasculitis in adults. Ann Ophthalmol 1980; 12:1369-1371.
- Fukumoto S, Kinjo M, Hokamura K, Tanaka K. Subarachnoid hemorrhage and granulomatous angiitis of the basilar artery: demonstration of the varicella-zoster-virus in the basilar artery lesions. Stroke 1986; 17:1024-1028.
- Hayman M, Henderson G, Poskitt KJ, Connolly MB. Postvaricella angiopathy: report of a case with pathologic correlation. Pediatr Neurol 2001; 24:387-389.
- Kleinschmidt-DeMasters BK, Gilden DH. Varicella-zoster virus infections of the nervous system: clinical and pathologic correlates. Arch Pathol Lab Med 2001; 125:770-780.
- Caruso JM, Tung GA, Brown WD. Central nervous system and renal vasculitis associated with primary varicella infection in a child. Pediatrics 2001; 107:E9.
- Koo EH, Massey EW. Granulomatous angiitis of the central nervous system: protean manifestations and response to treatment. J Neurol Neurosurg Psychiatry 1988; 51:1126-1133.
- Schmitt JA, Dietzmann K, Muller U, Krause P. [Granulomatous vasculitis—an uncommon manifestation of herpes simplex infection of the central nervous system]. Zentralbl Pathol 1992; 138:298-302.
- Shiozaki Y, Takeshima M, Itoshima T, Nose S, Hamaya K. [Granulomatous angiitis of the central nervous system complicated by the syndrome of inappropriate antidiuretic hormone]. No To Shinkei 1995; 47:595-599.
- Ban S, Goto Y, Kamada K, Takahama M, Watanabe H, Iwahori T, et al. Systemic granulomatous arteritis associated with Epstein-Barr virus infection. Virchows Arch 1999; 434:249-254.
- Lande MB, Mowry JA, Houghton DC, White CR Jr, Borzy MS. Immune complex disease associated with Epstein-Barr virus infectious mononucleosis. Pediatr Nephrol 1998; 12:651-653.
- Murakami K, Ohsawa M, Hu SX, Kanno H, Aozasa K, Nose M. Large-vessel arteritis associated with chronic active Epstein-Barr virus infection. Arthritis Rheum 1998; 41:369-373.
- Nakagawa A, Ito M, Iwaki T, Yatabe Y, Asai J, Hayashi K. Chronic active Epstein-Barr virus infection with giant coronary aneurysms. Am J Clin Pathol 1996; 105:733-736.
- Muso E, Fujiwara H, Yoshida H, Hosokawa R, Yashiro M, Hongo Y, et al. Epstein-Barr virus genome-positive tubulointerstitial nephritis associated with Kawasaki disease-like coronary aneurysms. Clin Nephrol 1993; 40:7-15.
- Kikuta H, Sakiyama Y, Matsumoto S, Hamada I, Yazaki M, Iwaki T, et al. Detection of Epstein-Barr virus DNA in cardiac and aortic tissues from chronic, active Epstein-Barr virus infection associated with Kawasaki disease-like coronary artery aneurysms. J Pediatr 1993; 123:90-92.
- Naides SJ. Rheumatic manifestations of parvovirus B19 infection. Rheum Dis Clin North Am 1998; 24:375-401.
- Aygoren-Pursun E, Scharrer I. A multicenter pharmacosurveillance study for the evaluation of the efficacy and safety of recombinant factor VIII in the treatment of patients with hemophilia A. German Kogenate Study Group. Thromb Haemost 1997; 78:1352-1356.
- Corman LC, Dolson DJ. Polyarteritis nodosa and parvovirus B19



- infection. *Lancet* 1992; 339:491.
40. Delannoy D, Balquet MH, Savinel P. Vasculitis with mixed cryoglobulin in a case of human parvovirus B19 infection. *Presse Med* 1993; 22:175.
  41. Finkel TH, Torok TJ, Ferguson PJ, Durigon EL, Zaki SR, Leung DYM, et al. Chronic parvovirus B19 infection and systemic necrotizing vasculitis: opportunistic infection or aetiological agent? *Lancet* 1994; 343:1255-1258.
  42. Martinelli C, Azzi A, Buffini G, Comin CE, Leoncini F. Cutaneous vasculitis due to human parvovirus B19 in an HIV-infected patient: report of a case. *AIDS* 1997; 11:1891-1893.
  43. Erdman DD, Anderson BC, Torok TJ, Finkel TH, Anderson LJ. Possible transmission of parvovirus B19 from intravenous immune globulin. *J Med Virol* 1997; 53:233-236.
  44. Prowse C, Ludlam CA, Yap PL. Human parvovirus B19 and blood products. *Vox Sang* 1997; 72:1-10.
  45. Yee TT, Cohen BJ, Pasi KJ, Lee CA. Transmission of symptomatic parvovirus B19 infection by clotting factor concentrate. *Br J Haematol* 1996; 93:457-459.
  46. Flunker G, Peters A, Wiersbitzky S, Modrow S, Seidel W. Persistent parvovirus B19 infections in immunocompromised children. *Med Microbiol Immunol* 1998; 186:189-194.
  47. Inman RD, Hodge M, Johnston ME, Wright J, Heathcote J. Arthritis, vasculitis, and cryoglobulinemia associated with relapsing hepatitis A virus infection. *Ann Intern Med* 1986; 105:700-703.
  48. Press J, Maslovitz S, Avinoach I. Cutaneous necrotizing vasculitis associated with hepatitis A virus infection. *J Rheumatol* 1997; 24:965-967.
  49. Costa MM, Lisboa M, Romeu JC, Caldeira J, De Q, V. Henoch-Schönlein purpura associated with coxsackie-virus B1 infection. *Clin Rheumatol* 1995; 14:488-490.
  50. Okano M, Thiele GM, Sakiyama Y, Matsumoto S, Purtilo DT. Adenovirus infection in patients with Kawasaki disease. *J Med Virol* 1990; 32:53-57.
  51. Embil JA, McFarlane ES, Murphy DM, Krause VW, Stewart HB. Adenovirus type 2 isolated from a patient with fatal Kawasaki disease. *Can Med Assoc J* 1985; 132:1400.
  52. Chia JK, Bold EJ. Life-threatening leukocytoclastic vasculitis with pulmonary involvement due to echovirus 7. *Clin Infect Dis* 1998; 27(5):1326-1327.
  53. Riikonen RS. Retinal vasculitis caused by rubella. *Neuropediatrics* 1995; 26:174-176.
  54. Duhaut P, Bosshard S, Calvet A, Pinede L, Demolombe-Rague S, Dumontet C, et al. Giant cell arteritis, polymyalgia rheumatica, and viral hypotheses: a multicenter, prospective case-control study. *Groupe de Recherche sur l'Arterite a Cellules Geantes. J Rheumatol* 1999; 26:361-369.
  55. Forster W, Bialasiewicz AA, Busse H. Coxsackievirus B3-associated panuveitis. *Br J Ophthalmol* 1993; 77:182-183.
  56. Corbeel L, Gewillig M, Baeten E, Casteels-Van Daele M, Eggermont E. Carotid and coronary artery involvement in infantile periarteritis nodosa possibly induced by Coxsackie B4 infection. Favourable course under corticosteroid treatment. *Eur J Pediatr* 1987; 146:441-442.
  57. Roden VJ, Cantor HE, O'Connor DM, Schmidt RR, Cherry JD. Acute hemiplegia of childhood associated with Coxsackie A9 viral infection. *J Pediatr* 1975; 86:56-58.
  58. Kodo K, Hida M, Omori S, Mori T, Tokumura M, Kuramochi S, et al. Vasculitis associated with septicemia: case report and review of the literature. *Pediatr Nephrol* 2001; 16:1089-1092.
  59. Conti T, Barnet B. The diagnostic challenge of infective endocarditis: cutaneous vasculitis leading to the diagnosis of infective endocarditis. *J Am Board Fam Pract* 2001; 14:451-456.
  60. Mylonakis E CSB. Infective endocarditis in adults. *N Engl J Med* 2001; 345(18):1318-1330.
  61. Steitz A, Orth T, Feddersen A, Fischer T, Marker-Hermann E, Husmann M. A case of endocarditis with vasculitis due to *Actinobacillus actinomycetemcomitans*: a 16S rDNA signature for distinction from related organisms. *Clin Infect Dis* 1998; 27:224-225.
  62. Cohen CA, Almeder LM, Israni A, Maslow JN. *Clostridium septicum* endocarditis complicated by aortic-ring abscess and aortitis. *Clin Infect Dis* 1998; 26:495-496.
  63. Elzouki AY, Akthar M, Mirza K. Brucella endocarditis associated with glomerulonephritis and renal vasculitis. *Pediatr Nephrol* 1996; 10:748-751.
  64. Bani-Sadr F, Hamidou M, Richard P, Tiab M, Lalande S, Grolleau JY. [Cutaneous vasculitis and acute renal failure disclosing endocarditis caused by *Actinobacillus actinomycetemcomitans*]. *Presse Med* 1993; 22:446.
  65. Gladstone JL, Friedman SA, Cerruti MM, Jomain SL. Treatment of *Candida* endocarditis and arteritis. *J Thorac Cardiovasc Surg* 1976; 71:835-838.
  66. Martinez AJ, Sotelo-Avila C, Alcalá H, Willaert E. Granulomatous encephalitis, intracranial arteritis, and mycotic aneurysm due to a free-living amoeba. *Acta Neuropathol (Berl)* 1980; 49:7-12.
  67. Vyas SK, Law NW, Loehry CA. Mycotic aneurysm of left subclavian artery. *Br Heart J* 1993; 69:455-456.
  68. Jenckes GA III. Aspergillus aortitis. *J Thorac Cardiovasc Surg* 1990; 99:375-376.
  69. Julke M, Leu HJ. [Extra-aortic aneurysms. Analysis of 163 aneurysms in 142 patients]. *Schweiz Med Wochenschr* 1985; 115:10-13.
  70. La Civita L, Fadda P, Olivieri I, Ferri C. Cryoglobulinaemic vasculitis as presenting manifestation of infective endocarditis. *Ann Rheum Dis* 2002; 61:89-90.
  71. Yerly P, Chuard C, Pugin P, Regamey C. [Cryoglobulins and endocarditis, a case report.] *Rev Med Suisse Romande* 2001; 121:573-576.
  72. Agarwal A, Clements J, Sedmak DD, Imler D, Nahman NS Jr, Orsinelli DA, et al. Subacute bacterial endocarditis masquerading as type III essential mixed cryoglobulinemia. *J Am Soc Nephrol* 1997; 8:1971-1976.
  73. Lum PN, Woo PC, Wong SS, Yuen K. Leukocytoclastic vasculitis complicating *Klebsiella pneumoniae* bacteremia. *Diagn Microbiol Infect Dis* 2000; 37:275-277.
  74. Garcia-Porrua C, Gonzalez-Gay MA. Bacterial infection presenting as cutaneous vasculitis in adults. *Clin Exp Rheumatol* 1999; 17:471-473.
  75. Houston TP. Small-vessel vasculitis following simultaneous influenza and pneumococcal vaccination. *N Y State J Med* 1983; 83:1182-1183.
  76. David J, Ansell BM, Woo P. Polyarteritis nodosa associated with streptococcus. *Arch Dis Child* 1993; 69:685-688.
  77. Walker DH, Cain BG, Olmstead PM. Laboratory diagnosis of Rocky Mountain spotted fever by immunofluorescent demonstration of Rickettsia in cutaneous lesions. *Am J Clin Pathol* 1978; 69:619-623.
  78. George F, Brouqui P, Boffa MC, Mutin M, Drancourt M, Brisson C, et al. Demonstration of *Rickettsia conorii*-induced endothelial injury in vivo by measuring circulating endothelial cells, thrombomodulin, and von Willebrand factor in patients with Mediterranean spotted fever. *Blood* 1993; 82:2109-2116.
  79. Davi G, Giammarresi C, Vigneri S, Ganci A, Ferri C, Di Francesco L, et al. Demonstration of *Rickettsia conorii*-induced coagulative and platelet activation in vivo in patients with Mediterranean spotted fever. *Thromb Haemost* 1995; 74:631-634.
  80. Reich JM. Pulmonary gangrene and the air crescent sign. *Thorax* 1993; 48:70-74.
  81. Henocq E, Hutinel B, Jacob J, Olivier C. [Immunopathologic aspects of recurrent phlebitis and nodular vasculitis. Therapeutic applications]. *Phlebologie* 1976; 29:125-132.
  82. Strnad BT, McGraw JK, Heatwole EV, Clark P. Tuberculous aneurysm of the aorta presenting with uncontrolled hypertension. *J Vasc Interv Radiol* 2001; 12:521-523.
  83. Allins AD, Wagner WH, Cossman DV, Gold RN, Hiatt JR. Tuberculous infection of the descending thoracic and abdominal aorta: case report and literature review. *Ann Vasc Surg* 1999; 13:439-444.
  84. Tuder RM, Renya GS, Bensch K. Mycobacterial coronary arteritis in a heart transplant recipient. *Hum Pathol* 1986; 17:1072-1074.
  85. Nenoff P, Kellermann S, Horn LC, Keiner S, Bootz F, Schneider S, et al. Case report. Mycotic arteritis due to *Aspergillus fumigatus* in a diabetic with retrobulbar aspergillosis and mycotic meningitis. *Mycoses* 2001; 44:407-414.
  86. Oaks TE, Pae WE, Pennock JL, Myers JL, Pierce WS. Aortic rup-

- ture caused by fungal aortitis: successful management after heart transplantation. *J Heart Transplant* 1988; 7:162-164.
87. de Carvalho CA, Allen JN, Zafran A, Yates AJ. Coccidioidal meningitis complicated by cerebral arteritis and infarction. *Hum Pathol* 1980; 11:293-296.
  88. Kobayashi RM, Coel M, Niwayama G, Trauner D. Cerebral vasculitis in coccidioidal meningitis. *Ann Neurol* 1977; 1:281-284.
  89. Whitaker DC, Lynch PJ. Erythema nodosum and coccidioidomycosis. *Ariz Med* 1979; 36:887-889.
  90. Body BA. Cutaneous manifestations of systemic mycoses. *Dermatol Clin* 1996; 14:125-135.
  91. Mastroiardo M, Loconsole F, Conte A, Rantuccio F. Cutaneous vasculitis as the sole manifestation of disseminated gonococcal infection: case report. *Genitourin Med* 1994; 70:130-131.
  92. Garcia-Patos V, Barnadas MA, Domingo P, Esquius J, De Moragas JM. [Cutaneous vasculitis during bacteremia caused by meningococcus serogroup B]. *Rev Clin Esp* 1992; 190:311-313.
  93. Dearajomartins-Romeo D, Garcia-Porrúa C, Gonzalez-Gay MA. Cutaneous vasculitis is not always benign. *Rev Rhum Engl Ed* 1999; 66:240.
  94. Seaton RA, Nathwani D, Dick J, Smith D. Acute meningococcaemia complicated by late onset gastrointestinal vasculitis. *J Infect* 2000; 41:190-191.
  95. Versapuech J, Leaute-Labreze C, Thedenat B, Taieb A, Ragnaud JM. [Ecthyma gangrenosum caused by *Pseudomonas aeruginosa* without septicemia in a neutropenic patient]. *Rev Med Interne* 2001; 22:877-880.
  96. Bonduel M, Santos P, Turienzo CF, Chantada G, Paganini H. Atypical skin lesions caused by *Curvularia* sp. and *Pseudallescheria boydii* in two patients after allogeneic bone marrow transplantation. *Bone Marrow Transplant* 2001; 27:1311-1313.
  97. Mull CC, Scarfone RJ, Conway D. Ecthyma gangrenosum as a manifestation of *Pseudomonas* sepsis in a previously healthy child. *Ann Emerg Med* 2000; 36:383-387.
  98. Wu BY, Peng CT, Tsai CH, Chiu HH. Community-acquired *Pseudomonas aeruginosa* bacteremia and sepsis in previously healthy infants. *Acta Paediatr Taiwan* 1999; 40:233-236.
  99. Fergie JE, Huang DB, Purcell K, Milligan T. Successful treatment of *Fusarium solanae* ecthyma gangrenosum in a child with acute lymphoblastic leukemia in relapse. *Pediatr Infect Dis J* 2000; 19:579-581.
  100. Del Pozo J, Garcia-Silva J, Almagro M, Martinez W, Nicolas R, Fonseca E. Ecthyma gangrenosum-like eruption associated with *Morganella morganii* infection. *Br J Dermatol* 1998; 139:520-521.
  101. Burgner D, Eagles G, Burgess M, Procopis P, Rogers M, Muir D, et al. Disseminated invasive infection due to *Metarrhizium anisopliae* in an immunocompromised child. *J Clin Microbiol* 1998; 36:1146-1150.
  102. Repiso T, Garcia-Patos V, Martin N, Creus M, Bastida P, Castells A. Disseminated fusariosis. *Pediatr Dermatol* 1996; 13:118-121.
  103. Martino P, Gastaldi R, Raccach R, Girmenia C. Clinical patterns of *Fusarium* infections in immunocompromised patients. *J Infect Dis* 1994; 28(Suppl 1):7-15.
  104. Jang TN, Wang FD, Wang LS, Liu CY, Liu IM. *Xanthomonas maltophilia* bacteremia: an analysis of 32 cases. *J Formos Med Assoc* 1992; 91:1170-1176.
  105. Stotka JL, Rupp ME. *Klebsiella pneumoniae* urinary tract infection complicated by endophthalmitis, perinephric abscess, and ecthyma gangrenosum. *South Med J* 1991; 84:790-793.
  106. Edelstein H, Cutting HO. *Escherichia coli* as cause of ecthyma gangrenosum. *Postgrad Med* 1986; 79:44-45.
  107. Harris RL, Fainstein V, Elting L, Hopfer RL, Bodey GP. Bacteremia caused by *Aeromonas* species in hospitalized cancer patients. *Rev Infect Dis* 1985; 7:314-320.
  108. Cheng TO. Syphilitic aortitis is dying but not dead. *Catheter Cardiovasc Interv* 2001; 52:240-241.
  109. Aizawa H, Hasegawa A, Arai M, Naganuma F, Hatori M, Kanda T, et al. Bilateral coronary ostial stenosis and aortic regurgitation due to syphilitic aortitis. *Intern Med* 1998; 37:56-59.
  110. Samson L, Chalaoui J, Paradis B. Case of the day. General. Syphilitic aortitis, with saccular aneurysm of the descending aorta and fusiform aneurysm of the ascending aorta. *Radiographics* 1990; 10:508-510.
  111. Oksi J, Kalimo H, Marttila RJ, Marjamäki M, Sonninen P, Nikoskelainen J, et al. Intracranial aneurysms in three patients with disseminated Lyme borreliosis: cause or chance association? *J Neurol Neurosurg Psychiatry* 1998; 64:636-642.
  112. Keil R, Baron R, Kaiser R, Deuschl G. [Vasculitis course of neuroborreliosis with thalamic infarct]. *Nervenarzt* 1997; 68:339-341.
  113. Oksi J, Kalimo H, Marttila RJ, Marjamäki M, Sonninen P, Nikoskelainen J, et al. Inflammatory brain changes in Lyme borreliosis. A report on three patients and review of literature. *Brain* 1996; 119:2143-2154.
  114. Leys AM, Schonherr U, Lang GE, Naumann GO, Goubau P, Honore A, et al. Retinal vasculitis in Lyme borreliosis. *Bull Soc Belge Ophtalmol* 1995; 259:205-214.
  115. Giang DW. Central nervous system vasculitis secondary to infections, toxins, and neoplasms. *Semin Neurol* 1994; 14:313-319.
  116. Smith JL, Winward KE, Nicholson DF, Albert DW. Retinal vasculitis in Lyme borreliosis. *J Clin Neuroophthalmol* 1991; 11:7-15.
  117. Lang GE, Schonherr U, Naumann GO. Retinal vasculitis with proliferative retinopathy in a patient with evidence of *Borrelia burgdorferi* infection. *Am J Ophthalmol* 1991; 111:243-244.
  118. Pizzarello LD, MacDonald AB, Semler R, DiLeo F, Berger B. Temporal arteritis associated with *Borrelia* infection. A case report. *J Clin Neuroophthalmol* 1989; 9:3-6.
  119. Lock G, Berger G, Grobe H. [Neuroborreliosis: progressive encephalomyelitis with cerebral vasculitis]. *Monatsschr Kinderheilkd* 1989; 137:101-104.
  120. Veenendaal-Hilbers JA, Perquin WV, Hoogland PH, Doornbos L. Basal meningovascularitis and occlusion of the basilar artery in two cases of *Borrelia burgdorferi* infection. *Neurology* 1988; 38:1317-1319.
  121. Meier C, Grehl H. [Vasculitic neuropathy in the Garin-Bujadoux-Bannwarth syndrome. A contribution to the understanding of the pathology and pathogenesis of the neurological complications in Lyme borreliosis]. *Dtsch Med Wochenschr* 1988; 113:135-138.
  122. Uldry PA, Regli F, Bogousslavsky J. Cerebral angiopathy and recurrent strokes following *Borrelia burgdorferi* infection. *J Neurol Neurosurg Psychiatry* 1987; 50:1703-1704.
  123. MacDonald AB. Giant cell arteritis and *Borrelia* infection. *J Clin Neuroophthalmol* 1987; 7:180-181.
  124. Camponovo F, Meier C. Neuropathy of vasculitic origin in a case of Garin-Bujadoux-Bannwarth syndrome with positive *Borrelia* antibody response. *J Neurol* 1986; 233:69-72.
  125. Hamidou MA, Gueglio B, Cassagneau E, Treweek D, Grolleau JY. Henoch-Schönlein purpura associated with *Toxocara canis* infection. *J Rheumatol* 1999; 26:443-445.
  126. Revuelta R, Juambelz P, Balderrama J, Teixeira F. Contralateral trigeminal neuralgia: a new clinical manifestation of neurocysticercosis: case report. *Neurosurgery* 1995; 37:138-139.
  127. Pirisi M, Gutierrez Y, Minini C, Dolcet F, Beltrami CA, Pizzolito S, et al. Fatal human pulmonary infection caused by an *Angiostrongylus*-like nematode. *Clin Infect Dis* 1995; 20:59-65.
  128. Rakita RM, White AC Jr, Kielhofner MA. *Loa loa* infection as a cause of migratory angioedema: report of three cases from the Texas Medical Center. *Clin Infect Dis* 1993; 17:691-694.