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Successful Antiviral Treatment of Giant Cell Arteritis and Takayasu Arteritis

Don Gilden, MD, Teresa M. White, BS, Lidia Nagae, MD, William H. Gurdin, MD, Philip J. Boyer, MD, PhD, and Maria A. Nagel, MD

Department of Neurology, University of Colorado School of Medicine, Aurora (Gilden, White, Nagel); Department of Microbiology and Immunology, University of Colorado School of Medicine, Aurora (Gilden); Department of Radiology, University of Colorado School of Medicine, Aurora (Nagae); Lutheran Medical Center, Wheat Ridge, Colorado (Gurdin); Department of Pathology, University of Colorado School of Medicine, Aurora (Boyer)

A patient who satisfies American College of Rheumatology criteria for both giant-cell arteritis (GCA) and Takayasu arteritis had a dramatic favorable response to antiviral treatment. The virological and pathological findings followed by successful antiviral treatment support earlier notions that GCA and Takayasu arteritis may represent a spectrum of the same disease produced by varicella-zoster virus (VZV).

Report of a Case

A woman in her 70s developed severe right-sided temporal pain and jaw claudication. Two months later, she developed bilateral arm pain, which was worse on the left; chest pain on exertion; and shortness of breath. No arm pulses were detected and blood pressure was unobtainable by auscultation or Doppler. Angiography findings revealed bilateral subclavian artery stenosis and left axillary artery occlusion without intracranial vasculopathy. Her erythrocyte sedimentation rate was normal and C-reactive protein level was 1.6 mg/0.1 L (normal <1.0 mg/0.1 L; to convert to nanomoles per liter, multiply by 9.524). Results from a temporal artery (TA) biopsy were initially negative for GCA. Despite treatment with oral prednisone, 30 mg twice daily, she experienced progressive arm pain, intractable fatigue, anorexia, and weight loss. She underwent additional angiograms, one complicated by deep-seated right hemispheric infarction. Seven months later, she developed gangrene in her left hand and underwent bilateral carotid to brachial artery bypass surgery. She continued prednisone, 20 mg daily, and stopped 2 months later.

Sixteen months after initial presentation, she was cachectic and weighed 30.8 kg. Her fingers were bright red and hyperesthetic with flexion contractures. Except for weak right popliteal artery pulse, there were no temporal or radial artery pulses, no pulses over the supraclavicular or left popliteal fossa, and both dorsalis pedis pulses were absent. Deep

Corresponding Author: Don Gilden, MD, Department of Neurology, University of Colorado School of Medicine, 12700 E 19th Ave, Box B182, Aurora, CO 80045 (don.gilden@ucdenver.edu).

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tendon reflexes were increased in the legs with a left extensor plantar response. The erythrocyte sedimentation rate was 30 mm/h (normal <20 mm/h) and C-reactive protein level was 0.3 mg/ 0.1 L. Computed tomographic angiography revealed extensive large-artery disease involving the right brachiocephalic, left subclavian, and vertebral, bilateral axillary and common carotid arteries; the celiac trunk; and the right renal artery (Figure 1).

Based on detection of VZV in GCA-positive TAs,¹ documented involvement of other large arteries in most patients with GCA,² and pathological changes of extensive arteritis with giant cells in both GCA and Takayasu arteritis,³ we treated our patient with intravenous acyclovir, 15 mg/kg 3 times daily for 2 weeks, followed by oral valacyclovir, 1 g 3 times daily. Immunohistochemical analysis of the TA biopsy obtained 14 months earlier detected VZV antigen, and histopathological examination of 17 sections revealed GCA (Figure 2). The response to antiviral therapy was dramatic. Within a week, she felt energetic and began to eat voraciously. Two weeks later, both TA pulses, left supraclavicular fossa pulse, and left radial and popliteal artery pulses were present. Erythrocyte sedimentation rates and C-reactive protein level during the next 4 months were normal or mildly elevated. Our patient continues to improve. Four months later, she weighed 39.5 kg, and pulses noted here remain patent. Permanent finger contractures limit mobility and other activities of daily living.

Discussion

Herein, we describe a remarkable case that satisfies American College of Rheumatology criteria for both GCA and Takayasu arteritis. Noteworthy features include development of GCA followed months later by Takayasu arteritis, consistent with findings that large-artery disease frequently complicates GCA.⁴ Furthermore, although the original TA biopsy was GCA negative, histopathological examination confirmed the diagnosis of GCA, underscoring the close relationship between VZV antigen and GCA pathology.^{1,5} Most important, however, was the patient's rapid clinical response to antiviral treatment as manifested by improved energy, appetite, and weight gain, as well as detection of multiple pulses that were absent 2 weeks earlier.

Overall, the virological and pathological findings in this case followed by the favorable response to antiviral therapy support earlier assumptions that GCA and Takayasu arteritis may represent a spectrum of the same disease⁶ produced by VZV.

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Figure 1. Computed Tomographic Angiograms of Upper Extremities

A, Coronal maximum intensity projection reconstructions at the origin of the great vessels show moderate focal narrowing of the right brachiocephalic artery (black arrowhead) and multiple focal areas of narrowing along the left subclavian and axillary arteries (blue arrowheads) with segmental occlusion distally; the right subclavian artery was partially obscured by contrast in the adjacent vein, although severe stenosis and occlusion were seen distally in the right axillary artery (red arrowhead). Focal narrowing was seen at the origin of the left vertebral artery (yellow arrowhead). B, Volume rendering shows the origin of the great vessels with focal narrowing of the left subclavian artery (blue arrowhead), as well as areas of occlusion distally (red arrowheads). Failure to reconstruct the proximal right subclavian artery is due to reflux of contrast in the adjacent vein, as detailed in panel A. C, An axial section at the level of the common carotid arteries demonstrates bilateral wall thickening, up to 3 mm on the left side (blue arrowheads). Note severe focal narrowing at the origin of the celiac trunk (D, blue arrowhead) and moderate focal narrowing at the origin of the right renal artery (E, blue arrowhead). Irregularities seen along the aorta (D and E, red arrowheads) reflect calcified atherosclerotic disease.

Figure 2. Pathologic and Virologic Analysis of the Temporal Artery in a Patient With Giant Cell Arteritis and Takayasu Arteritis

A, Hematoxylin-eosin stain shows inflammation and necrosis (arrowheads) with epithelioid cells (inset, arrowhead) in the arterial media. Immunohistochemical stain with rabbit anti-varicella-zostervirus (VZV) IE63 antibody¹ revealed VZV antigen in the arterial adventitia (B) that was not seen with normal rabbit serum (C). Immunostaining with mouse anti-VZV gE IgG1 antibody¹ confirms the presence of VZV antigen in the arterial media (D and E, yellow arrowheads), in the intima adjacent to the internal elastic membrane (D and E, blue arrowheads), and in the adventitia surrounding the vasa nervorum (F, arrowheads) that was not seen when mouse isotype IgG1 antibody was used as the primary antibody (G-I). Original magnification $\times 600$.