Revised Nomenclature of Systemic Vasculitides (CHCC2012) and Kawasaki disease

Kei Takahashi, MD

Professor of Department of Pathology, Toho University Ohashi Medical Center, Tokyo, Japan

2012 Revised International Chapel Hill Consensus Conference Nomenclature of Systemic Vasculitides

Because of advances in our understanding of vasculitis, another International Chapel Hill Consensus Conference was convened to improve the CHCC1994 nomenclature, change names and definitions as appropriate, and add important categories of vasculitis that were not included in CHCC1994.

First, the use of each vasculitis eponym was carefully deliberated to determine if a non-eponymous replacement term was suitable. In the result, three of five eponymous vasculitis, Wegener's granulomatosis, Churg-Strauss syndrome and Henoch-Schönlein purpura listed in CHCC1994, were changed to the following non-eponymous terms, granulomatosis with polyangiitis (Wegener's), eosinophilic granulomatosis with polyangiitis (Churg-Strauss) and IgA vasculitis (Henoch-Schönlein), respectively. On the other hand, two eponyms, Takayasu arteritis and Kawasaki disease were retained because these eponyms are more effective than any alternatives that were proposed. Next, major vasculitis categories were made based on the predominant type of vessels involved. Four new categories in addition to three categories in CHCC1994 were proposed in CHCC2012. Each vasculitis disease was classified into appropriate categories and definitions of each disease was made. Finally, 26 vasculitis diseases were described in CHCC2012.

It will be expected to be used as a new Chapel Hill classification in a number of areas in the future.

Kawasaki disease

Kawasaki disease (KD) was first described in 1967 by Dr. Tomisaku Kawasaki as mucocutaneous lymph node syndrome. The etiology of this disease remains still unknown and this disease affects most commonly infants and young children. KD is considered as a kind of systemic vasculitis syndrome, and it invades primarily the medium-sized muscular arteries. This disease has attracted special interest because death from this disease is most frequently attributable to ischemic heart disease in children caused by thrombosed coronary artery aneurysms, secondary to coronary arteritis.

Histopathologically, coronary arteritis in KD begins as edematous dissociation of the tunica media 6 to 8 days after the onset of KD. On about the 10th day of disease, lymphocyte and macrophage infiltration into the arterial wall from the luminal side and adventitial side begins, leading immediately to inflammation of all layers of the artery. The inflammation spreads completely around the artery, and the internal elastic lamina, smooth muscle cells of the media and other structural components of the artery undergo intense damage; the artery then begins to dilate. Aneurysms develop on about the 12th day after onset when the damage is severe. The blood eddies in the aneurysm makes it easy for thrombi to form, and thrombotic occlusion is found in the coronary artery aneurysm of many autopsy cases of acute-stage KD. Arteritis in KD is characterized by proliferative inflammation that consists of marked accumulation of monocytes/macrophages, and aberrant activation of those macrophages is thought to be involved in the formation of vascular lesions. However, the lesions in the initial stage of inflammation contain not only macrophages and lymphocytes but also many neutrophils. The inflammatory cell infiltration continues until about the 25th day of disease, after which the inflammatory cells gradually decrease in number and are almost completely gone by about the 40^{th} day of the disease. A scar from the inflammation remains for a long time thereafter.

I will mention the characteristics of epidemiology and pathogenesis in addition to pathology of KD.

References

1. Jennette JC, Falk RJ, Bacon PA, et al. 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 2013, 65:1-11
2. Kawasaki T. Acute febrile mucocutaneous syndrome with lymphoid involvement with specific desquamation of fingers and toes in children. Clinical observation of 50 patients. [in Japanese] *Jpn J Allergy* 1967;16:178-222
3. Kawasaki T, Kosaki F, Okawa S, et al. A new infantile acute febrile mucocutaneous lymph-node syndrome (MLNS) prevailing in Japan. *Pediatrics* 1974; 54: 271-276
4. Ayusawa M, Sonobe T, Uemura S, et al. Kawasaki Disease Research Committee.: Revision of diagnostic guidelines for Kawasaki disease (the 5th revised edition). *Pediatr Int.* 2005;47:232-234.
5. Masuda H, Naoe S, Tanaka N. A pathological study of coronary artery in Kawasaki disease (MCLS) - with special reference to morphogenesis of aneurysm. [in Japanese] *J Jpn Coll Angiol* 1981;21:899-912
6. Takahashi K, Oharaseki T, Naoe S, et al. Neutrophilic involvement in the damage to coronary arteries in acute stage of Kawasaki disease. *Pediatr Int* 2005;47:305–310
7. Takahashi K, Oharaseki T, Naoe S. Pathological study of postcoronary arteritis in adolescents and young adults, with reference to the relationship between sequelae of Kawasaki disease and atherosclerosis *Pediatr Cardiol*, 2001;22:138–142

CHCC2012 Names	CHCC2012 Definitions
Large Vessel Vasculitis (LVV)	Vasculitis affecting large arteries more often than other vasculitides. Large arteries are the aorta and its major branches. Any size artery may be affected.
Takayasu Arteritis (TAK)	Arteritis, often granulomatous, predominantly affecting the aorta and/or its major branches. Onset usually in patients younger than 50.
Giant Cell Arteritis (GCA)	Arteritis, often granulomatous, usually affecting the aorta and/or its major branches, with a predilection for the branches of the carotid and vertebral arteries. Often involves the temporal artery. Onset usually in patients older than 50 and often associated with polymyalgia rheumatica.
Medium Vessel Vasculitis (MVV)	Vasculitis predominantly affecting medium arteries defined as the main visceral arteries and their branches. Any size artery may be affected. Inflammatory aneurysms and stenoses are common.
Polyarteritis Nodosa (PAN)	Necrotizing arteritis of medium or small arteries without glomerulonephritis or vasculitis in arterioles, capillaries, or venules; and not associated with ANCA.
Kawasaki Disease (KD)	Arteritis associated with the mucocutaneous lymph node syndrome and predominantly affecting medium and small arteries. Coronary arteries are often involved. Aorta and large arteries may be involved. Usually occurs in infants and young children.
Small Vessel Vasculitis (SVV)	Vasculitis predominantly affecting small vessels, defined as small intraparenchymal arteries, arterioles, capillaries and venules. Medium arteries and veins may be affected.
ANCA Associated Vasculitis (AAV)	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (i.e., capillaries, venules, arterioles and small arteries), associated with MPO-ANCA or PR3-ANCA. Not all patients have ANCA. Add a prefix indicating ANCA reactivity, e.g. PR3-ANCA, MPO-ANCA, ANCA-negative.
Microscopic Polyangiitis (MPA)	Necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (i.e., capillaries, venules, or arterioles). Necrotizing arteritis involving small and medium arteries may be present. Necrotizing glomerulonephritis is very common. Pulmonary capillaritis often occurs. Granulomatous inflammation is absent.
Granulomatosis with Polyangiitis (Wegener's) (GPA)	Necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small to medium vessels (e.g., capillaries, venules, arterioles, arteries and veins). Necrotizing glomerulonephritis is common.
Eosinophilic Granulomatosis with Polyangiitis (Churg Strauss) (EGPA)	Eosinophil-rich and necrotizing granulomatous inflammation often involving the respiratory tract, and necrotizing vasculitis predominantly affecting small to medium vessels, and associated with asthma and eosinophilia. ANCA is more frequent when glomerulonephritis is present.
Immune Complex Vasculitis	Vasculitis with moderate to marked vessel wall deposits of immunoglobulin and/or complement components predominantly affecting small vessels (i.e., capillaries, venules, arterioles and small arteries). Glomerulonephritis is frequent.
Anti-GBM Disease	Vasculitis affecting glomerular capillaries, pulmonary capillaries, or both, with basement membrane deposition of anti-basement membrane autoantibodies. Lung involvement causes pulmonary hemorrhage, and renal involvement causes glomerulonephritis with necrosis and crescents.
Cryoglobulinemic Vasculitis (CV)	Vasculitis with cryoglobulin immune deposits affecting small vessels (predominantly capillaries, venules, or arterioles) and associated with cryoglobulins in serum. Skin, glomeruli and peripheral nerves are often involved.

IgA Vasculitis (IgAV) *(Henoch-Schönlein)*	Vasculitis, with IgA1-dominant immune deposits, affecting small vessels (predominantly capillaries, venules, or arterioles). Often involves skin and gastrointestinal tract, and frequently causes arthritis. Glomerulonephritis indistinguishable from IgA nephropathy may occur.
Hypocomplementemic Urticarial Vasculitis (HUV) *(Anti-C1q Vasculitis)*	Vasculitis accompanied by urticaria and hypocomplementemia affecting small vessels (i.e., capillaries, venules, or arterioles), and associated with anti-C1q antibodies. Glomerulonephritis, arthritis, obstructive pulmonary disease, and ocular inflammation are common.
Variable Vessel Vasculitis (VVV)	Vasculitis with no predominant type of vessel involved that can affect vessels of any size (small, medium, and large) and type (arteries, veins, and capillaries).
Behçet's Disease (BD)	Vasculitis occurring in patients with Behçet's disease that can affect arteries or veins. Behçet's disease is characterized by recurrent oral and/or genital aphthous ulcers accompanied by cutaneous, ocular, articular, gastrointestinal, and/or central nervous system inflammatory lesions. Small vessel vasculitis, thromboangiitis, thrombosis, arteritis and arterial aneurysms may occur.
Cogan's Syndrome (CS)	Vasculitis occurring in patients with Cogan's syndrome. Cogan's syndrome is characterized by ocular inflammatory lesions, including interstitial keratitis, uveitis, and episcleritis, and inner ear disease, including sensorineural hearing loss and vestibular dysfunction. Vasculitic manifestations may include arteritis (affecting small, medium or large arteries), aortitis, aortic aneurysms, and aortic and mitral valvulitis.
Single Organ Vasculitis (SOV)	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 a systemic vasculitis. The involved organ and vessel type should be included in the name (e.g. cutaneous small vessel vasculitis, testicular arteritis, central nervous system vasculitis). Vasculitis distribution may be unifocal or multifocal (diffuse) within an organ. Some patients originally diagnosed with SOV will develop additional disease manifestations that warrant re-defining the case as one of the systemic vasculitides (e.g. cutaneous arteritis later becoming systemic polyarteritis nodosa, etc.).
Vasculitis Associated with Systemic Disease	Vasculitis that is associated with and may be secondary to (caused by) a systemic disease. The name (diagnosis) should have a prefix term specifying the systemic disease (e.g. rheumatoid vasculitis, lupus vasculitis, etc.).
Vasculitis Associated with Probable Etiology	Vasculitis that is associated with a probable specific etiology. The name (diagnosis) should have a prefix term specifying the association (e.g. hydralazine-associated microscopic polyangiitis, hepatitis B virus-associated vasculitis, hepatitis C virus-associated cryoglobulinemic vasculitis, etc.).

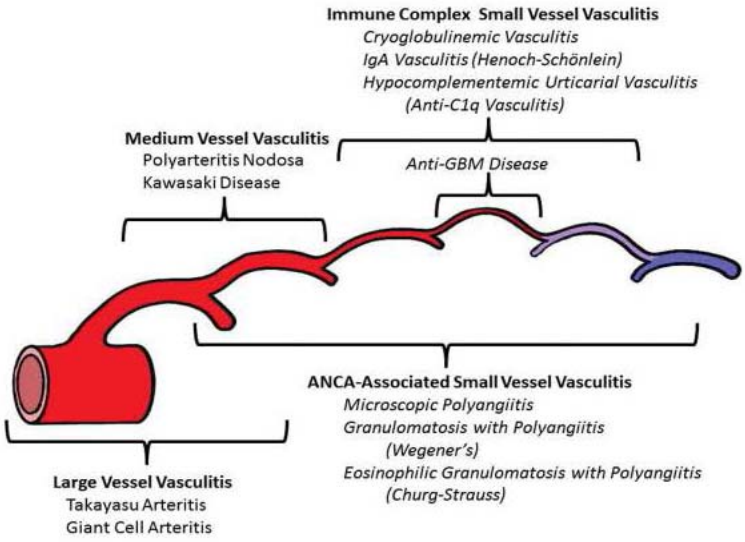

Figure 2. Distribution of vessel involvement by large vessel vasculitis, medium vessel vasculitis, and small vessel vasculitis. Note that there is substantial overlap with respect to arterial involvement, and an important concept is that all 3 major categories of vasculitis can affect any size artery. Large vessel vasculitis affects large arteries more often than other vasculitides. Medium vessel vasculitis predominantly affects medium arteries. Small vessel vasculitis predominantly affects small vessels, but medium arteries and veins may be affected, although immune complex small vessel vasculitis rarely affects arteries. Not shown is variable vessel vasculitis, which can affect any type of vessel, from aorta to veins. The diagram depicts (from left to right) aorta, large artery, medium artery, small artery/arteriole, capillary, venule, and vein. Anti-GBM = anti–glomerular basement membrane; ANCA = antineutrophil cytoplasmic antibody.

J. C. Jennette, R. J. Falk, P. A. Bacon, N. Basu, M. C. Cid, F. Ferrario, L. F. Flores-Suarez, W. L. Gross, L. Guillevin, E. C. Hagen, G. S. Hoffman, D. R. Jayne, C. G. M. Kallenberg, P. Lamprecht, C. A. Langford, R. A. Luqmani, A. D. Mahr, E. L. Matteson, P. A. Merkel, S. Ozen, C. D. Pusey, N. Rasmussen, A. J. Rees, D. G. I. Scott, U. Specks, J. H. Stone, K. Takahashi, and R. A. Watts: 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 65(1), 2013, 1–11.