A CanVasc project

CAVALI

CAnadian VAsculitis Learning Initiative

An approach to vasculitis through interactive clinical cases

Corisande Baldwin, MD · Raphael Rush, MD · Medha Soowamber, MD

Under the direction and guidance of Christian Pagnoux, MD

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Contents

List of commonly used abbreviations

ACR: American College of Rheumatology

ANA: Antinuclear antibody

ANCA: Anti-neutrophil cytoplasm(ic) antibodies

AZA: Azathioprine

BVAS: Birmingham vasculitis activity score

CD: Cluster of differentiation (e.g. CD4+ T cell, CD19+ B cells)

CRP: C-reactive protein

CT (scan): Computerized tomography (scanner)

CYC: Cyclophosphamide

DCVAS: Diagnostic and classification criteria for primary systemic vasculitis

EBV: Epstein-Barr virus

EGPA: Eosinophilic granulomatosis with polyangiitis

ELISA: Enzyme-linked immunosorbent assay

ENA: Extractable nuclear antigens

ENT: Ear, nose and throat

EULAR: European League Against Rheumatism

ESR: Erythrocyte sedimentation rate

GBM: Glomerular basal membrane (such as anti-GBM antibody)

G6PD: Glucose-6-phosphate dehydrogenase

GC: Glucocorticoid(s)

GCA: Giant cell arteritis

GPA: Granulomatosis with polyangiitis

HBV: Hepatitis B virus

HCV: Hepatitis C virus

HIV: Human immunodeficiency virus

HLA: Human leukocyte antigen

KD: Kawasaki disease

IgA: Immunoglobulin A

IgG4-RD: Immunoglobulin G4-related disease

(I)IF: (indirect) Immunofluorescence (study)

IV: Intravenous

IVIg: Intravenous immunoglobulins

LCV: Leukocytoclastic vasculitis

LEF: Leflunomide

MMF: Mycophenolate mofetil

MPA: Microscopic polyangiitis

MPO: Myeloperoxidase (such as MPO-ANCA)

MRA: Magnetic resonance angiography

MRI: Magnetic resonance imaging

MTX: Methotrexate

PAN: Polyarteritis nodosa

(18F-FDG-)PET: (18-fluorodeoxyglucose) Positron emission tomography

PR3: Proteinase 3 (such as PR3-ANCA)

RA: Rheumatoid arthritis

RCT: Randomized controlled trial

RF: Rheumatoid factor

RTX: Rituximab

SSc: Systemic scleroderma

TAK: Takayasu arteritis

TCZ: Tocilizumab

TNF-alpha: Tumour necrosis factor-alpha

TPMT: Thiopurine methyltransferase

VDI: Vasculitis damage index

Introduction

Christian Pagnoux

Cavali, First edition, February 2017

The Canadian Vasculitis Network (CanVasc) was founded in November 2010. Its core committee includes more than 20 physicians from various medical specialties across Canada, with expertise and interest in vasculitis, and many more collaborators (updated list on the CanVasc website – http://www.canvasc.ca). CanVasc ultimately aims at optimizing the management of vasculitis patients in Canada, throughout the development of (or assistance with the development of) guidelines, educational and awareness programs for health care providers, and studies on vasculitides.

Since its creation, CanVasc core members have initiated and achieved several important projects. The first CanVasc/Canadian recommendations, for the diagnosis and management of ANCA-associated vasculitis, have been published (McGeoch et al. J Rheumatol 2016;43:97-120). Work is in progress to develop similar recommendations for other vasculitides. Several descriptive studies have also been completed and published, and projects for prospective studies and cohorts are underway.

In parallel, several tools have been developed to provide and help disseminate continuous, up-to-date educational materials to physicians who manage patients with vasculitides and increase awareness on these rare and potentially life-threatening diseases. The CanVasc website offers practical information and resources. Conferences and presentations during sessions organized with Vasculitis Foundation Canada, the Canadian patients' support group, helped to reach more diversified audiences, including patients of course, but also their health care allied professionals and general practitioners.

The development of 'Cavali, a CAnadian VAsculitis Learning Initiative: An approach to vasculitis through interactive clinical cases' aims to further support the continuous learning of physicians and health care providers managing vasculitis patients and training residents. Cavali is the result of hundreds of hours of work to develop practical cases and have them reviewed by CanVasc core physicians. It would not have been possible and this book would not be in your hands today without the contribution or support of several individuals, listed in the Contributors' page, and the educational grants obtained from the Canadian Initiative for Outcomes in Rheumatology cAre (CIORA) and Hoffmann-La Roche. Corisande Baldwin, Raphael Rush and Medha Soowamber helped develop several cases, at the time they were (outstanding!) vasculitis and/or rheumatology fellows in the Vasculitis clinic at Mount Sinai Hospital (Toronto, ON). Of course, as new studies will come up, Cavali will need some periodical updates.

There are multiple aspects involved in attempting to improve patient outcomes. We hope that Cavali will contribute in some way towards this important goal, by raising or nurturing the interest for vasculitis in our current and future Canadian health care colleagues, and by providing them in a playful manner with some practical updates.

After having read the cases in this book, readers who wish to go even further, test their knowledge on vasculitides and/or receive a certificate to support a claim for CME credits, can complete two additional cases online at http://www.cavali.ca.

Case 1

Giant cell arteritis

A 72-year-old woman with hypertension, dyslipidemia and a 50 pack-year smoking history presents with a two-week history of worsening left-sided temporal headache, scalp tenderness, especially in the left temporal area, general malaise and an 8-kg weight loss. C-reactive protein is elevated at 55 mg/l (normal <10 mg/l). The patient is diagnosed with presumed giant cell arteritis (GCA) and started on prednisone 60 mg/day. Ten days later, a temporal artery biopsy is done. The histopathology is negative (normal artery with minimal, chronic atherosclerotic changes). She is referred to you for further diagnostic evaluation and management.

1. *Describe the clinical manifestations of GCA. What are the possible neurological, ocular, and extra-cranial vascular complications of GCA?*
2. *Describe the existing diagnostic and classification criteria for GCA. What are the limitations of these criteria?*
3. *What is the sensitivity and specificity of temporal artery biopsy in patients with suspected GCA? How does treatment with glucocorticoids impact the sensitivity and specificity of temporal artery biopsy?*
4. *Which imaging modalities can be of use in the diagnosis of GCA?*

The patient followed a gradual prednisone tapering regimen. At 6 months, she is on 10 mg/day prednisone (tapered down from 15 mg/day two weeks ago). She complains of returning temporal headache and fatigue. The physical examination is normal. C-reactive protein is high again at 68 mg/l (versus 6 mg/l a month ago).

5. *How would you now manage and treat this patient?*

Learning objectives

1. To describe the prevalence, the typical demographics and clinical characteristics of GCA.
2. To describe the classic laboratory results, histopathology and imaging of GCA.
3. To describe the role and limitations of temporal artery biopsy and imaging modalities in the diagnosis of GCA.
4. To describe the evidence for the use of glucocorticoids, glucocorticoid-sparing agents, and biologics in the treatment of GCA.
5. To list the possible complications of GCA and its treatment.

Answers

1. Describe the clinical manifestations of GCA. What are the possible neurological, ocular, and extra-cranial vascular complications of GCA?

GCA is one of the most common forms of vasculitis in adults ≥50 years of age, with incidence peaking at 70-80 years. It is more common in women (sex ratio, 2.5), at least in Northern European countries. GCA seems rarer in African, Asian, Hispanic and Arab populations.

GCA affects large vessels and can cause systemic manifestations and ischemic complications. Systemic manifestations are common at the time of diagnosis, with fatigue, general malaise, symptoms of polymyalgia rheumatica, fever, weight loss, or dry cough. In some instances, these unspecific systemic symptoms can precede by weeks or months the other and more suggestive signs of GCA. The latter relate to the vessels predominantly involved (mainly the external carotid artery and its branches, uni- or bilaterally, but other large vessels can be affected). The most frequent clinical symptoms include headache, often fronto-temporal and of sub-acute onset, scalp tenderness, temporal artery induration and tenderness, and jaw claudication. More severe ischemic complications include vision loss in 10-20% of patients. Vision loss may be transient (amaurosis fugax due to acute anterior ischemic optic neuritis) or permanent. Visual loss in one eye may lead to involvement of the contralateral eye in up to 25-50% if initially unrecognized. Other ischemic complications include diplopia, stroke or transient ischemic attack, tongue or scalp infarct, and, more exceptionally, myocardial infarction. Extra-cranial large vessels can be involved in up to 30–50% of patients, depending on the detection technique used, and can cause limb ischemia, digital ischemia with ulcers and/or gangrene. Other important possible vascular complications of GCA include aortitis in up to 10–30% of patients with aortic aneurysm and/or dissection (Figure 1.1), which can develop years after the diagnosis, when the disease is otherwise in remission, and aortic valvular insufficiency.

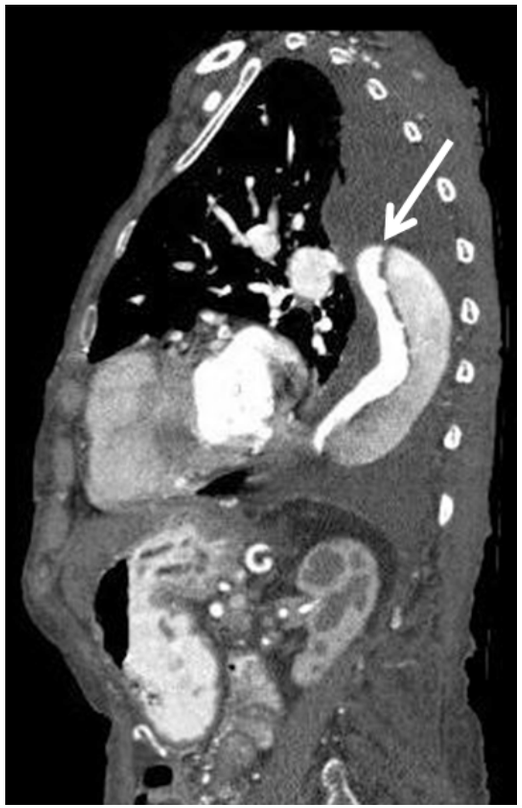

Figure 1.1. Parasagittal thoraco-abdominal CT in an 80-year-old female with a diagnosis of giant cell arteritis, made 2 years earlier, showing a thoracic aorta dissection (arrow). Vessel imaging was normal at the time of diagnosis.

2. Describe the existing diagnostic and classification criteria for GCA. What are the limitations of these criteria?

There are currently no diagnostic criteria for GCA. The 1990 American College of Rheumatology (ACR) classification criteria are validated for research classification purposes only, and should therefore be used with caution in clinical settings.