

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

A CanVasc project



---

# CAVALI

## Canadian VAsculitis Learning Initiative

An approach to vasculitis through interactive clinical cases

---

**Corisande Baldwin, MSc, MD, FRCPC**

**Raphael Rush, MD, FRCPC**

**Medha Soowamber, MD, FRCPC**

**Under the direction and guidance of Christian Pagnoux, MD, MSc, MPH**

**Contributors:** CanVasc core members (updated list: <http://www.canvasc.ca>);

Mercedes Chan, MD; and Kristin Houghton, MD

**Developed and published with funding support and grants from:**

- **Canadian Initiative for Outcomes in Rheumatology cAre (CIORA):** CanVasc Project “Improving the Care of Patients with Systemic Vasculitis through the Development of Management Recommendations and Educational Materials: A Canadian Vasculitis Network (CanVasc) Initiative” (main applicant: Dr. C. Pagnoux)
- **Hoffmann-La Roche** educational grant-in-aid

## Contributors' Affiliations and Acknowledgments

### **Christian Pagnoux, MD, MSc, MPH**

Vasculitis Clinic, Division of Rheumatology, Department of Medicine, Mount Sinai Hospital, University of Toronto, 60 Murray Street, Room 2-220, Toronto, ON, M5T 3L9, Canada  
Email: christian.pagnoux@sinaihealthsystem.ca

### **Corisande Baldwin, MSc, MD, FRCPC**

Division of Rheumatology, Richmond Road Diagnostic and Treatment Centre, University of Calgary, 1820 Richmond Rd SW, Calgary, AB, T2T 5C7, Canada  
Email: corisande.baldwin@albertahealthservices.ca

### **Raphael Rush, MD, FRCPC**

Division of Rheumatology, Department of Medicine, Mount Sinai Hospital, University of Toronto, 60 Murray Street, Room 2-220, Toronto, ON, M5T 3L9, Canada

### **Medha Soowamber, MD, FRCPC**

Vasculitis Clinic, Division of Rheumatology, Department of Medicine, Mount Sinai Hospital, University of Toronto, 60 Murray Street, Room 2-227, Toronto, ON, M5T 3L9, Canada

### **Mercedes Chan, MD**

Edmonton Clinic Health Academy (ECHA), 3505 11405 87 Ave NW, Edmonton, AB, T6G 1C9, Canada

### **Kristin Houghton, MD, MSc, FRCPC**

Division of Rheumatology Department of Pediatrics, UBC BC Children's Hospital, 4480 Oak Street, Vancouver, BC, V6H 3V4, Canada

Each case in this book has been peer-reviewed by at least one of the **CanVasc core members** (updated list and affiliations: <http://www.canvasc.ca>): **Volodko Bakowsky, Lillian Barra, Susan Benseler, David A. Cabral, Simon Carette, Natasha Dehghan, Navjot Dhindsa, Christine Dipchand, Leilani Famorca, Aurore Fifi-Mah, Michelle Goulet, Nader Khalidi, Majed M. Khraishi, Patrick Liang, Nataliya Milman, Frédéric Morin, Christian A. Pineau, David Robinson, Dax G. Rumsey, Regina Taylor-Gjevre, Tanveer E. Towheed, Judith Trudeau, Marinka Twilt, Elaine Yacyshyn, Rae Yeung.**

In addition, the main authors wish to thank the following persons for their help or support, direct or indirect, in developing this book: Mark Atkinson (Ardeane Healthcare Solutions), Christina Clark, Thao Nguyen, Ariel Lefkowitz, Mark Kearney, Diana Fung, Stewart Campbell, Loïc Guillevin, and the patients and their families who generously supported CanVasc initiatives since its creation.

Copyright © CanVasc February 2017

Printed and bound in Canada

1st edition, March 2017

## Contents

### **Introduction | 7**

### **Cases**

- 1 Giant cell arteritis | 8**
- 2 Takayasu arteritis | 14**
- 3 Aortitis and imaging of large-vessel vasculitis | 19**
- 4 Polyarteritis nodosa | 25**
- 5 Kawasaki disease | 32**
- 6 Granulomatosis with polyangiitis – diagnosis and induction treatment of severe disease | 37**
- 7 Limited granulomatosis with polyangiitis | 47**
- 8 Granulomatosis with polyangiitis with subglottic stenosis | 54**
- 9 Microscopic polyangiitis – maintenance treatment | 60**
- 10 Relapsing microscopic polyangiitis | 69**
- 11 Eosinophilic granulomatosis with polyangiitis | 77**
- 12 Eosinophilic granulomatosis with polyangiitis – cardiac involvement and glucocorticoid dependency | 84**
- 13 Isolated cutaneous vasculitis | 89**
- 14 CNS vasculitis | 95**
- 15 CNS vasculitis in children | 102**
- 16 Cryoglobulinemic vasculitis | 106**
- 17 Behçet's disease | 114**
- 18 Cogan's syndrome | 122**
- 19 IgA vasculitis | 127**
- 20 Vasculitis and risk of late cancers and cardiovascular disease | 132**

### **Evaluation cases | 136**

## List of commonly used abbreviations

ACR: American College of Rheumatology	IgA: Immunoglobulin A
ANA: Antinuclear antibody	IgG4-RD: Immunoglobulin G4-related disease
ANCA: Anti-neutrophil cytoplasm(ic) antibodies	(I)IF: (indirect) Immunofluorescence (study)
AZA: Azathioprine	IV: Intravenous
BVAS: Birmingham vasculitis activity score	IVIg: Intravenous immunoglobulins
CD: Cluster of differentiation (e.g. CD4+ T cell, CD19+ B cells)	LCV: Leukocytoclastic vasculitis
CRP: C-reactive protein	LEF: Leflunomide
CT (scan): Computerized tomography (scanner)	MMF: Mycophenolate mofetil
CYC: Cyclophosphamide	MPA: Microscopic polyangiitis
DCVAS: Diagnostic and classification criteria for primary systemic vasculitis	MPO: Myeloperoxidase (such as MPO-ANCA)
EBV: Epstein-Barr virus	MRA: Magnetic resonance angiography
EGPA: Eosinophilic granulomatosis with polyangiitis	MRI: Magnetic resonance imaging
ELISA: Enzyme-linked immunosorbent assay	MTX: Methotrexate
ENA: Extractable nuclear antigens	PAN: Polyarteritis nodosa
ENT: Ear, nose and throat	(18F-FDG-)PET: (18-fluorodeoxyglucose) Positron emission tomography
EULAR: European League Against Rheumatism	PR3: Proteinase 3 (such as PR3-ANCA)
ESR: Erythrocyte sedimentation rate	RA: Rheumatoid arthritis
GBM: Glomerular basal membrane (such as anti-GBM antibody)	RCT: Randomized controlled trial
G6PD: Glucose-6-phosphate dehydrogenase	RF: Rheumatoid factor
GC: Glucocorticoid(s)	RTX: Rituximab
GCA: Giant cell arteritis	SSc: Systemic scleroderma
GPA: Granulomatosis with polyangiitis	TAK: Takayasu arteritis
HBV: Hepatitis B virus	TCZ: Tocilizumab
HCV: Hepatitis C virus	TNF-alpha: Tumour necrosis factor-alpha
HIV: Human immunodeficiency virus	TPMT: Thiopurine methyltransferase
HLA: Human leukocyte antigen	VDI: Vasculitis damage index
KD: Kawasaki disease	

## 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  $\geq 50$  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.