Case report

Giant Cell Arteritis or Formerly Known as Horton's Disease- When the Puzzle is Complete: A Case Report

Abstract :

Giant cell arteritis, formerly known as Horton's disease, is a vasculitis affecting the large vessels, specifically the aorta, with a preference for the supra-aortic trunks. Its etiology remains unknown, but two risk factors have been identified: a genetic predisposition and the hypothesis of a likely viral infectious agent. The pathophysiology is increasingly understood due to advances in immunological and genetic knowledge. It generally affects patients over 50 years old and clinically manifests as headaches, scalp paresthesias, and jaw claudication, evolving in a context of low-grade fever and general deterioration. It is often associated with polymyalgia rheumatica, and the most feared complication is blindness. Clinical examination reveals a decrease or abolition of temporal pulses. Diagnosis is histological, via temporal artery biopsy or, failing that, through a PET-CT scan. The condition is highly sensitive to corticosteroids, with a favorable prognosis under treatment. However, relapses can occur during corticosteroid tapering, potentially necessitating a minimally effective maintenance dose of at least 1 mg/day of corticosteroids such as prednisone.

Introduction :

Giant cell arteritis, formerly known as Horton's disease, is an inflammatory condition classified as vasculitis, affecting large arterial trunks, specifically the aorta and its branches, with a strong preference for the supra-aortic trunks. This condition primarily affects elderly patients (starting from age 50 with a peak at 70 years) and has a female predominance with a sex ratio of 3:1. Clinically, it is characterized by a triad: deterioration of general health (weight loss, fatigue, and anorexia), scalp paresthesia or persistent headache, and jaw claudication. Diagnosis is confirmed histologically by temporal artery biopsy or radiologically by MRI/PET scan. The main complication is functional, as it threatens the visual prognosis due to involvement of the ophthalmic artery or its branches, and rarely the vital prognosis. The prognosis is very good once treated, but frequent relapses necessitate low-dose corticosteroid therapy.

We report a classic case of Giant Cell Arteritis confirmed by all clinical, radiological, and histological criteria.

Case Presentation:

A 65-year-old male patient with a history of depression for 3 years controlled by treatment presented with significant weight loss of 27 kg (30% of body weight) over 6 months, progressively worsening fatigue, and inflammatory arthralgia of both shoulders, complicated by headache resistant to first and second-level analgesics, prompting consultation at CHU Ibn Rochd in Casablanca.

Clinical examination revealed a cachectic, dehydrated patient with skin fold persisting for more than 3 seconds, conscious with a Glasgow score of 15/15, well-oriented in time and space, with slight conjunctival discoloration. Palpation of pulses revealed diminished temporal pulses with asymmetry of supraclavicular pulses and a thrill on the left side. Blood pressure was low at 106/68 mmHg with a mean arterial pressure of 80 mmHg. The patient was urgently hospitalized in the Internal Medicine department at CHU Ibn Rochd, where an urgent ophthalmologic examination showed no signs of anterior ischemic optic neuropathy with visual acuity preserved at 9/10 in the right eye and 10/10 in the left eye with correction, and tortuosity of retinal vessels.

Echo-Doppler of the temporal arteries showed normal caliber arteries without significant thickening. Echo-Doppler of the supra-aortic trunks showed circumferential thickening of the right carotid and calcification of the left carotid. Thoraco-abdominopelvic CT scan revealed inflammatory wall thickening of large and medium caliber arteries without stenosis or tumor mass.

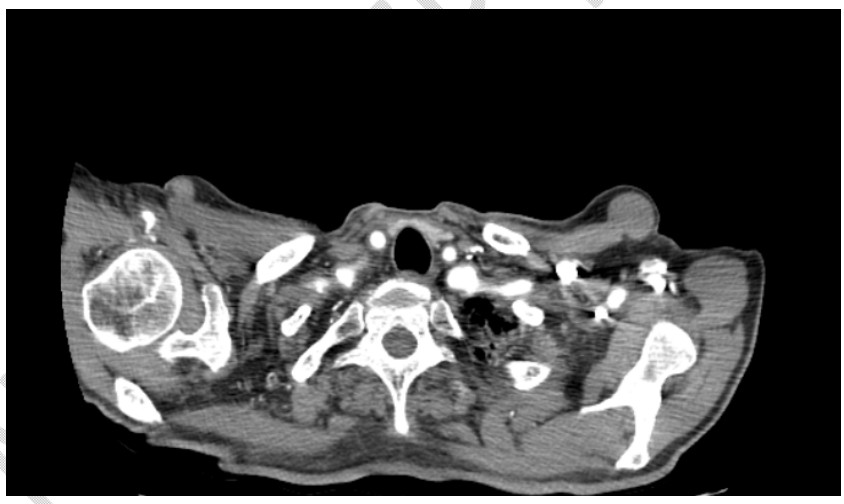


Fig 1. Transverse thoracic high CT scan showing circumferential wall thickening of the common carotids, more pronounced on the right side.

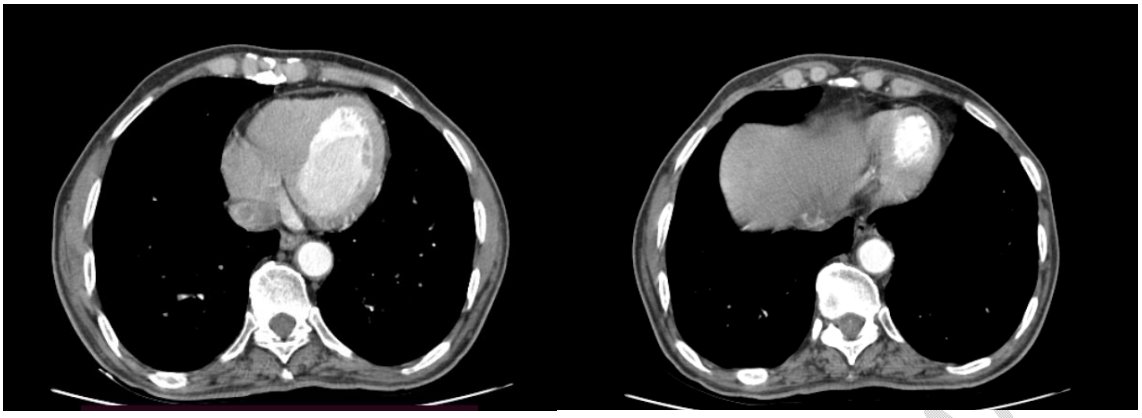


Fig 2. Transverse low thoracic CT scan showing circumferential wall thickening of the descending thoracic aorta.

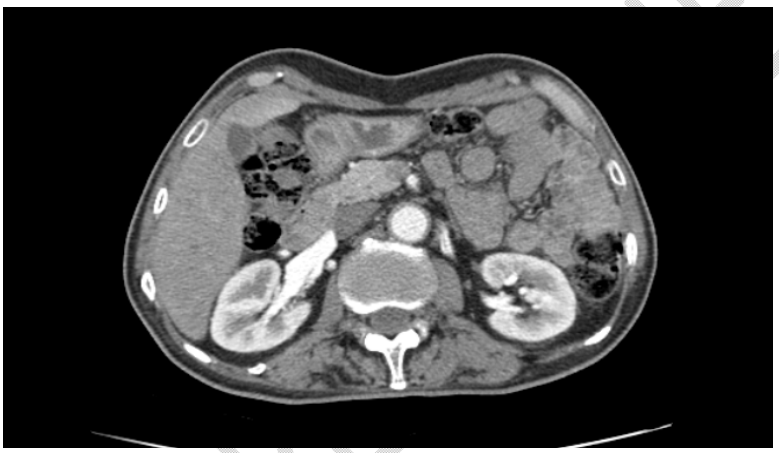


Fig 3. Transverse abdominal CT scan showing circumferential wall thickening of the abdominal aorta.

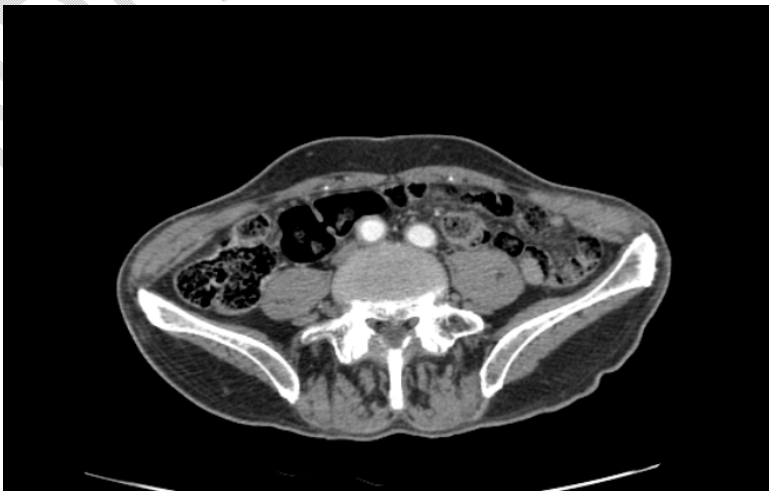
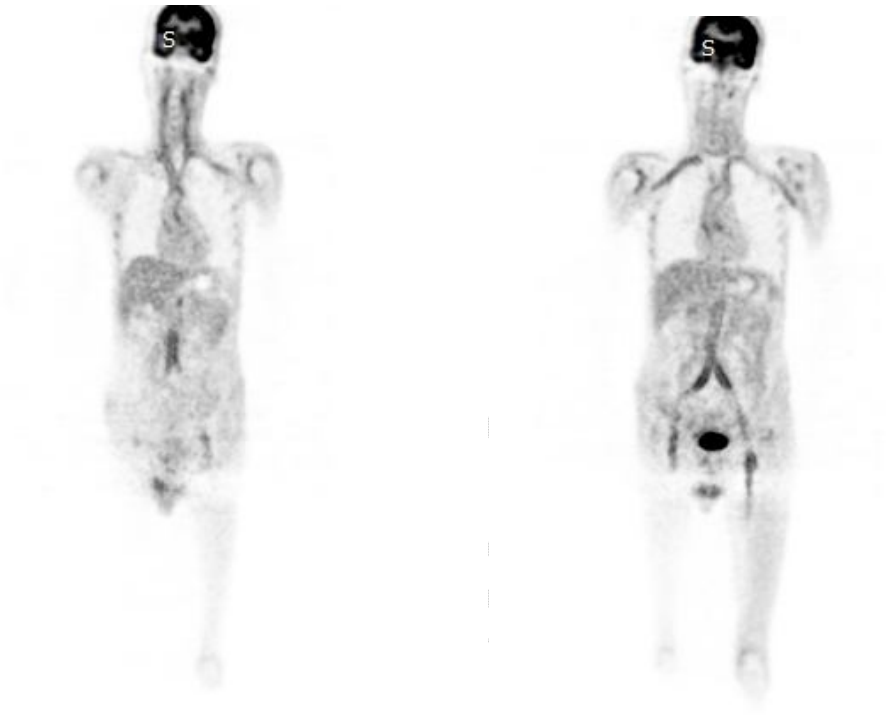


Fig 4. Transverse pelvic CT scan showing circumferential wall thickening of both iliac arteries.

PET scan showed an appearance of extensive active grade III vasculitis with hypermetabolic foci at the shoulder joints, suggesting polymyalgia rheumatica.



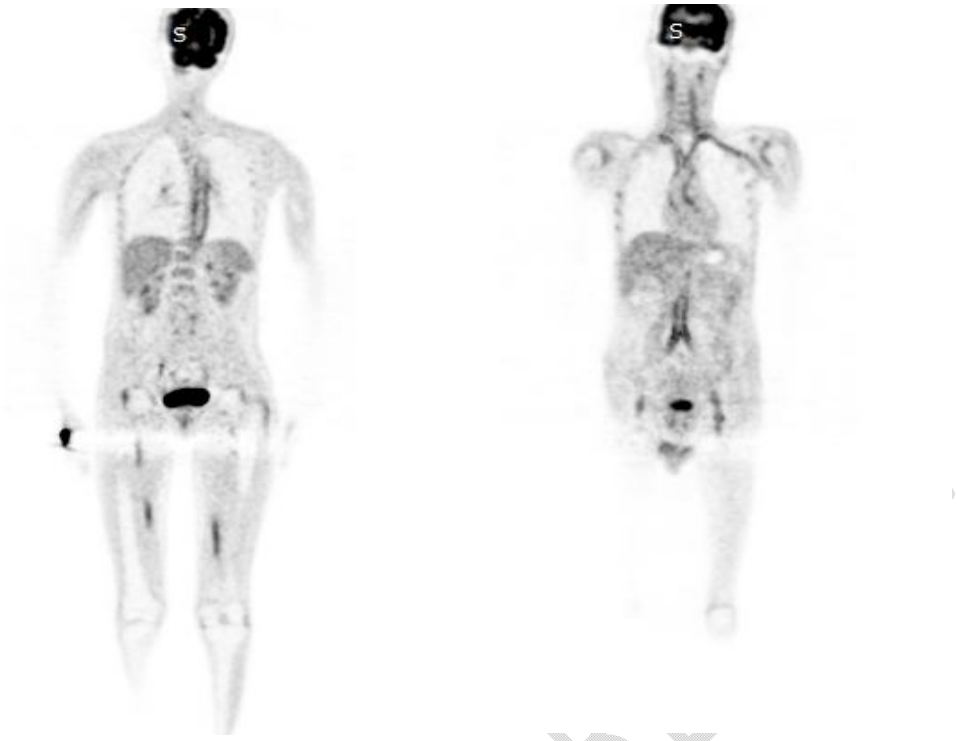


Fig 5. Coronal PET-Scan of the patient showing hypermetabolic uptake in nearly the entire aorta as well as the subclavian and carotid branches, corresponding to grade III vasculitis with hypermetabolic foci in both shoulder joints

Biological assessment showed an inflammatory syndrome with CRP at 32 mg/l and ESR accelerated to 92 mm in the first hour. Immunological assessment was negative for anti-CCP and RF, hyponatremia at 131 mEq/l, creatinine at 13 mg/l, urea at 0.6 g/l, low blood glucose at 0.7 g/l, and mild hypochromic microcytic anemia at 11.5 g/dl. Temporal artery biopsy confirmed granulomatous arteritis of the Horton type.

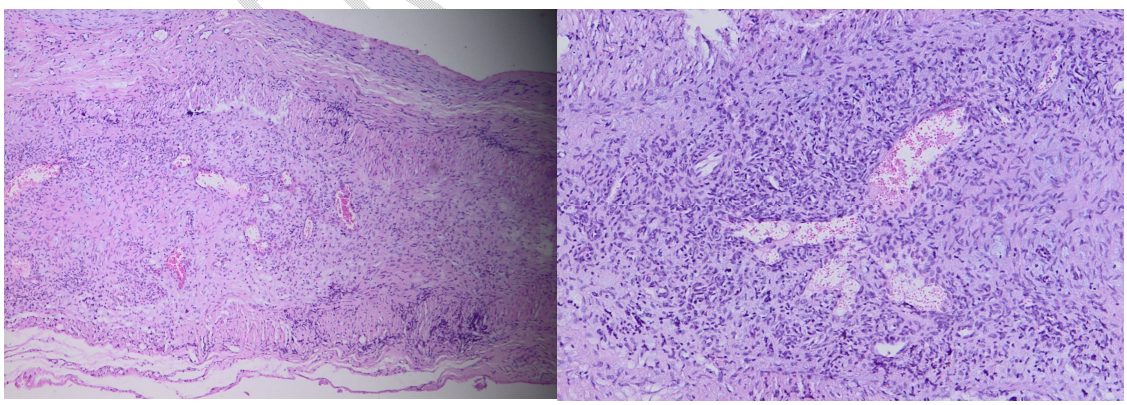


Fig 6. Large caliber vascular wall with significant inflammatory infiltrate of lymphocytes, epithelioid histiocytes, and altered neutrophils.

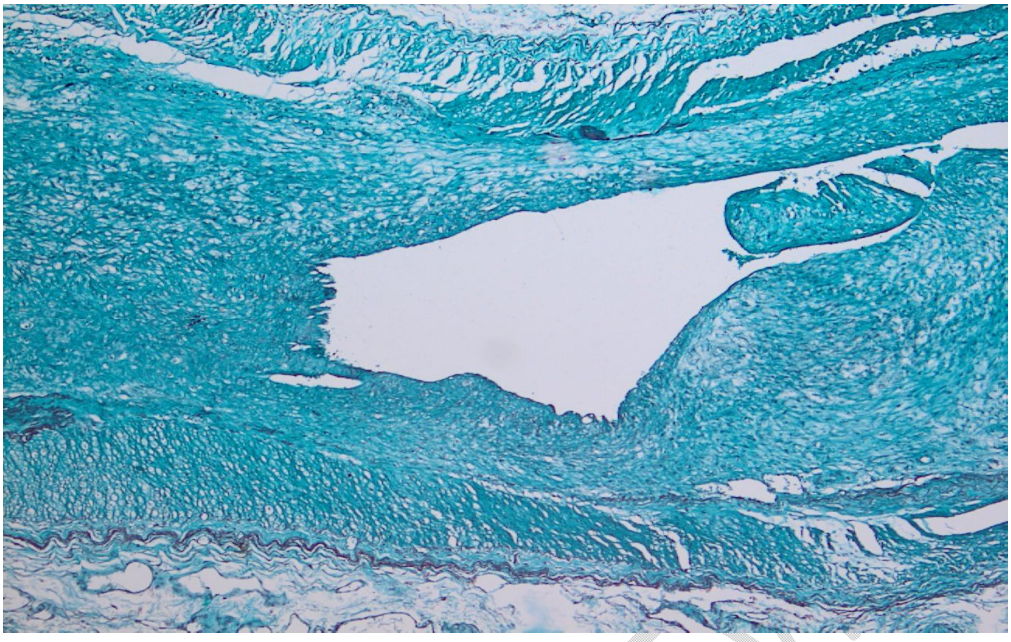


Fig 7. Special orcein staining showing loss of elastic fibers.

The pre-therapeutic assessment was normal, and the patient was started on oral corticosteroid therapy at 0.7 mg/kg/day with spectacular clinical and biological improvement after 3 days.

Discussion:

Giant cell arteritis is a vasculitis of large vessels, affecting the artery and its branches, with a preference for the supra-aortic trunks. The first pathological entity associating blindness with the abolition of temporal pulses was described in the 10th century by Ali Ibn Sina of Baghdad. In the late 19th century, Hutchinson first described giant cell arteritis, and in the early 20th century, Bayard Taylor Horton and Thomas B. Magath histologically described temporal arteritis with giant cells. [1]

Epidemiologically, it is the most common vasculitis, affecting patients over 50 years old with a peak at 70 years, and predominantly affects women (3:1). The etiology remains unknown, although risk factors have been identified, categorized into two types:

- Genetic: A genetic predisposition has been suggested due to familial cases of giant cell arteritis among first-degree relatives [2]. Studies have identified predisposing genes, including HLA-DRB1-04 (class II MHC) [3], HLA-B15 (class I), MICA (class I polypeptide-related sequence A) [4], cytokine-related genes (IL-18, TNF-a, IFN-g, IL-10, IL-17), endothelial markers (ICAM-1, VEGF, eNOS, MMP-9), and components of innate immunity (TLR-4, NLRP-1). A recent genome-wide association study (GWAS) confirmed a strong association between SNPs in the class II HLA region and the development of giant cell arteritis [5,6], and an association with genes involved in vascular remodeling, angiogenesis, and lymphocyte recruitment. [7]
- Environmental: Infections, several studies have attempted to identify an infectious agent responsible, with an increased risk of giant cell arteritis. PCR has detected

genomes of Parvovirus B19, Herpes simplex virus, Varicella-Zoster virus, Human herpes Virus 6 and 7, Cytomegalovirus, and Epstein-Barr virus in temporal artery biopsies. [8-9-10-11-12-13-14]

Pathophysiology is complex but better understood, with vascular walls rich in immature dendritic cells activated by a danger signal (likely a viral infection), remaining in the arterial walls and producing chemokines to recruit CD4 T cells and macrophages. Activated T cells produce pro-inflammatory cytokines, recruiting and activating more macrophages, forming giant cells and granulomas. Endothelial cells produce nitric oxide and giant cells produce reactive oxygen species, causing apoptosis of vascular smooth muscle cells, leading to arterial wall remodeling.

Clinically, giant cell arteritis manifests with an insidious and progressive onset, although it can be sudden. It causes low-grade fever in 10-15% of cases, which our patient did not report, and is characterized by general deterioration, as seen in our patient's 30% weight loss over 6 months and debilitating fatigue. Headaches, present in 60% of cases, were parietal and bilateral in our patient without scalp paresthesia or jaw claudication. Horton's disease can present with pseudopolyarthritis rheumatica (PPZ) in 40-50% of cases, causing shoulder pain and stiffness. Our patient had inflammatory arthralgia of both shoulders without stiffness. The pelvic girdle may also be affected, with thigh root pain. Rarely, arthralgia affects large peripheral joints. Other rare clinical manifestations include dry cough, pleural effusions, pulmonary infiltrates, scalp or lingual necrosis, and peripheral neurological symptoms like mono or multineuritis. Central neurological deficits are even rarer. Horton's disease can cause aortic involvement in 10-15% of cases, leading to asymptomatic or symptomatic aortic arch syndrome with subclavian artery stenosis or thrombosis, causing arm claudication or vasomotor extremity disorders. The most feared ophthalmological complication, affecting 15-20% of patients, is anterior ischemic optic neuropathy due to posterior ciliary artery involvement, rarely causing acute retrobulbar optic neuropathy or central retinal artery occlusion. Blindness can occur suddenly, often bilaterally within 25-50% of cases, and is usually irreversible. Any ophthalmic warning signs (amaurosis fugax, transient diplopia, ocular pain) warrant immediate treatment. [15-16-17-18-19-20-21-22-23]

Biologically, giant cell arteritis is characterized by an inflammatory syndrome with ESR above 50 mm and highly elevated CRP, sometimes exceeding 100 mg/l, with increased alkaline phosphatase in one-third of cases. Temporal artery and supra-aortic trunk exploration by ultrasound Doppler shows luminal narrowing, decreased blood flow, and segmental circumferential thickening, indicating the "Halo" sign. Angio-CT and angio-MRI show arterial wall thickening, particularly in the aorta and encephalic branches, but definitive diagnosis is histological via temporal artery biopsy or, failing that, by PET-CT. Our patient's ultrasound Doppler did not show thickening of the temporal arteries but circumferential thickening of the right carotid, while angio-CT showed inflammatory wall thickening of large and medium caliber arteries without stenosis. PET-CT showed extensive active grade III large vessel vasculitis with hypermetabolic foci at both shoulder joints, suggesting pseudopolyarthritis rheumatica. Finding such a comprehensive presentation clinically, radiologically, and histologically makes our patient an excellent case study.

Conclusion:

Giant cell arteritis, formerly known as Horton's disease, is a vasculitis of large vessels, primarily affecting elderly patients with a female predominance. The major risk is blindness due to ophthalmic artery involvement, and it can rarely be fatal. It should be considered in any elderly patient with prolonged headache or visual acuity decline. Diagnosis is histological via temporal artery biopsy or, if necessary, imaging. Highly corticosteroid-sensitive, the condition shows.

References :

[1] Charles Masson, « La Maladie de Horton », HEGEL, ALN édi ons, 2012, pages 30 à 42. https://dx.doi.org/https%3A//doi.org/10.3917/heg.022.0030

[2] RaptisL, Pappas G, Akritidis N. Horton'sthree sisters: familial clustering of temporal arteritis. Clin Rheumatol 2007;26:1997–8. http://dx. doi.org/10.1007/s10067-007-0610-5.

[3] Gonzalez-Gay MA, Garcia-Porrua C, Hajeer AH, Dababneh A, Ollier WE. HLA-DRB1*04 may be a marker of severity in giant cell arteritis. Ann Rheum Dis 2000;59:574–5.

[4] Gonzalez-Gay MA, Rueda B, Vilchez JR, Lopez-Nevot MA, Robledo G, Ruiz MP, et al. Contribution of MHC class I region to genetic susceptibility for giant cell arteritis. Rheumatol Oxf Engl 2007;46:431–4. http:// dx.doi.org/10.1093/rheumatology/kel324.

[5] Amoli MM, Gonzalez-Gay MA, Zeggini E, Salway F, Garcia-Porrua C, Ollier WER. Epistatic interactions between HLA-DRB1 and interleukin 4, but not interferon-gamma, increase susceptibility to giant cell arteritis. J Rheumatol 2004;31:2413–7

[6] Rodríguez-Pla A, Beaty TH, Savino PJ, Eagle RC, Seo P, Soloski MJ. Association of a nonsynonymous single nucleotide polymorphism of matrix metalloproteinase 9 with giant cell arteritis. Arthritis Rheum 2008;58:1849–53. http://dx.doi.org/ 10.1002/art.23457.

[7] Carmona FD, Vaglio A, Mackie SL, Hernández-Rodríguez J, Monach PA, Castañeda S, et al. A genome wide association study identifies risk alleles in plasminogen and P4HA2 associated with giant cell arteritis. Am J Hum Genet 2017;100:64–74. http://dx.doi.org/ 10.1016/j.ajhg.2016.11.013

[8] Gabriel SE, Espy M, Erdman DD, Bjornsson J, Smith TF, Hunder GG. The role of parvovirus B19 in the pathogenesis of giant cell arteritis: a preliminary evaluation. Arthritis Rheum 1999;42:1255–8 [doi:10.1002/1529-0131 (199906)42:63.0.CO;2-P]

[9] Alvarez-Lafuente R, Fernández-Gutiérrez B, Jover JA, Júdez E, Loza E, Clemente D, et al. Human parvovirus B19, varicella zoster virus, and human herpes virus 6 in temporal artery biopsy specimens of patients with giant cell arteritis: analysis with quantitative real time polymerase chain reaction. Ann Rheum Dis 2005;64:780–2. http://dx.doi.org/10.1136/ ard.2004.025320

[10] Powers JF, Bedri S, Hussein S, Salomon RN, Tischler AS. High prevalence of herpes simplex virus DNA in temporal arteritis biopsy specimens. Am J Clin Pathol 2005;123:261–4.

[11] Helweg-Larsen J, Tarp B, Obel N, Baslund B. No evidence of parvovirus B19, Chlamydia pneumoniae or human herpes virus infection in temporal artery biopsies in patients with giant cell arteritis. Rheumatol Oxf Engl 2002;41:445–9.

[11] Cankovic M, Zarbo RJ. Failure to detect human herpes simplex virus, cytomegalovirus, and Epstein-Barr virus viral genomes in giant cell arteritis biopsy specimens by real time quantitative polymerase chain reaction. Cardiovasc Pathol 2006;15:280–6. http://dx. doi.org/10.1016/j.carpath.2006.05.007.

[12] Nagel MA, White T, Khmeleva N, Rempel A, Boyer PJ, Bennett JL, et al. Analysis of Varicella Zoster virus in temporal arteries biopsy positive and negative for giant cell arteritis. JAMA Neurol 2015;72:1281–7. http://dx.doi.org/ 10.1001/jamaneurol.2015.2101.

[13] Cooper RJ, D'Arcy S, Kirby M, Al-Buhtori M, Rahman MJ, Proctor L, et al. Infection and temporal arteritis: a PCR-based study to detect pathogens in temporal artery biopsy specimens. J Med Virol 2008;80:501–5. http://dx.doi.org/10.1002/jmv.21092.

[14] Nordborg C, Nordborg E, Petursdottir V, LaGuardia J, Mahalingam R, Wellish M, et al. Search for varicella zoster virus in giant cell arteritis. Ann Neurol 1998;44:413–4. http://dx.doi.org/10.1002/ana.410440323.

[15] Gonzalez-Gay MA, Lopez-Diaz MJ, Barros S, Garcia-Porrua C, Sanchez-Andrade A, et al. Giant cell arteritis: disease patterns of clinical presentation in a series of 240 patients. Medicine (Baltimore) 2005; 84:269.

[16] Calamia KT, Hunder GG. Giant cell arteritis (temporal arteritis) presenting as fever of undetermined origin. Arthritis Rheum 1981;24:1414.

[17] Olopade CO, Sekosan M, Schraufnagel DE. Giant cell arteritis manifesting as chronic cough and fever of unknown origin. Mayo Clin Proc 1997;72:1048.

[18] Salvarani C, Giannini C, Miller DV, Hunder G. Giant cell arteritis: Involvement of intracranial arteries. Arthritis Rheum 2006;55:985.

[19] Nuenninghoff DM, Hunder GG, Christianson TJ, Matteson EL. Incidence and predictors of large-artery complication (aortic aneurysm, aortic dissection, and/or large-artery stenosis) in patients with giant cell arteritis: a population-based study over 50 years. Arthritis Rheum 2003;48:3522.

[20] Ninet JP, Bachet P, Dumontet CM, Du Colombier PB, Stewart MD, Pasquier JH. Subclavian and axillary involvement in temporal arteritis and polymyalgia rheumatica. Am J Med 1990;88:13.

[21] Blockmans D. Utility of imaging studies in assessment of vascular inflammation. Cleve Clin J Med 2002;69(Suppl. 2):SII95.

[22] Evans JM, Bowles C, Bjornsson JJ, Mullany CJ, Hunder GG. Thoracic aortic aneurysm and rupture in giant cell arteritis: A descriptive study of 41 cases. Arthritis Rheum 1994;37:1539.

[23] Aiello PD, Trautmann JC, McPhee TJ, Kunselman AR, Hunder GG. Visual prognosis in giant cell arteritis. Ophthalmology 1993;100:550.