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Agnieszka Ciba-Stemplewska[1, 2], Dorota Krzos[3], Anna Kaczmarczyk[1, 2], Magdalena Dolecka-Ślusarczyk[1, 2], Ewa Pater[4], Joanna Roskal-Wałek[2, 5]

[1]Clinical Department of Internal Medicine, Voivodeship Combined Hospital, Kielce, Poland
[2]*Collegium Medicum*, Jan Kochanowski University, Kielce, Poland
[3]Rheumatology Outpatient Clinic, Gorno, Poland
[4]Department of Rheumatology, John Paul II District Hospital, Wloszczowa, Poland
[5]Department of Ophthalmology, Voivodeship Combined Hospital, Kielce, Poland

Giant cell arteritis: Diagnostic difficulties

ABSTRACT

Giant cell arteritis (GCA) is the most common form of vasculitis present in adults. Its symptoms result from ischemia of the areas supplied by the arteries or the severity of the inflammatory reaction: headache, jaw and limb claudication, visual disturbances, blindness, stroke, polymyalgia, and fever. Because of the variety of symptoms, the disease is often overlooked in diagnostics, possibly leading to permanent ischemic complications. The current classification criteria and the gold standard for diagnostics – temporal artery biopsy – apply to the cranial form of the disease. European Alliance of Associations for Rheumatology guidelines have systematized diagnostics, based mainly on simple and reproducible ultrasound examination (ultrasonography). Despite the widespread availability of this imaging method, GCA is still diagnosed too late, and therefore the authors analyzed the possible diagnostic difficulties, based on a group of 21 patients.

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KEY WORDS: giant cell arteritis; blindness; ultrasonography

INTRODUCTION

Giant cell arteritis (GCA) is the most common form of vasculitis diagnosed in patients over the age of 50 (15–25 cases/100 000 people). Women develop the disease twice as often [1]. The essence of the disease is an inflammatory process involving the walls of large and medium-sized arteries, usually the aorta and/or its branches, initiated from the adventitia (vasa vasorum), leading to the formation and infiltration of giant cells, hypertrophy of the intima-media layer (IMT, intima-media thickness), and subsequent deformation of the entire vessel wall [2, 3]. The symptoms are due to ischemia in the supplied areas, while the disrupted structure of the artery wall promotes the formation of aneurysms. The symptoms most commonly identified with GCA are due to extracranial artery involvement: headaches, jaw claudication, tenderness of the temporal region, visual disturbances, and irreversible blindness. There is coexisting polymyalgia rheumatica in 40% of cases. Nevertheless, more nonspecific symptoms may also predominate, related to the extracranial localization of the inflammation and the severity of the inflammatory response: limb claudication, mesenteric ischemia, myocardial infarction, cerebral stroke, fatigue, fever [1]. Giant cell arteritis should be treated as an emergency because of the consequences of vascular complications in cases of delayed diagnosis. The authors analyzed cases of patients hospitalized in the Department of Internal Medicine and Ophthalmology between 2012 and 2023, who were eventually diagnosed with GCA during the diagnostic process.

CASE REPORT

The characteristics of the patients are shown in Table 1.

Medical records of 21 patients (18 patients with the cranial form of GCA and 3 patients with the extracranial form) were analyzed. The mean age was: 75.1 years. Women accounted for 66.7%. At the time of admission, as many

Address for correspondence:
Dorota Krzos, MD
Rheumatology Outpatient Clinic,
Górno 80b,
26–008 Górno, Poland
e-mail: krzosd@wp.pl

Table 1. Patient characteristics

Clinical Data	All patients (n = 21)	GCA, cranial phenotype (n = 18)	GCA, extracranial form (n = 3)
Age (mean ± SD)	75.1 (8.6)	77.4 (6.2)	61.3 (8.6)
Sex			
Female	14 (66.7%)	13 (72.2%)	1 (33.3%)
Male	7 (33.3%)	5 (27.8%)	2 (66.7%)
ESR [mm/h] (mean ± SD)	83.7 (44.6)	79.6 (46.1)	108.3 (28.9)
CRP [mg/L] (mean ± SD)	78.8 (46.5)	75.3 (47.5)	100 (40.9)
Headache (%)	n = 19; 12 (63.2%)	n = 16; 11 (68.8%)	1 (33.3%)
Jaw claudication	n = 19; 9 (47.5%)	n = 16; 9 (56.2%)	0 (0.0%)
Tenderness of the temporal area	8 (42.1%)	8 (50.0%)	0 (0.0%)
Polymyalgia	n = 19; 12 (63.2%)	n = 16; 9 (56.2%)	3 (100.0%)
Weight loss	n = 19; 7 (36.8%)	n = 16; 4 (25.0%)	3 (100.0%)
Subfebrile states	n = 19; 11 (57.9%)	n = 16; 8 (50.0%)	3 (100.0%)
Duration of symptoms (months), mean ± SD	n = 19; 4.1 (2.9)	n = 16; 3.4 (2.2)	8.0 (3.5)
Monocular blindness	n = 17; 11 (64.7%)	n = 14; 11 (78.6%)	0 (0.0%)
Binocular blindness	n = 17; 4 (19.0%)	n = 14; 4 (22.2%)	0 (0.0%)
CT or MR imaging diagnostics with contrast	16 (76.2%)	13 (72.2%)	3 (100.0%)

CRP — C-reactive protein; CT — computed tomography; ESR — erythrocyte sedimentation rate; GCA — giant cell arteritis; MR — magnetic resonance; SD — standard deviation

as 64.9% had monocular blindness, while 19% had binocular blindness. The mean erythrocyte sedimentation rate (ESR) value was: 83.7 mm/h, wherein patients with the extracranial form of GCA had a higher ESR value (108.3 mm/h). Patients with the cranial phenotype declared headaches (68.8%) and jaw claudication (56.2%). The mean duration of symptoms until diagnostics was 4.1 months. The duration of symptoms was longer (8 months) in patients with the extracranial form.

During hospitalization, all patients underwent ultrasound of the head and neck arteries (temporal, carotid, and vertebral arteries, axillary arteries were not evaluated). The IMT complex was not measured in all patients. The examination was performed by radiologists. The halo sign of the temporal artery was visualized in two cases. Computed tomography (CT) or magnetic resonance imaging scan of the head was performed in 72.2% of patients with the cranial form. An magnetic resonance imaging device with a magnetic field strength of 1.5 T (Tesla) was used. Computed tomography scans of the thorax, abdomen, and pelvis with contrast were performed in all patients with the extracranial form. One case included thickening of the aortic wall on a CT scan in a patient without cranial symptoms, diagnosed because of high inflammatory parameters. The suspicion of GCA was suggested by the radiologist in that case. Ultimately, the diagnosis was confirmed by positron emission tomography (PET)/CT with fluoro-18-deoxyglucose radiopharmaceutical (^{18}F-FDG-PET/CT) or temporal artery biopsy. The diagnosis was based on the typical clinical picture and response to treatment in 6 patients of the Ophthalmology Department when a biopsy of the temporal artery was impossible. Treatment based on steroid pulses was started in all patients with visual disturbances before the biopsy result was obtained, based on the high clinical probability, with diagnostics carried out at the same time.

DISCUSSION

It seems that GCA is characterized by low awareness among doctors. The pre-hospital diagnostics took several months. Visual disturbance or diagnostics of elevated parameters of inflammation were the reason for hospitalization. The percentage of patients with visual impairment was high.

What causes diagnostic difficulty and how to improve it?

The current 1990 American College of Rheumatology classification criteria refer to cranial symptoms [4]. These include 5 clinical aspects:

— age > 50 years;
— ESR > 50 mm/h;

— new localized headache;
— tenderness of the temporal artery on palpation;
— temporal artery biopsy result.

These criteria have limitations. Neither of these constitute diagnostic criteria. They concern cranial localization and do not include progress in terms of new imaging methods. New validated 2022 classification criteria include:

— age ≥ 50 years;
— six clinical criteria (morning stiffness of the neck or shoulder girdle, sudden blindness, jaw or tongue claudication, new headache of the temporal region, tenderness of the scalp area, abnormalities on temporal artery examination);
— lab, imaging, and biopsy results (ESR > 50 mm/h or C-reactive protein > 10 mg/L, positive temporal artery biopsy or temporal artery "halo" sign on ultrasound, bilateral axillary artery involvement on imaging tests, abnormal glucose uptake in the descending and abdominal aorta on PET scan) [5].

The 2018 European Alliance of Associations for Rheumatology (EULAR) recommendations systematized diagnostics, recommending temporal artery ultrasound as the first imaging method in patients with suspected cranial manifestations of GCA [6]. The sensitivity of this test is 77%, with a specificity of 96%. The "halo" signs, which are not subject to compression, is representative of GCA [7–9]. If temporal artery evaluation does not yield valid diagnostic results, the axillary arteries or other extracranial arteries should be evaluated next. This is because the axillary arteries and other large vessels may be involved in 50% of cases [10]. Atherosclerotic lesions are localized less frequently in the axillary arteries than in the carotid arteries, making reliable imaging assessment difficult.

The Omeract Group (Outcome Measures in Rheumatology Clinical Trials) for ultrasound in large vessel vasculitis defines normal appearance of the extracranial artery ("pulsatile, hardly compressible, with anechoic lumen"), IMT complex ("homogeneous, hypoechoic or anechoic structure delineated by two hyperechoic lines"), and halo sign as "homogeneous, hypoechoic thickening of the wall, well delineated in the direction of the lumen, visible in both longitudinal and transverse planes, usually concentric in transverse scans" [11]. The cutoff points for minimum IMT in GCA are not established in the recommendations. Atherosclerosis is a common pathology in the GCA patient age group, and results in an IMT increase [12]. Various studies have used different IMT cutoff points, yet there is no defined consensus to date [13–18]. Giant cell arteritis on the axillary artery ultrasound is characterized by the specific "slope sign" — the nature of increased IMT thickness transition to normal thickness [19]. EULAR recommendations also specify the technical parameters of the equipment: 15 MHz linear transducers for temporal arteries and 7–15 MHz for extracranial supra-aortic arteries, and sectoral or convex transducers for aortic arch evaluation. The sensitivity and specificity of ultrasound in GCA were estimated based on tests involving equipment with recommended parameters. CT angiography can be used as a tool in extracranial artery assessment. The thickening of the arterial wall and post-contrast enhancement of the vessel wall in the delayed venous phase, which can manifest as a double ring (inner hypoechoic ring and outer hyperechoic ring), are typical for this condition. Berthod et al. [20] suggest 2.2 mm for assessing aortic thickness as the optimal threshold for diagnosing GCA.

EULAR guidelines recommend using equipment with a magnetic field strength of 3 T (3 Teslas) in GCA diagnostics, particularly for extracranial artery evaluation. The sensitivity and specificity of this test are 75% and 89%, respectively. ^{18}F-FDG-PET/CT allows evaluation of all arteries, including aortic branches, which can be difficult with CT alone, due to vessel size, and also enables differential diagnosis of diseases with similar symptoms (tumors, infections). The sensitivity of the test is estimated at 67–77%, with specificity at 66–100%.

The value of positive radiographic imaging results is increased by EULAR's recommendation not to perform temporal artery biopsies in cases with high clinical probability [6].

Based on history, physical examination, and diagnostic imaging, a rapid diagnostic pathway algorithm for confirming or ruling out GCA was proposed by Sebastian et al. [21]. Southend Pretest Probability Score classifies patients into low, intermediate, and high clinical probability categories for GCA. Probability is assessed based on clinical data: age, sex, duration of symptoms, CRP value, headache, polymyalgia symptoms, ischemic symptoms, visual disturbances, and temporal and extracranial artery abnormalities that are

scored accordingly. The next step is to recommend further diagnostic tests if GCA is likely, with the first test being ultrasonography of the temporal and axillary arteries (a value > 0.29–0.42 mm was considered to be abnormal wall thickness in the temporal, and > 1 mm in the axillary artery, respectively), possibly followed by other imaging tests.

It should be noted that the foregoing algorithm is based on cooperation between the clinician and the ultrasonographer.

The examples provided by our patients prove that this disease is overlooked in diagnostics. The authors hoped that the awareness of both its symptoms and radiological picture, already well documented in the literature and recommendations, will be increased among physicians, resulting in an accelerated diagnostic pace and reduced severe complication rate.

SUMMARY

Giant cell arteritis is overlooked in outpatient diagnostics, as evidenced by months of symptoms and a high rate of ischemic complications in patients admitted to the hospital. At the same time, the paper points out that diagnostic imaging is problematic in facilities with less experience. An ultrasound protocol aimed at ultrasonographers and radiologists describing the arterial evaluation, IMT values, ultrasound signs of GCA well documented in the literature, and technical parameters of medical devices could be helpful.

ARTICLE INFORMATIONS AND DECLARATIONS

DATA AVAILABILITY STATEMENT

The authors declared that the manuscript meets the requirements of the Declaration of Helsinki.

AUTHOR CONTRIBUTIONS

ACS and JRW — development of concepts and assumptions, writing of the paper. EP — methodology. DK and AK —statistics and data analysis. MDŚ — interpretation of results.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

SUPPLEMENTARY MATERIAL

None.

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