

Widespread headache as the first clinical manifestation of giant cell arteritis in patients affected by polymyalgia rheumatica

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Abstract

Introduction: In giant cell arteritis (GCA) headache of new onset due to inflammatory involvement of the temporal artery (TA) represents a diagnostic criterion. A widespread headache (WH) with scalp tenderness due to cranial arteritis can represent another manifestation of GCA.

Material and methods: In 225 elderly patients with polymyalgia rheumatica (PMR) followed in our rheumatologic outpatient clinic from 2004 until June 2016, the frequency of WH as the first clinical manifestation of GCA was evaluated.

Results: Among 26 patients with GCA+PMR (11.6% of total), 5 (23.07%) had WH as first clinical manifestation of GCA without TA. In all these patients TA colour duplex sonography (CDS) and 18-fluorodeoxyglucose positron emission tomography (FDG-PET) with total body contrast-enhanced CT was consistent with the diagnosis of arteritis. TA biopsy was not performed. High doses of prednisone (1 mg/kg/day) led to the immediate and total disappearance of the headache.

Conclusions: The widespread headache should be considered as the first symptom GCA and in cases of suspicion of vasculitis patients should have a full diagnostics examination. Colour duplex sonography and FDG-PET with total body contrast-enhanced CT are useful tools for non-invasive diagnosis of GCA.

Key words: polymyalgia rheumatica, giant cell arteritis, tension headache, widespread headache.

Introduction

Giant cell arteritis (GCA) is considered one of the most common vasculitides in older persons [1]. The branches of the external carotid (including the temporal arteries) are typically involved but every medium- and large-size vessel can be involved. 40–60% of GCA patients have also manifestations of polymyalgia rheumatica (PMR) whereas 10–16% of PMR patients can have manifestations of GCA [2]. Headache of new onset is the most frequent clinical manifestation and represents a diagnostic criterion [3]. Typically it is due to inflammatory involvement of temporal artery (TA), is associated with TA tenderness and decreased pulsation and with a significant increase of inflammatory markers (erythro-

cyte sedimentation rate– ESR; C-reactive protein – CRP). A widespread headache (WH) with scalp tenderness due to cranial arteritis can represent another manifestation of GCA: when it is associated with TA (as usually), there are no diagnostic difficulties; but when it is not and the inflammatory markers are in the normal ranges, differential diagnosis with tension-type headache (TTH) (a type of headache with different therapy and prognosis) is very difficult. As TA, WH can be associated with other typical GCA manifestations such as visual loss (due to ischemia in the territory of the ophthalmic artery) and/or jaw claudication (due to insufficient blood flow to the masseter and pterygoid muscles). Therefore its recognition is essential for the adjustment of corticosteroid therapy.

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Material and methods

We followed 225 elderly patients with PMR in our rheumatologic outpatient clinic from 2004 to June 2016. In PMR+GCA patients we evaluated the frequency of WH as first clinical manifestation of GCA. In all patients with PMR and WH, a TA clinical examination, a TA colour duplex sonography (TA-CDS), the determination of ESR and CRP serum levels, a fundus oculi examination and a 18-fluorodeoxyglucose positron emission tomography (FDG-PET) with total body contrast-enhanced computerized tomography (CT) were performed. TA-CDS was performed by the same ultrasonographer, who was unaware of the patient's clinical data. TA-CDS was carried out after a variable time period (from 2 to 4 months) after the onset of headache: the presence of a headache not controlled by analgesics and present even at night was the main warning, even without inflammatory markers raised. FDG-PET was performed by the same diagnostic center (outside our hospital); it was considered positive for diagnosis in the presence of vascular glucose uptake greater than liver uptake. TA biopsy was not performed.

Results

Among 26 patients (18 females; 8 males, median age = 76 years) with GCA+PMR (11.6% of total), 5 (23.07%) had WH as first clinical manifestation of GCA without TA and without elevation of ESR and CRP. In all these patients TA CDS showed a halo sign (Fig. 1) and all had a FDG-PET picture consistent with the diagnosis of arteritis. The characteristics of these patients are reported in Table I.

When we compared PMR-GCA/WH group (5 patients) vs. PMR-GCA/TA group (21 patients), some significant differences were highlighted: the average time for a correct diagnosis was statistically significant (3 months as average vs. 2 weeks); the onset of vision loss was more frequent in the second group in which the vision loss was the first clinical GCA manifestation in two patients; ESR and CRP were (obviously) much higher in TA group (Table II). No other vascular symptoms occurred in our patients. The switch of corticosteroid dosages from 10/12.5 mg pred-

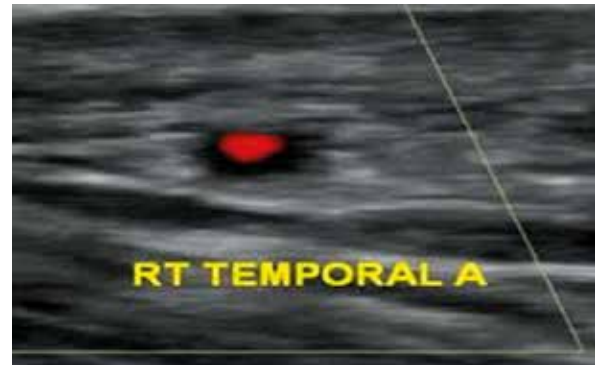


Fig. 1. HALO-SIGN in temporal artery colour duplex sonography.

Table I. Baseline characteristics of the five patients

Gender, n (%)	Male – 1 (20%) Female – 4 (80%)
Age at the date of examination, average (min-max) [years]	73 (68–84)
ESR (min-max) [mm/h]	22–30
CRP (min-max) [mg/l]	2.2–6.00
Disease duration before the diagnosis of WH, min-max [months]	2–8
Patients with halo sign in TA CDS (%)	100
Patients with FDG-CT positive (%)	100

ESR – erythrocyte sedimentation rate; CRP – C-reactive protein; TA CDS – temporal artery colour duplex sonography; FDG-CT – 18fluorodeoxyglucose positron emission tomography with total body contrast-enhanced computerized tomography

nisone or equivalent/day (as average) to 1 mg/kg/day allowed a prompt and permanent resolution of WH.

Discussion

Rarely WH can be the initial manifestations of GCA in PMR patients, in absence of TA. The possibility that GCA can present without elevation of inflammatory markers is well known [4–6]: up to 25% of biopsy-confirmed GCA

Table II. Patients with WH [5] vs. patients with classical TA [21] as first clinical manifestation of GCA overlapping PMR

Parameter	WH	TA	p value*
Gender, n (M, F)	1 M, 4 F	7 M, 14 F	< 0.000
Age at the date of examination – min-max [years]	68–84	70–85	NS
ESR – min-max [mm/h]	22–30	68–110	< 0.0000
CRP – min-max [mg/l]	2.2–6.00	12–66.4	< 0.0000
Disease duration before diagnosis, min-max [months]	2–8	0.5–1.00	< 0.005
Visual loss, n	0	2	< 0.000

*Fisher exact test. P value was considered significant when < 0.05.

patients present with a normal ESR and CRP before corticosteroids are started [7, 8].

TA biopsy is one of the diagnostic criteria for GCA [3, 9] but it is to consider that the absence of typical biopsy features does not exclude diagnosis of GCA [5]. In 1995 Schmidt et al. first described using Doppler ultrasonography a 'halo' sign [10] that is a hypoechoic halo in the artery wall probably caused by oedema. In a meta-analysis published in 2010, Ball et al. [11] highlighted that in the presence of the halo sign the probability of a positive biopsy is high (sensitivity = 75%; specificity = 83%). Besides, the presence of halo sign was even more specific when measured against the ACR criteria instead of TA biopsy (sensitivity = 69%; specificity = 89%) [11]. TA-CDS has been proposed as a useful alternative tool when temporal biopsy cannot be performed [12–14]. A complementary contrast-enhanced CT was acquired immediately after FDG. The metabolic information obtained from 18F-FDG PET combined with the demonstration of wall enhancement and thickness in cranial and extracranial vessels assessed by contrast-enhanced CT is considered more useful for diagnosis of GCA [15]. In other words, in our five patients the absence of TA biopsy did not exclude the diagnosis of GCA since other important clinical and instrumental elements were present.

When WH is present without raised inflammatory markers, TTH must be considered in the differential diagnosis [16]. TTH is known to have a very different therapy and prognosis. The presence of WH during the night and an absence of efficacy of drugs commonly used for TTH should represent important warnings. In our experience, WH (when is a GCA manifestation) is always associated with subclinical involvement of other medium and large-size vessels but no vascular symptom was clinically observed when diagnosis of GCA was made. The very small size of our cohort is a limitation. Therefore the data presented deserve to be confirmed on data from multicenter cohorts. Nevertheless, in consideration of the close relationship between GCA and PMR, WH of recent onset – even if not associated with raised inflammatory markers in PMR patient – should be considered as a possible manifestation of overlapping GCA and specific diagnostic investigations implemented [17, 18].

The possibility that WH without TA involvement can be a favorable prognostic factor for the onset of vision loss should be evaluated in broader statistics.

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