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CORRESPONDENCE

Sir,

Giant cell arteritis with normal ESR and/or CRP is rare, but not unique!

We read the paper by Levy *et al*[1] with interest, however, we believe that it contains several weaknesses which should be discussed.

As it is well known the diagnosis of GCA is based on the combination of clinical symptoms, laboratory test (CRP and ESR), and histopathology.[2] The treatment must be started immediately, thus the temporal artery biopsy result usually confirms presumed diagnosis made on the basis of clinical picture and laboratory tests.

It is well known that laboratory tests in GCA have some limited sensitivity: CRP 86.9% and ESR 84.1%.[2] Both combined gave specificity 97%, but it was shown and discussed in several studies that they might be normal in GCA:[2–5] ESR was normal in 5–30% of patients with GCA.[3] The authors[1] inappropriately stated that 'including their case there are only three published cases of isolated CRP-negative GCA and only two cases of simultaneous ESR and CRP negativity' as they did not notice nor analyze many similar cases (Table 1). Noteworthy, it was postulated that elevated ESR with normal CRP might occur even in 1.7% of GCA patients,[3] and that these markers can be normal at the early stage of the disease.[4]

Having in mind problems with ESR and CRP in GCA, the role of clinical picture of the disease seems to be very important. They include usually headache, tenderness of the scalp, jaw claudication and some systemic symptoms, including malaise, fever, anorexia, and weight loss.[5] The symptoms are based on ischemia and/or inflammation. Thus, it is hard to understand why in the discussed case none of the clinicial symptomes was presented.

Concluding, we agree that diagnosis of GCA might be problematic, but it must be based on clinical picture and laboratory tests, including ESR and CRP, and confirmed by temporal artery biopsy. GCA with normal ESR and/or normal CRP level is rare, but many cases of this form of disease were already described.

Table 1 Some publications reporting normal ESR and/or CRP

References	*Normal ESR (number of cases/ percentage of cases)*	*Normal CRP*
Raja *et al*[6]	1	1
Rahman and Rahman[7]	5–30%	—
Ellis and Ralston[8]	22.5%	—
Kermani *et al*[9]	18 (4%)	18 (4%)
Man and Dayan[10]	1	1
Weintraub[11]	1	—
Wong and Korn[12]	36	—
Parikh *et al*[13]	1 (0.8%)	2 (1.7%)
Laria *et al*[14]	4–15%	0.8%
Yoeruek *et al*[15]	1	1
Myklebust and Gran[16]	1.2%	1.2%

Conflict of interest

The authors declare no conflict of interest.

References

1 Levy SL, Bull AD, Nestel AR. How common is inflammatory marker-negative disease in giant cell arteritis? *Eye* 2013; **27**: 106–108

2 Kermani TA, Schmidt J, Crowson CS, Ytterberg SR, Hunder GG, Matteson EL *et al*. Utility of erythrocyte sedimentation rate and C-reactive protein for the diagnosis of giant cell arteritis. *Semin Arthritis Rheum* 2012; **41**: 866–871.

3 Martínez-Taboada VM, Blanco R, Armona J, Uriarte E, Figueroa M, Gonzalez-Gay MA *et al*. Giant cell arteritis with an erythrocyte sedimentation rate lower than 50. *Clin Rheumatol* 2000; **19**: 73–75.

4 Hall JK. Giant-cell arteritis. *Curr Opin Ophthalmol*. 2008; **19**: 454–460.

5 Grzybowski A, Misiuk-Hojlo M, Szalinski M. A need for new diagnostic tools for giant cell arteritis. *Acta Ophthalmol* 2009; **87**: 109.

6 Raja MK, Proulx AA, Allen LH. Giant cell arteritis presenting with aortic aneurysm, normal erythrocyte sedimentation rate, and normal C-reactive protein. *Can J Ophthalmol* 2007; **42**: 136–137.

7 Rahman W, Rahman FZ. Giant cell (temporal) arteritis: an overview and update. *Surv Ophthalmol* 2005; **50**: 415–428.

8 Ellis ME, Ralston S. The ESR in the diagnosis and management of the polymyalgia rheumatica/giant cell arteritis syndrome. *Ann Rheum Dis* 1983; **42**: 168–170.

9 Kermani TA, Schmidt J, Crowson CS, Ytterberg SR, Hunder GG, Matteson EL *et al*. Utility of erythrocyte sedimentation rate and C-Reactive protein for the diagnosis of giant cell arteritis. *Semin Arthritis Rheum* 2012; **41**: 866–871.

10 Man P, Dayan MR. Giant cell arteritis with normal inflammatory markers. *Acta Ophthalmol Scand* 2007; **85**: 460.

11 Weintraub MI. Temporal arteritis. *Arch Neurol*. 1978; **35**: 183.

12 Wong RL, Korn JH. Temporal arteritis without an elevated erythrocyte sedimentation rate. Case report and review of the literature. *Am J Med* 1986; **80**: 959–964.

13 Parikh M, Miller NR, Lee AG, Savino PJ, Vacarezza MN, Cornblath W *et al*. Prevalence of a normal C-reactive protein with an elevated erythrocyte sedimentation rate in biopsy-proven giant cell arteritis. *Ophthalmology* 2006; **113**: 1842–1845.

14 Laria A, Zoli A, Bocci M, Castri F, Federico F, Ferraccioli GF. Systematic review of the literature and a case report informing biopsy-proven giant cell arteritis (GCA) with normal C-reactive protein. *Clin Rheumatol* 2012; **31**: 1389–1393.

15 Yoeruek E, Szurman P, Tatar O, Weckerle P, Wilhelm H. Anterior ischemic optic neuropathy due to giant cell arteritis with normal inflammatory markers. *Graefes Arch Clin Exp Ophthalmol* 2008; **246**: 913–915.

16 Myklebust G, Gran JT. A prospective study of 287 patients with polymyalgia rheumatica and temporal arteritis: clinical and laboratory manifestations at onset of disease and at the time of diagnosis. *Br J Rheumatol* 1996; **35**: 1161–1168.

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Sir,

Response to Grzybowski and Justynska

We thank Dr Grzybowski and Justynska[1] for their interest in our article.

In response to their comments on our report[2] we acknowledge the inadvertent omission of articles that emphasize the occurrence of inflammatory-marker-negative disease seen in giant cell arteritis (GCA). Unfortunately some papers referred to were not published at the time of writing.[3,4] The table provided by Dr Grzybowski and Justynska highlights some important articles, some of which were referenced in our original report[5] and others which were summarized by key articles referenced.[6,7,8]

Dr Grzybowski and Justynska remark that typical features commonly associated with GCA were not presented in our case. However, the patient we described was indeed unique in that the patient did not display symptoms usually found in GCA other than AION-induced loss of vision and corresponding RAPD in a patient with known polymyalgia rheumatica. These features were described in our report. We fully agree that scrutinizing the clinical picture is critical in the diagnosis of GCA but would like to emphasize that this is exactly what we did. We specifically looked at the clinical presentation including increased pre-test probability due to ethnicity in order to come to the conclusion that the negative CRP needed to be ignored!

We are very grateful for the additional case reports and have integrated them into our original table, thereby giving a more detailed understanding of inflammatory-marker-negative disease (Table 1).

Table 1 Summary of current literature—revised and updated according to comments by Grzybowski and Justynska

	ESR-negative disease	*CRP-negative disease*	*ESR- and CRP-negative disease*
Parikh *et al*[5]	14.3%	1.7%	0.8%
Ellis and Ralston[9]	22.5% at initial presentation		
Weintraub[10]	1 case report		
Levy *et al*[2]		1 case report	
Laria *et al*[4]			1 case report
Kermani *et al*[3]			4%
Yoeruek *et al*[11]			1 case report
Raja *et al*[12]			1 case report
Man and Dayan[13]			1 case report
Poole *et al*[14]			1 case report

Conflict of interest

The authors declare no conflict of interest.

References

1 Grzybowski A, Justynska A. Giant cell arteritis with normal ESR and/or CRP is rare, but not unique! *Eye* 2013; **27**: 1418–1419.
2 Levy SL, Bull AD, Nestel AR. How common is inflammatory marker-negative disease in giant cell arteritis? *Eye* 2013; **27**: 106–108
3 Kermani TA, Schmidt J, Crowson CS, Ytterberg SR, Hunder GG, Matteson EL *et al*. Utility of erythrocyte sedimentation rate and C-reactive protein for the diagnosis of giant cell arteritis. *Semin Arthritis Rheum* 2012; **41**: 866–871.
4 Laria A, Zoli A, Bocci M, Castri F, Federico F, Ferraccioli GF. Systematic review of the literature and a case report informing biopsy-proven giant cell arteritis (GCA) with normal C-reactive protein. *Clin Rheumatol* 2012; **31**: 1389–1393.
5 Parikh M, Miller NR, Lee AG, Savino PJ, Vacarezza MN, Cornblath W *et al*. Prevalence of a normal C-reactive protein with an elevated erythrocyte sedimentation rate in biopsy-proven giant cell arteritis. *Ophthalmology* 2006; **113**(10): 1842–1845.
6 Rahman W, Rahman FZ. Giant cell (temporal) arteritis: an overview and update. *Surv Ophthalmol* 2005; **50**: 415–428.
7 Wong RL, Korn JH. Temporal arteritis without an elevated erythrocyte sedimentation rate. Case report and review of the literature. *Am J Med* 1986; **80**: 959–964.
8 Myklebust G, Gran JT. A prospective study of 287 patients with polymyalgia rheumatica and temporal arteritis: clinical and laboratory manifestations at onset of disease and at the time of diagnosis. *Br J Rheumatol* 1996; **35**: 1161–1168.
9 Ellis ME, Ralston S. The ESR in the diagnosis and management of the polymyalgia rheumatica/giant cell arteritis syndrome. *Ann Rheum Dis* 1983; **42**: 168–170.
10 Weintraub MI. Temporal arteritis. *Arch Neurol* 1978; **35**: 183.
11 Yoeruek E, Szurman P, Tatar O, Weckerle P, Wilhelm H. Anterior ischemic optic neuropathy due to giant cell arteritis with normal inflammatory markers. *Graefes Arch Clin Exp Ophthalmol* 2008; **246**(6): 913–915.
12 Raja MK, Proulx AA, Allen LH. Giant cell arteritis presenting with aortic aneurysm, normal erythrocyte sedimentation rate, and normal C-reactive protein. *Can J Ophthalmol* 2007; **42**: 136–137.
13 Man P, Dayan MR. Giant cell arteritis with normal inflammatory markers. *Acta Ophthalmol Scand* 2007; **85**: 460.
14 Poole TR, Graham EM, Lucas SB. Giant cell arteritis with a normal ESR and CRP. *Eye* 2003; **17**(1): 92–93.

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