Assessing the role of pentraxin-3 in Takayasu's arteritis

Comment on: Plasma pentraxin-3 levels in patients with Takayasu's arteritis during routine follow-up

Alibaz-Oner F *et al*.

Sirs,

We read with great interest the article 'Plasma pentraxin-3 levels in patients with Takayasu's arteritis during routine follow-up', by Alibaz-Oner *et al*. (1). In this cross-sectional study, plasma Pentraxin-3 (PTX3) levels were significantly higher in 94 Takayasu's arteritis (TAK) patients compared to healthy controls, but no differences were found between active and inactive patients. The authors then suggested that PTX3 is of limited aid in the assessment of TAK disease activity. However, this conclusion deserves some comments.

To date, several studies point at PTX3 as a useful biomarker for distinguishing active from inactive inflammation in patients with TAK and other vasculitides (2-4). Previous studies from our group showed that PTX3 determinations are more accurate than CRP and ESR in differentiating between active or inactive TAK (2). Also, PTX3 levels (but not CRP levels) may allow discriminating between patients with active vascular inflammation and those with quiescent disease at imaging (3).

The assessment of disease activity in TAK remains a challenge, as neither clinical symptoms nor currently available biomarkers can accurately differentiate active from inactive disease. Marked limitations of physical examination emerged from a study comparing the predictive value of imaging techniques and physical signs (5). Enhanced-ultrasound and MR angiography may be more accurate in differentiating active from inactive disease (6-7), but are not yet widely available. Variations in erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are neither sensitive nor specific to monitor disease activity: in particular, up to 23% of TAK patients may have active disease despite normal laboratory parameters (8), while a separate study reported elevated ESR levels in 72% of patients with active and in 44% of patients with inactive disease (9).

The discrepancy between our results and those reported by Alibaz-Oner *et al*. (1) resides primarily in the different definitions of active disease adopted by the two studies. Specifically, Alibaz-Oner *et al*. evaluated disease activity with the physician's global assessment (PGA), the NIH-criteria, and the new composite index Indian Takayasu Clinical Activity Score (ITAS2010), also including ESR or CRP (10). Noteworthy, the ITAS2010 scoring system relies solely on clinical examination for the assessment of various parameters, not taking into account imaging data. Given the above-discussed limitations of physical examination and acute phase reactants in differentiating active from inactive TAK, the usefulness of these scores in the routine clinical assessment of disease activity is debatable. Also of note, the scoring system of ITAS2010 places particular emphasis on cardiovascular and larger vessel involvement, thus having limited applicability to cases characterised by subclinical vascular inflammation or mild clinical symptoms. Finally, while acknowledging the relevance of this attempt for a quantitative clinical scoring system in TAK, ITAS2010 should be validated in more sizeable and differentiated cohorts as well as in larger clinical studies before it is incorporated into the clinical practice.

In our previous studies, we relied on particularly stringent criteria to define active and inactive disease at different time points. These included the repeated detection (or absence) of new arterial lesions on angiography, new onset of carotodynia or pain over large vessels, new ischaemic episodes, bruit or asymmetry in pulses, and fever without evidence of infection. When objective readouts are used to determine disease activity over time, PTX3 levels can accurately discriminate between active and inactive TAK (2). In conclusion, sound experimental evidence indicates that PTX3 levels correlate with disease activity in TAK patients (2-4). We advocate for additional investigations to unequivocally confirm and validate the usefulness of this biomarker in the clinical and research settings.

G. De Luca, *MD*
G. Cavalli, *MD*
E. Baldissera, *MD*
L. Dagna, *MD*

Unit of Immunology, Rheumatology, Allergy, and Rare Diseases, IRCCS San Raffaele Scientific Institute Vita-Salute, San Raffaele University, Milan, Italy.

Address correspondence to:
Prof. Lorenzo Dagna,
FEFIM Unit of Immunology, Rheumatology, Allergy and Rare Diseases,
IRCCS San Raffaele Scientific Institute Vita-Salute, San Raffaele Univeristy,
Via Olgettina 60, 20132 Milan, Italy.
E-mail lorenzo.dagna@unisr.it

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References

1. Alibaz-Oner F, Aksu K, Yentur SP, Keser G, Saruhan-Direskeneli G, Direskeneli H: Plasma pentraxin-3 levels in patients with Takayasu's arteritis during routine follow-up. *Clin Exp Rheumatol* 2016; 34 (Suppl. 97):S73-6.
2. Dagna L, Salvo F, Tiraboschi M *et al*.: Pentraxin-3 as a marker of disease activity in Takayasu arteritis. *Ann Intern Med* 2011; 155: 425-33.
3. Tombetti E, Di Chio MC, Sartorelli S *et al*.: Systemic pentraxin-3 levels reflect vascular enhancement and progression in Takayasu arteritis. *Arthritis Res Ther* 2014; 16: 479.
4. Ishihara T, Haraguchi G, Kamiishi T, Tezuka D, Inagaki H, Isobe M: Sensitive assessment of activity of Takayasu's arteritis by pentraxin3, a new biomarker. *J Am Coll Cardiol* 2011; 57: 1712-3.
5. Grayson PC, Tomasson G, Cuthbertson D *et al*.: Vasculitis Clinical Research Consortium. Association of vascular physical examination findings and arteriographic lesions in large vessel vasculitis. *J Rheumatol* 2012; 39: 303-9.
6. Magnoni M, Dagna L, Coli S, Cianflone D, Sabbadini MG, Maseri A: Assessment of Takayasu arteritis activity by carotid contrast-enhanced ultrasound. *Circ Cardiovasc Imaging* 2011; 4: e1-2.
7. Papa M, De Cobelli F, Baldissera E *et al*.: Takayasu arteritis: intravascular contrast medium for MR angiography in the evaluation of disease activity. *Am J Roentgenol* 2012; 198: W279-84.
8. Kerr GS, Hallahan CW, Giordano J *et al*.: Takayasu arteritis. *Ann Intern Med* 1994; 120: 919-29.
9. Maksimowicz-McKinnon K, Clark TM, Hoffman GS: Limitations of therapy and a guarded prognosis in an American cohort of Takayasu arteritis patients. *Arthritis Rheum* 2007; 56: 1000–9.
10. Misra R, Danda D, Rajappa SM *et al*.: Indian Rheumatology Vasculitis (IRAVAS) group. Development and initial validation of the Indian Takayasu Clinical Activity Score (ITAS2010). *Rheumatology* 2013; 52: 1795-801.