in a cohort where biopsy-negative patients were followed for extended periods without long-term corticosteroid treatment [4]. In Monti *et al.*'s cohort [1], nine patients with a positive CDS underwent TAB. Of these, only four (44%) had a positive TAB. This is in keeping with another recent paper published in this journal [5] where only 13/23 (57%) patients with a halo on CDS had corresponding transmural inflammation on US-guided biopsy. Clearly a halo on CDS does not equate with a positive TAB and thus clinicians must be mindful of not attributing the prognostic implications of a positive TAB to patients with a halo on CDS.

Our final comment regarding this study relates to our own dedicated vascular US laboratory experience. As a centre that scans patients for primary vascular diseases, we have found that patients with traditional or novel cardiovascular risk factors with atherosclerosis of the carotid arteries may exhibit increased intima-media thicknesses of the axillary artery in the absence of vasculitis. Indeed, it is not uncommon for these patients to have an axillary intima-media thickness of >1 mm. Furthermore, our centre is reluctant to report vasculitis of the STA in the absence of clearly hypoechoic artery walls with a thickness $\geqslant 0.6$ mm. We believe that the minimum wall thickness cut-offs quoted by Monti *et al.* [1] for axillary arteries of 0.9 mm and STA of 0.4 mm may be normal for some patients with atherosclerotic disease. Further study is clearly needed to better define the confounding effects of atherosclerosis on axillary and STA wall thickness [6].

In summary, we applaud Monti *et al.* [1] for their report of temporal and axillary artery US findings in their GCA cohort. However, we caution clinicians against inferring from this study that a positive CDS has a specificity of 100% for GCA and that a halo on CDS has the same prognostic implications as a positive TAB.

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Comment on: IgG4-related disease presenting with raised serum IgG2—real timeline of IgG4-RD?

Sir, Dunkley and Mudhar [1] describe an infrequent presentation of IgG4-related disease (IgG4-RD) manifesting initially with adult-onset asthma and periorbital xanthogranulomatosis, in addition to an apparently isolated elevation of serum IgG2 (with a normal IgG4). After 3 years, the patient was noted to have elevations of both serum IgG2 and IgG4 (see Table 1). Our group suspects that this evolution of the clinical laboratory findings primarily reflects analytical errors associated with immunonephelometric IgG subclass measurement, rather than the hypothesized evolution of disease from an IgG2-predominant phase to a later phase involving elevation in serum IgG4.

Two major analytical errors that may affect the immunonephelometric IgG subclass methods, when used in patients with IgG4-RD or any patient with an elevation of serum IgG4, have been described: antigen excess, leading to falsely low serum IgG4 measurement in a patient who in fact has a marked elevation of serum IgG4 [2]; and cross-reactivity of the reagent used to measure IgG2 with serum IgG4, leading to falsely high serum IgG2 measurement (this may be attributable to a direct and specific recognition of IgG4 epitopes or to non-specific novel RF interaction) [3, 4].

The means by which these immunonephelometric errors might have affected the clinical laboratory results presented in the report by Dunkley and Mudhar [1] is described in Table 1.

As the methodology used for the serial measurements of IgG subclasses was not described, the proposed interpretations are not definitive. However, in order to understand whether serum IgG2 concentrations are significantly associated with the presence and severity of IgG4-RD in this case, or any other, requires the use of an IgG subclass method, such as mass spectrometry, which has been documented as free from error in the setting of high IgG4 concentrations [4].

TABLE 1 Clinical laboratory IgG subclass concentrations from Dunkley and Mudhar [1], with suggested interpretation

Date	Therapy	Serum IgG2 (1.2–6.6), g/l	Serum IgG4 (0–1.3), g/l	Interpretation
March 2013	Initial	7.24	0.38	Reported IgG2 elevation owing to cross-reactivity of test reagents with IgG4 (i.e. reported IgG2 = actual IgG2 + actual IgG4) Reported IgG4 is normal, instead of markedly elevated, owing to error of antigen excess
February 2014	CS	6.27	0.4	Reported IgG2 decreased modestly owing to a decrease in the actual sum of IgG2 and IgG4 Reported IgG4 is normal, instead of markedly elevated, owing to error of antigen excess
June 2016	MTX	6.43	5.26	Reported IgG2 relatively unchanged with change from CS to MTX, suggesting no marked change in the sum of IgG2 and IgG4 Reported IgG4 increased compared with previous because the error of antigen excess was corrected,[a] allowing the reported IgG4 value to reflect the actual value
December 2016	No therapy for 3 months	11.7	11.5	Off treatment, the actual IgG4 increases, resulting in both the reported IgG4 and the reported IgG2 (= IgG2 + IgG4) concentrations increasing by the same amount, 5.75 (±0.5) g/L

[a]The IgG4 analytical error of antigen excess was published in a major clinical journal in 2014 [2] and, consequently, solutions to the error of antigen excess were published, facilitating clinical laboratory correction of antigen excess errors [5].

In addition, this article highlights the need to reconsider the diagnosis of IgG4-RD in patients who were historically assessed as unlikely to have the disease, on the basis of a low serum IgG4 concentration (that was potentially affected by the error of antigen excess).

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Comment on: IgG4-related disease presenting with raised serum IgG2—real timeline of IgG4-RD?: reply

SIR, We note with interest the response from Mattman *et al.* [1]. We agree that serum IgG subclass measurement is known to be associated with potential analytical errors as described. The methodology for serial IgG subclass measurement in this case was the binding site assays for the Siemens BNII™ nephelometer (latex enhanced for IgG3 and IgG4). The settings were changed between 2014 and 2015 to correct for antigen excess errors.