Reply to the comment on: IgG4-related prostatitis: expanding the spectrum of IgG4-related disease. A systematic review

Sirs,

We thank Suzuki and colleagues for their thoughtful commentary on our systematic review of IgG4-related prostatitis and for sharing an instructive case illustrating key diagnostic pitfalls (1).

In their report, a 72-year-old man with retroperitoneal and pancreatic involvement consistent with IgG4-related disease (IgG4-RD) was found – during malignancy screening – to have a markedly elevated PSA (40.2 ng/mL) and acinar adenocarcinoma confirmed on prostate biopsy, with definitive oncologic management preceding initiation of glucocorticoids for IgG4-RD. This case compellingly reinforces two central messages that align with our review: (i) serum markers and imaging are insufficiently specific to discriminate IgG4-related inflammatory lesions from malignancy at the prostatic level, and (ii) tissue confirmation remains indispensable when clinical, biochemical, or radiologic features are discordant or potentially attributable to cancer.

Our synthesis of 66 reported cases showed wide variability in both serum IgG4 and PSA values, supporting the contention that neither parameter is reliable as a stand-alone discriminator or longitudinal monitoring tool in suspected IgG4-related prostatitis (2). Moreover, malignancy was reported in 18.5% of evaluable cases in our dataset and was associated with poorer outcomes, including higher mortality – observations that heighten the clinical importance of systematic malignancy assessment in this setting. The case presented by Suzuki *et al*. adds important real- world granularity to this signal by demonstrating how prostatic cancer can be clinically subtle on imaging and yet clinically decisive, and how immunosuppression without adequate oncologic exclusion could plausibly delay diagnosis or confound response assessment (1).

We fully agree with the authors that confirmation of IgG4-RD in one organ should not prematurely anchor attribution of additional lesions to IgG4-RD without organ-specific evaluation (3, 4). In practical terms, for patients with known or suspected IgG4-RD who develop lower urinary tract symptoms, disproportionate PSA elevation, or focal prostatic abnormalities, a structured approach is warranted: parallel assessment for systemic IgG4-RD involvement and independent evaluation of the prostate, with biopsy prioritised when malignancy remains plausible. This approach is consistent with the overarching principle – also emphasised in our review – that histopathology is the diagnostic cornerstone for IgG4-RD organ involvement and for excluding mimics, particularly malignancy.

Finally, Suzuki *et al*. highlight emerging discussions regarding paraneoplastic phenotypes and malignancy co-occurrence in IgG4-RD. While case-based literature cannot establish causality, convergent observations across cohorts support heightened vigilance, especially at diagnosis and when atypical features arise (5). Our field would benefit from prospective, multicentre registries with standardised reporting of cancer timing, histopathology, treatment sequencing, and long-term outcomes to clarify (i) the magnitude and timing of malignancy risk and (ii) whether specific IgG4-RD phenotypes, including prostatic involvement, carry differential oncologic associations.

We again thank Suzuki and colleagues for their valuable contribution, which strengthens the clinical take-home message of our review: in IgG4-RD, prostatic involvement should be a diagnosis secured by careful clinicopathologic correlation, not inferred by biomarkers or imaging alone, and malignancy must remain an active consideration even after IgG4-RD has been confirmed elsewhere.

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