Anti-RNA Polymerase III Antibodies as a Risk Marker for Early Gastric Antral Vascular Ectasia (GAVE) in Systemic Sclerosis

To the Editor:

We read with the greatest interest the recent article by Ingraham *et al*, on predictors of gastric antral vascular ectasia (GAVE) in systemic sclerosis (SSc)[1]. In a series of 28 patients with GAVE, only 1 patient was positive for anti-topoisomerase I (topo I), whereas 1 patient had anti-RNA polymerase III (RNAP III) antibodies, and 4 (all with rapidly progressive diffuse cutaneous involvement) had a speckled antinuclear antibody (ANA) pattern. These 4 patients were not tested for anti-RNAP III antibodies, but the authors considered likely that the patients in this group would have anti-RNAP III because of their typical clinical appearance and the absence of anti-topo I. They also reported that, in their clinical practice, another 4 patients with diffuse cutaneous SSc and GAVE were found to be anti-RNAP III positive. For these reasons, they raised the suggestion that anti-RNAP III antibodies may act as predictors for early development of GAVE in SSc patients[1].

We recently reported the clinical data of a series of anti-RNAP III positive SSc patients followed in our center[2]. Interestingly, 3 out of 18 (16.7%) anti-RNAP III positive SSc patients had been diagnosed with GAVE[2]. This proportion is relatively high, considering that GAVE prevalence was estimated at 5.7% in a population of 264 consecutive patients with SSc[3], and suggests a possible predictive role of anti-RNAP III antibodies, as reported by Ingraham, *et al*.

In order to verify the hypothesis that anti-RNAP III and anti-topo I antibodies are associated with different risk for early GAVE in SSc patients, we reevaluated the clinical charts of 453 consecutive patients with SSc and anti-RNAP III or anti-topo I antibodies. More than 99% of patients were Caucasian. The presence of GAVE was identified through endoscopic visual evidence in patients with SSc and unexplained iron deficiency anemia. Anti-topo I were detected by counterimmunoelectrophoresis and anti-RNAP III by ELISA.

Sixteen patients with isolated anti-RNAP III antibodies (16/453; 3.5%) and 101 patients with anti-topo I (101/453; 22.2%) were identified. Three additional patients with anti-RNAP III in combination with other antinuclear specificities (anti-NOR90, anti-topo I, anti-centromere, one case each) were excluded, due to the confounding effect of the double antinuclear specificity. Patients with anti-RNAP III antibodies had more rapid disease onset, defined as the interval from appearance of Raynaud's phenomenon to first symptom other than Raynaud's ($p = 0.0013$). They also had faster skin thickening in the first months after SSc onset ($p = 0.0002$), in comparison with anti-topo I positive SSc patients.

GAVE was diagnosed in 4/16 (25%) SSc patients with anti-RNAP III antibodies, while no SSc patient with anti-topo I antibodies had GAVE (0/101; $p<0.0001$). In two patients with GAVE the main sources of bleeding were the jejunum and the ileum, identified by video-capsule endoscopy. All 4 patients were diagnosed with GAVE within the first year of disease (mean 7 mo; SD: 1 mo), and they suffered from rapid progression of skin involvement.

Therefore, even considering the limitations of a retrospective study, our data suggest that SSc patients with rapid progression of cutaneous disease and anti-RNAP III antibodies are particularly at risk for the early development of GAVE. On the other hand, GAVE seems infrequent in patients with anti-topo I, as reported by others[1,3]. These observations lend further support to the role of SSc specific autoantibodies, such as anti-RNAP III and anti-topo I, which are differently associated with demographic, clinical, systemic, and survival features[4]. Thus, SSc autoantibodies can be very helpful in determining prognosis, as well as options for monitoring and treating patients with SSc. In particular, we agree with the suggestion by Ingraham, *et al* that, with commercial tests now available[1], anti-RNAP III antibodies should be evaluated in all patients with SSc. Lastly, our experience suggests that video-capsule endoscopy may be a useful tool for SSc patients suspected to have early GAVE[5].

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