Improvements in PET/CT results and serum cytokine profile of HLA-B52-positive patients with Takayasu’s arteritis and ulcerative colitis post-tofacitinib

Sir,

We present two cases of patients with Takayasu’s arteritis (TAK) complicated with ulcerative colitis (UC) who successfully sustained remission after the introduction of tofacitinib (TOF), as seen on 18F-fluorodeoxyglucose positron emission tomography (PET) with computed tomography (CT) (PET-CT). The alternation of serum cytokines before and after TOF administration was also evaluated.

The first patient was a 19-year-old male who had been suffering from UC for 2 years. As his colitis was prednisone (PSL) dose-dependently by combination with mesalazine and azathioprine, infliximab (IFX) was initiated in May 2019. However, the patient’s bowel symptoms did not improve, and symptoms like headache, cervical pain, and myalgia in upper limbs with progressive C-reactive protein (CRP) elevation were reported. We suspected complicated aortitis and performed PET-CT, observing high intensities in the thickened aortic wall and in the entire colon, which prompted a diagnosis of TAK. PSL 50 mg/day was administered initially and TOF 20 mg/day was done additionally, causing the prompt amelioration of the disease activity. PSL was...

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**Fig.1.** The interval changes of PET-CT and cytokines.

PET-CT in the chest (A) and pelvis (B) recorded before induction and during tofacitinib monotherapy (C, D) in a male patient (patient #1) with refractory ulcerative colitis to infliximab. Chest PET-CT before (E) and after (F) induction in a female patient (patients #2) with severe arterial valvar regurgitation. Cytokine changes (in pg/ml) before induction therapy and during the maintenance phase in two patients with TA and UC and a patient with TAK alone positive (patient #3) or negative (patient #4) for HLA-B52 (G). The values in the left and right columns in corresponding to patient represent the serum value of each cytokine measured before induction therapy and maintenance, respectively. Cytokines highlighted in red indicate elevation after treatment (thick: approximately more than 2 folds, thin: less than 2 fold), blue highlights indicate a decrease (thick: approximately more than 2 folds, thin: less than 2 fold), and gray highlights indicate almost unchanged values.
tapered-off in April 2020 while keeping a TOF dose. Follow-up PET-CT revealed the suppression of aortitis, and it revealed a significant decrease in the thickening of the aortic wall as well as colon (Fig. 1 A-D). The second patient was a 26-year-old-female who had been suffering from UC for 7 years and managed with mesalazine. She had chest pain followed by dyspnoea exacerbated by exercise in May 2019. A cardiac ultrasound scan revealed severe aortic regurgitation. PET-CT showed diffuse high intensities in the ascending aortic wall, leading to the diagnosis of TAK. We initiated PSL 25 mg/day and TOF 10 mg/day, causing a rapid normalisation of the CRP level. In October 2019, follow-up PET-CT revealed significantly lower intensities in ascending aorta under PSL 12.5 mg/day and TOF (Fig. 1 E, F).

Many cytokines have been associated with TAK and UC (1-3). After comparing cytokine profiles before the introduction of PSL with TOF with those during the maintenance phase with TOF and little to no consecutive PSL, interleukin (IL)-1α, 2, 4, 5, and 23 were all elevated in both patients with UC and TAK. We also studied two patients with TAK only, one of which was positive for HLA-B52, and both were being treated with tocilizumab (TCZ) (Fig. 1 G). If the common pathogenesis is associated with HLA-B52, which can be a risk factor commonly observed in both TAK and UC (4), this mechanism can involve innate immune hyperactivation, leading to the upregulation of many systemic and local cytokines and chemokines. Indeed, more cytokines were altered in patients positive for HLA-B52 compared to those who tested negative for HLA-B52. Actually, recent reports have demonstrated the efficacy of TOF for patients with both TAK and UC (5, 6).

In conclusion, multi-cytokine-targeting drugs like TOF can be reasonable and advantageous for patients with TAK complicated with UC, because of a suggested common pathogenesis involved in both these diseases.

K. INO, MD
N. KINOSHITA, MD
Y. ARINUMA, MD, PhD
Y. MATSUEDA, MD, PhD
K. YAMAOKA, MD, PhD

Department of Rheumatology and Infectious Diseases, Kitasato University School of Medicine, Kanagawa, Japan.

Please address correspondence to:
Dr. Y. Arinuma,
Department of Rheumatology and Infectious Diseases,
Kitasato University School of Medicine,
1-15-1 Kitasato, Minami-ku, Sagamihara,
Kanagawa 252-0374, Japan.
E-mail: y-arinuma@med.kitasato-u.ac.jp

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