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FRI0477 IMMUNOGENICITY OF INFLIXIMAB AMONG PATIENTS WITH BEHÇET'S SYNDROME: A CONTROLLED STUDY

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Background: Immunogenicity of anti-TNFs has been recognised as an important problem that may cause loss of efficacy and adverse events such as infusion reactions. Anti-TNFs are being increasingly used among patients with Behçet's syndrome (BS).

Objectives: We aimed to investigate the prevalence of anti-drug antibodies against infliximab (IFX) in patients with BS together with controls.

Methods: We collected serum samples from 66 consecutive BS patients (51 M, 15 F and mean age 37±9 years) who were treated with IFX. IFX was used for eye involvement in 43, vascular involvement in 12, nervous system involvement in 8 and arthritis in 2 patients. Additionally, 53 ankylosing spondylitis (AS), 25 Crohn's disease (CD) and 27 rheumatoid arthritis (RA) patients, and 31 healthy subjects were included as controls. We included patients who had received at least 4 cycles of IFX. Samples were collected just before an infusion, stored at -80° C until analysis, and serum IFX trough levels and anti-IFX antibodies were measured by ELISA at the same time. We used a cut-off value of 1 µg/mL for serum IFX trough level, extrapolating from RA studies. After serum sampling, we continued to follow up patients.

Results: Anti-IFX antibodies were detected in 4 (6%) BS, 5 (18.5%) RA, 3 (12%) CD, and 1 (%2) AS patient, and in none of the healthy subjects. The mean number of IFX cycles was 19±14 in BS, 21±13 in RA, 19±21 in CD, and 33±18 in AS patients. Allergic reactions had occurred in 9 (14%) BS, 6 (22%) RA, 5 (20%) CD, and 4 (7.5%) AS patients. 3/6 RA patients and 3/5 CD patients who had experienced an allergic reaction had anti-IFX antibodies whereas none of BS and AS patients did.

The median serum IFX trough level was significantly lower in patients with anti-IFX antibodies compared to those without antibodies (2.32 (IQR: 0.6–3.6) vs 3.35 (IQR: 1.63–5.6; p=0.019). The serum IFX trough level was lower than the cut off value in 6/13 patients with anti-IFX antibodies and in 25/158 without anti-IFX antibodies (46% vs 16%; p=0.015).

We were able to get samples before at least 2 consecutive infusions in 27 BS patients and the presence of anti-IFX antibodies was consistent across the samples in all of these patients. We were able to get samples before the infusion and at week 2 in 5 BS patients. Serum IFX level was below 1 µg/mL before IFX and above 1 µg/mL at week 2 in all of these 5 patients.

During a median follow up of 1.5 years, 2/4 BS patients with anti-IFX antibodies had flares. Among the 62 patients without anti-IFX antibodies, 49 are still on IFX and IFX was stopped due to remission in 12 and due to infusion reaction in one patient. Overall, 5 infusion reactions occurred during the follow up (4 without anti-IFX antibodies and 1 with anti-IFX antibodies; 6.5% vs 25%).

Conclusions: Immunogenicity does not seem to be an important problem in BS patients treated with IFX. The frequency of anti-IFX antibodies was lower than RA and CD patients. This might be related to concomitant immunosuppressive and corticosteroid use among BS patients. The presence of anti-IFX antibodies may not be associated with efficacy loss in BS. However, longer follow-up is needed to make that statement as BS has a relapsing-remitting course.

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FRI0478 OCCURRENCE OF GENUINE VASCULITIS IN PATIENTS WITH EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS

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Background: Many patients with eosinophilic granulomatosis with polyangiitis (EGPA) lack a "vasculitic" phenotype and/or are ANCA negative. Recently, the Groupe d'Etudes et de Recherche sur les Maladies Orphelines Pulmonaires developed a revised nomenclature for EGPA and proposed to differentiate it from hypereosinophilic asthma with systemic (nonvasculitic) manifestations (HASM).

Objectives: To evaluate the occurrence of genuine polyangiitis and HASM in a cohort of patients with EGPA.

Methods: We retrospectively studied the medical records of patients with EGPA that fulfilled the classification criteria of the American College of Rheumatology. Patients with genuine vasculitis were identified by at least one of the following criteria:¹ definite vasculitis feature as defined: biopsy-proven necrotizing vasculitis of any organ, biopsy-proven necrotizing glomerulonephritis or crescentic glomerulonephritis, alveolar haemorrhage, palpable purpura, myocardial infarction due to proven coronary arteritis;² strong surrogate of vasculitis as defined: haematuria associated with red casts or ≥10% dysmorphic erythrocytes, or haematuria and 2 +proteinuria on urinalysis related to the systemic disease; and any organ manifestation other than ENT or bronchopulmonary manifestation associated with leukocytoclastic capillaritis and/or eosinophilic infiltration of the arterial wall;³ mononeuritis multiplex;⁴ ANCA with at least one extra-thoracic non-ENT manifestation of disease.

Results: We followed 68 patients with EGPA for a mean ±SD of 6.3±6.5 years (587.7 patient-years). There were 19 males and 49 females. Their mean ±SD age was 49.5±13.8 years. In 18 patients (26.5%) with EGPA diagnosis was revised in favour of HASM using the new criteria (table 1). Notably, 19 of 50 patients (38%) with genuine polyangiitis were ANCA-negative but have histological evidence or clinical signs (rapidly progressive glomerulonephritis in 1, mononeuritis multiplex 7, palpable purpura in 5) of definite vasculitis. The majority of patients in both groups were females of similar age at disease onset. The occurrence of constitutional symptoms, except myalgia, nasal involvement, cardiovascular and pulmonary manifestations did not differ between patients with genuine polyangiitis and HASM. However, patients with EGPA usually required more intensive immunosuppressive treatment, including cyclophosphamide, while monotherapy with moderate to high dose corticosteroids was adequate for the majority of patients with HASM.

Table 1 Clinical and demographic characteristics of patients with genuine EGPA and HASM

	All, n=68	HASM, n=18	EGPA, n=50	p
Age at diagnosis, years	49.5 (36; 56)	50 (35; 55)	49.0 (37; 57)	0.91
Females, n (%)	49 (72.1)	17 (94.4)	32 (64.0)	0.014
Follow up, months	52.5 (22; 89)	57 (33; 92)	49.0 (19; 83)	0.44
Asthma, n (%)	64 (94.1)	16 (88.9)	48 (96.0)	0.28
Chronic rhinosinusitis, n (%)	56 (82.4)	14 (77.8)	42 (84.0)	0.72
Nasal polyposis, n (%)	28 (41.2)	6 (33.3)	22 (44.0)	0.58
General manifestation				
Fever >38°, n (%)	49 (72.0)	11 (61.1)	38 (76.0)	0.24
Weight loss, n (%)	19 (27.9)	5 (27.8)	14 (28.0)	1.00
Myalgia, n (%)	32 (47.1)	4 (22.2)	28 (56.0)	0.026
Arthralgia, n (%)	40 (58.8)	13 (72.2)	27 (54.0)	0.26
Arthritis, n (%)	17 (25.0)	4 (22.2)	13 (26.0)	1.00
Definite vasculitis features				
Alveolar hemorrhage, n (%)	1 (1.5)	0	1 (2.0)	1.00
Purpura, n (%)	13 (19.1)	0	13 (26.0)	0.015
Strong vasculitis surrogates				
Haematuria, n (%)	11 (16.2)	1 (5.6)	10 (20.0)	0.26
Other features of polyangiitis				
Mononeuritis multiplex, n (%)	19 (27.9)	0	16 (32.0)	0.001
ANCA, n (%)	31 (45.6)	0	31 (62.0)	<0.0001
Cardiac and vascular manifestations				
Pericarditis (echocardiography and/or CT), n (%)	11 (16.2)	2 (11.1)	9 (18.0)	0.71
Myocarditis, n (%)	9 (13.2)	1 (5.6)	8 (16.0)	0.43
Venous thrombo-embolism, n (%)	7 (10.3)	0	7 (14.0)	0.18
Renal manifestation				
Renal disease, n (%)	6 (10.3)	0	6 (12.0)	0.18
Proteinuria, n (%)	4 (5.9)	0	4 (8.0)	0.30
Urinary syndrome, n (%)	14 (20.6)	0	14 (28.0)	0.014
The increase in creatinine, n (%)	5 (7.4)	0	5 (10.0)	0.31
Other glomerulonephritis, n (%)	3 (4.4)	0	3 (6.0)	0.56
Neurologic manifestations				
Peripheral neuropathy, n (%)	50 (73.5)	8 (44.4)	42 (84.0)	0.004
Cutaneous manifestations				
Livedo, n (%)	3 (4.4)	1 (5.6)	2 (4.0)	1.00
Urticaria, n (%)	7 (10.3)	3 (16.7)	4 (8.0)	0.37
Erythema, n (%)	12 (17.7)	3 (16.7)	9 (18.0)	1.00
Papules, n (%)	6 (8.8)	2 (11.1)	4 (8.0)	0.65
Gastro-intestinal manifestations				
Eosinophilic gastroenteritis, n (%)	5 (7.4)	1 (5.6)	4 (8.0)	1.00
Abdominal pain, n (%)	6 (8.8)	0	6 (12.0)	0.18
Other manifestations				
Lung infiltrates, n (%)	35 (51.5)	12 (66.7)	23 (46.0)	0.17
Pleural effusion, n (%)	6 (8.8)	1 (5.6)	5 (10.0)	1.00
Perforation of the nasal septum, n (%)	5 (7.4)	0	5 (10.0)	0.31

Conclusions: At least a quarter of patients with EGPA classified according to the ACR criteria do not have genuine polyangiitis. The revised criteria of EGPA and HASM may have a significant value for choosing treatment options.

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