POS1341

TOCILIZUMAB FOR THE TREATMENT OF IMMUNE-RELATED ADVERSE EVENTS TO IMMUNE CHECKPOINT INHIBITORS: A CASE SERIES

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Background: Immune checkpoint inhibitors (ICI) are pharmacological agents effectively used in the treatment of several malignant tumors. The hyperactivation of the immune system induced by ICI may trigger an inflammatory involvement of healthy tissues, a phenomenon referred to as immune-related adverse event (irAE). No clinical trials are available to guide the management of irAEs. Observational data suggest tocilizumab might be effective in severe cases of irAEs, but data are scant. The possibility of continuing ICI treatment despite the development of irAE and the subsequent initiation of tocilizumab has never been evaluated.

Objectives: To evaluate the efficacy and safety of tocilizumab, as monotherapy or alongside the continuation of ICI treatment, in the management of irAEs.

Methods: We retrospectively identified patients who developed irAEs and were referred to our specialized Clinic between May 2018 and December 2020. Among these patients, we identified those who had been treated with tocilizumab and collected information about their oncologic history and outcome, ICI therapy and irAEs.

Results: Thirty-nine patients were referred to our outpatient Clinic following the development of irAEs. Five of them were treated with tocilizumab. Disease and demographic features are reported in Table 1. At irAEs onset all patients were treated with glucocorticoids. A steroid-sparing agent was started to permit an adequate prednisone tapering without the irAE relapsing. Before tocilizumab start, two patients were treated with methotrexate monotherapy, one with anakinra monotherapy, and one with methotrexate and anakinra combination therapy. A significant therapeutic effect was confirmed in all patients and no significant adverse reactions were reported. ICI therapy was permanently discontinued in two patients. In the other three cases, cancer immunotherapy was safely continued alongside tocilizumab without further irAEs occurring. Only one patient experienced tumor progression two years after ICI suspension and subsequently died despite the improvement of his myocardial inflammatory involvement.

Conclusion: In our cohort, tocilizumab proved to be an effective and safe therapy for the management of irAEs.

Our case series also supports the possibility of maintaining ICI while introducing tocilizumab for irAE treatment. This combined approach might represent a suitable therapeutic option to guarantee a significant anti-inflammatory activity without losing the oncologic response.

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Table 1. Clinical characteristics of patients who developed irAEs secondary to ICI therapy and who received tocilizumab.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age at irAE onset (years)	69	52	72	57	75
Sex	Male	Male	Male	Female	Female
Neoplastic histology	NSCLC	NSCLC	NSCLC	NSCLC	Pleural mesothelioma
ICI treatment	Nivolumab	Nivolumab	Pembrolizumab	Pembrolizumab	Pembrolizumab
irAE	Myocarditis	Arthritis	Arthritis	Arthritis	Large vessel vasculitis
ICI discontinuation due to irAE	Yes	No	No	No	Yes
PDN initial dose (mg daily)	50	37.5	25	25	37.5
DMARD therapy	T16: ANK T20: TCZ T26: TCZ + MMF	T5: MTX T6: MTX + ANK T11: MTX + TCZ	T3: MTX T11: MTX + TCZ	T4: MTX T6: MTX + TCZ	T3: TCZ
irAE outcome	Improvement	Low disease activity	Low disease activity	Remission	Remission
Follow-up length (months)	50 10	47 25	57 2	25 5	26 8
Since oncologic diagnosis					
Since TCZ start					
Oncological outcome	Progressive disease and death	Complete response	Stable disease	Stable disease	Complete response

* Treatment chronology is referred to as a T followed by the number of months since irAE onset. ANK, anakinra; ICI, immune checkpoint inhibitor; irAE, immune-related adverse events; DMARD, disease modifying anti-rheumatic drug; MTX, methotrexate; NSCLC, non-small cell lung cancer; PDN, prednisone; TCZ, tocilizumab.

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POS1342

CHEMOPROPHYLAXIS IN LATENT TUBERCULOSIS ASSOCIATED WITH RHEUMATIC IMMUNE-MEDIATED DISEASES. STUDY OF 240 PATIENTS FROM A SINGLE UNIVERSITY HOSPITAL

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Background: Tuberculosis (TB) may be increased with biologic therapy (BT). Diagnosis and treatment of latent TB infection (LTBI) is the best strategy to prevent TB. In Rheumatic Immune-Mediated Diseases (R-IMID) and LTBI, chemoprophylaxis must be used before BT. The drugs more frequently used are Isoniazid (INH), Rifampicin (RIF) and Fluoroquinolones (FQ). These drugs may be associated with side-effects, especially hepatotoxicity.

Objectives: To assess, in a single University Hospital, a) used chemoprophylactic drugs and, b) adverse events with these drugs.

Methods: We included all consecutive patients in the last five years (2016-2020) with a diagnosis of R-IMID and a positive LTBI test (positive tuberculin skin test and/or interferon-γ-release assay), who received chemoprophylaxis prior to BT. Dose of chemoprophylactic drugs were a) INH (5 mg/kg/d, maximum, 300 mg; for 9 months with vitamin B6), b) RIF (10 mg/kg/d, maximum, 600 mg for 4 months) and c) FQ levofloxacin (500 mg/day for 9 months).

In all patients analytic controls that included liver enzymes were performed at the 1st and 3rd month and then at a variable time.

Results: 240 patients were analyzed (165 women/ 75 men), mean age of 56±11 years. The underlying R-IMID of patients receiving chemoprophylaxis were rheumatoid arthritis (n=74, 30.8%), axial spondyloarthritis (n=59, 24.6%), psoriatic arthritis (n=62, 25.8%), connectivopathies (n=17, 7.1%), vasculitis (n=12, 5%), sarcoidosis (n=2, 0.8%), Behçet's disease (n=1, 0.4%), inflammatory myopathies (n=1, 0.4%) and other (n=12, 5%).

At the onset of chemoprophylaxis they were taking: Prednisone in 61 patients (24 of them above 10 mg/day) and the following conventional DMARD, methotrexate (n=109, 45.4%), hydroxychloroquine (n=20, 8.3%), sulfasalazine (n=11, 4.6%), leflunomide (n=4, 1.7%) and azathioprine (n=2, 0.8%).

The first-line chemoprophylactic drug was INH in 232 (96.7%) patients and RIF in the remaining 8 (3.3%). Due to adverse events, second-line therapy was used in 18 (RIF, n=17 and Levofloxacin, n=1) patients previously treated with INH.

Adverse events were more frequent with INH, being observed in 55 patients (23.7%) out of 232. (Table 1 next page, Figure 1 below). By contrast, only 1 out of 25 (4%) receiving RIF presented an adverse event, which was hepatotoxicity, requiring suspension of RIF. No adverse events were described in the only patient receiving levofloxacin.

Figure 1. Liver enzyme elevation over baseline in patients in treatment with isoniazid.* Patients with higher liver enzyme elevation are included in the previous groups.

Conclusion: INH is the most used first-line treatment for LTBI. RIF was mainly used as second-line therapy if an adverse event with INH was observed. Treatment was generally well tolerated and most adverse events did not require the withdrawal of the treatment. Hepatotoxicity was the most frequent adverse event with INH and the most frequent cause of treatment withdrawal.

Table 1. Adverse events with isoniazid at months 1 and 3 and after month 3

Adverse events, n (%)	Month 1 (n=232)			Month 3 (n=222)			After month 3 (n=214)		
	Total	Requiring switching	Requiring suspension	Total	Requiring switching	Requiring suspension	Total	Requiring switching	Requiring suspension
Hepatotoxicity	38 (16.4)	6 (2.6)	0	33 (14.9)	5(2.3)	2 (0.9)	16 (7.5)	2 (0.9)	0
Gastrointestinal side effects	4 (1.3)	3 (1.3)	1 (0.4)	3 (1.5)	0	3 (1.5)	2 (0.9)	0	1 (0.5)
Cutaneous toxicity	2 (0.9)	1 (0.4)	0	0	0	0	0	0	0
Dizziness	1 (0.4)	1 (0.4)	0	0	0	0	0	0	0
Total	44 (19)	11 (4.7)	1 (0.4)	36 (16.2)	5 (2.3)	5(2.2)	18 (8.4)	2 (0.9)	1 (0.5)

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POS1343

ABNORMAL ELECTROCHEMICAL SKIN CONDUCTANCE VALUES IN PATIENTS WITH AA AMYLOIDOSIS

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Background: Clinical manifestations are scarce in AA amyloidosis (AAA) and, contrary to other types of amyloidosis, involvement of the peripheral nervous system was rarely reported in AAA. However, the usual absence of hypertension despite chronic renal failure and the digestive involvement may be secondary to dysautonomia, but the autonomic nervous system has rarely been studied in AAA (1). Measure of the electrochemical skin conductance (ESC) is a simple and reproducible method to evaluate the function of eccrine sweat glands, which are innervated by small non-myelinated C fibers, and patients with AL and hereditary transthyretin amyloidoses show decreased ESC values (2,3).

Objectives: To evaluate ESC values by Sudoscan in patients with AAA.

Methods: Patients diagnosed as having AAA based on positive immunohistochemistry with an anti-serum amyloid A antibody followed at the national reference center for AAA in Tenon Hospital between July, 2017 and September, 2020, were routinely assessed for ESC with FDA approved Sudoscan (Impeto Medical, Paris, France). An ESC value above 60 microSiemens (μS) or 70 μS were considered normal for hands or feet, respectively. Categorical variables are reported as percentages and continuous variables are expressed as means±standard deviation. Correlations between age, body mass index (BMI), hemoglobin levels, C-reactive protein levels, estimated glomerular filtration rate using the Chronic Kidney Disease Epidemiology Collaboration equation (defined as 0 for dialysis patients) and ESC values were calculated using the nonparametric Spearman test. GraphPad Prism Version 7 software (GraphPad Software, San Diego, California, USA) was used for statistical analyses. A p-value <0.05 was considered as statistically significant.

Results: Overall, 32 patients (16 women) were included, with a mean age of 57.4±13.6 years and a mean BMI of 25.2±6.8 kg/m². Six (19%) had diabetes mellitus, and 5 (16%) had a kidney transplantation. The main causes of AAA were: monogenic autoinflammatory diseases (n=11, 34%, including 9 patients with familial Mediterranean fever), chronic and/or recurrent infections (n=5, 16%), obesity (n=3, 9%) and undefined (n=3, 9%). The mean hands' ESC values was normal at 65.5±21.1 μS, although 8 (25%) patients had ESC values below 60 μS, including 2 diabetic patients. In contrast, the mean feet's ESC values was abnormal at 62.7±23.7 μS, including half of the patients with ESC values below 70 μS (2 diabetic patients). Eight patients had abnormal ESC values only for feet, and 1 had abnormal values only for hands. Apart from a significant correlation between feet and hands' ESC values (p<0.0001), only the estimated glomerular filtration rate was significantly associated with hands' ESC values (p<0.01).

Conclusion: To our knowledge, this is the first study to assess ESC in AAA. Feet's ESC values were moderately impaired in half of the patients with AAA. Therefore, this study reinforces the previously reported alterations in the autonomic nervous system in patients with AAA that should probably be searched for in these patients. In addition, the identification of an alteration of the ESC values cannot allow to distinguish the type of amyloidosis.

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POS1344

EVALUATING THE MULTIVISCERAL INVOLVEMENT ON ADULT-ONSET STILL'S DISEASE TO RETRIEVE IMAGING-BASED DIFFERENCES IN PATIENTS WITH AND WITHOUT MACROPHAGE ACTIVATION SYNDROME; RESULTS FROM A SINGLE-CENTRE OBSERVATIONAL STUDY

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Background: Adult-onset Still's disease (AOSD) is a rare systemic inflammatory disorder usually affecting young adults, burdened by life-threatening complications, mainly macrophage activation syndrome (MAS), a secondary form of hemophagocytic lymphohistiocytosis [1]. In this context, the importance of an accurate assessment of AOSD is suggested to promptly recognise the multivisceral involvement of the disease which is associated with life-threatening complications. The assessment of the most aggressive subsets of the disease could guide the clinicians when to apply additional resources but avoiding unnecessary expenditures in patients with a less severe clinical picture.

Objectives: In this study, we aimed at describing the multivisceral involvement of the disease to retrieve imaging-based differences in AOSD patients with and without MAS.

Methods: The present evaluation has been designed as a cross-sectional study to descriptively compare the multivisceral involvement in AOSD patients with and without MAS. Patients admitted to our Institution, who underwent a total body CT scan, were selected from our historical cohort and assessed. Clinical and CT scan characteristics of AOSD patients with and without MAS were compared. Clinical and CT scan characteristics of AOSD patients with and without MAS were analysed by parametric or non-parametric t tests for all continuous variables, and chi squared test was used for categorical ones, as appropriate. Furthermore, possible correlations among radiological outcomes with laboratory markers and systemic score were estimated by using a point-biserial coefficient correlation.

Results: This study evaluated 39 AOSD patients (men 64.1%), mean age of 48.8±16.6 years). Out of those, 14 patients (35.9%) were complicated by MAS. These patients showed higher values of ferritin [AOSD: 770.0 (1306.5) ng/mL vs MAS: 2926.3 (4918.5) ng/mL p=0.003] and systemic score (AOSD: 4.6±1.4 vs MAS: 6.9±1.7, p<0.0001). AOSD patients with MAS presented a higher prevalence of lung disease than others (AOSD: 56.0% vs MAS 85.7% p=0.048). Lung disease correlated with the systemic score (coefficient 0.491, p=0.003). AOSD patients with MAS were more frequently characterised by hepatomegaly (AOSD: 12.0% vs MAS: 50.0% p=0.019) and splenomegaly (AOSD: 16.0% vs MAS 50.0% p=0.033), respectively, than others. Hepatomegaly correlated with CRP (coefficient 0.421, p=0.016), ferritin (coefficient 0.397, p=0.020), and systemic score (coefficient 0.391, p=0.022). Furthermore, the presence of splenomegaly correlated with the systemic score (coefficient 0.439, p=0.009). CT scan features of abdominal effusions were more frequently observed in AOSD patients with MAS than those without this complication (AOSD: 12.0% vs 57.1% p=0.007).