Cellular Analysis of Bronchoalveolar Lavage Fluid to Narrow Differential Diagnosis of Checkpoint Inhibitor-related Pneumonitis in Metastatic Melanoma

P501

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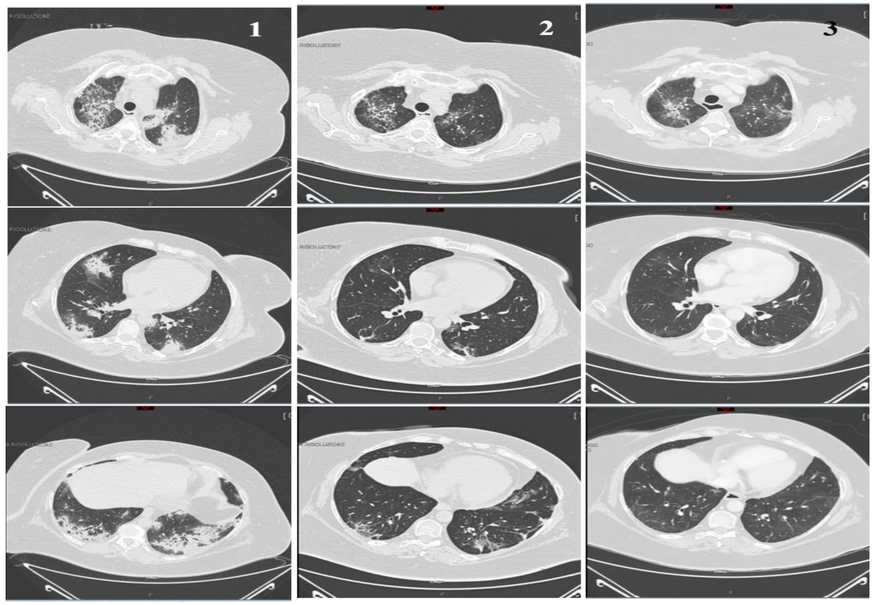
Background

The diagnosis of check-point inhibitor-related pneumonitis (CIP) relies on radiological and clinical patterns which are not specific and can mimic other conditions (cancer progression, infectious diseases or interstitial pneumonitis). Cell pattern analysis of bronchoalveolar lavage (BAL) is well-known to support the diagnosis of interstitial lung disease; nevertheless, this analysis is somewhat performed and not required by immune-toxicity management guidelines for CIP.

Methods and Materials

We conducted a single-center study by recruiting patients with stage IV melanoma treated with anti PD-1 alone or with anti-CTLA4 who underwent BAL after developing respiratory symptoms associated with computed tomography (CT) scan imaging suspected for CIP. We also correlated the BAL features with the computed tomography (CT) scan patterns and with various peripheral blood parameters to better define the profile of this patient population.

Fig. 1 CT images at different time points (1 at admission, 2 after 1 month and after i.v. methylprednisolone, 3 after 4 months) showing a COP pattern



Results

Among 112 patients treated with check-point inhibitors in 2018–2019 we identified 5 (4%) cases of CIP. There were 3 men, median age 58 years (43-77), in four cases the ongoing therapy was anti-PD1. Median time of onset was 44 weeks (6-88), according to CTCAE 5.0 we observed grade 3 toxicity in 2 cases, grade 4 in 2 cases and grade 2 in 1 case. One patient also had grade 3 colitis and two patients developed vitiligo as skin toxicity.BAL flow cytometer and cytopathology analyses showed typical and homogeneous features with increased lymphoid population, prevalent CD8+ T cells and inversion of the CD4/CD8 ratio. Moreover, the extent of activated CD3+HLA-DR+ T cells was related to the grading of adverse events (table 1). Blood leucocytosis, hypoxemia, normal values for procalcitonin and lactate dehydrogenase were also found together with a cryptogenic organizing pneumonia-like radiologic pattern. All patients recovered from pulmonary toxicity after corticosteroid treatment for a median time of 2 months (range 2-12). PD1 inhibitors were permanently discontinued in 4 patients, whereas one patient was re-started on treatment until disease progression. Interestingly, in all our patients CIP was associated with partial or complete response.

Fig. 2 – Aaa ccc

Conclusion

Identification of a specific BAL cellular pattern allows clinicians to place this investigation in the appropriate position of CIP diagnosis and management to avoid misdiagnosis or considering this condition as progressive disease and delaying proper treatment.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Normal range
Total cells (x 10^5/ml)	1,8	1,8	2,5	1,5	1,3	
Macrophages	78%	80%	77%	72%	66%	75-85%
Neutrophils	0	0	5%	3%	2%	1-2%
Lymphocytes	22%	20%	26%	24%	30%	8-12%
Eosinophils	0	0	2%	1%	2%	0-0,5%
T CD3+	99%	95.8%	96%	95%	93%	70-90%
T CD4+	35%	17.2%	41%	38%	39%	35-45%
T CD8+	60.3%	77%	52%	47%	50%	30-40%
Natural killer CD3- CD16+CD56+	0,70%	2,60%	3%	2%	3%	1-7%
B CD19+	0	0,50%	1%	1%	1%	0-7%
CD4/CD8 RATIO	0.6	0,2	0,7	0,8	0,7	0,8-2
CD3+HLA-DR+	25.8%	36%	31%	24%	13%	

Tab. 1 – Flow cytometer of BAL in 5 melanoma patients with CIP