T2 and T3 cytokine expression in asthma with chronic rhinosinusitis

V. Carriero[1],E. Arrigo[1], F. Bertolini[1], F. L. M. Ricciardolo[1]

[1]Department of Clinical and Biological Sciences, University of Turin- Orbassano,Turin (Italy),[2]Severe Asthma and Rare Lung Disease Unit, San Luigi Gonzaga University Hospital- Orbassano, Turin (Italy).

INTRODUCTION

Asthma and chronic rhinosinusitis (CRS) represent frequent comorbidities, leading to severe and poor-controlled disease.

Two phenotypes of CRS are distinguished whether nasal polyps are present (CRSwNP) or not (CRSsNP), the former with a better-known inflammatory and immunologic signature (T2), the latter being not yet clarified.

AIMS AND OBJECTIVES

The project aims to characterize asthmatic patients with CRS (both CRSwNP and CRSsNP) from a clinical, functional and bio-pathological point of view, and to identify specific biomarkers associated with the two phenotypes.

METHODS

We performed immunohistochemical staining on 33 bronchial biopsies (BB) of asthmatics divided into CRSwNP (N=11), CRSsNP (N=11) and no CRS (asthma without CRS, N=11).

We assessed the expression of T2 and T3 inflammatory cytokines (IL-5, IL-13, Eotaxin-3, IL-17F, IL-17A) in BB among the 3 groups in relation to the clinical and pulmonary functional data.

Table 1

Clinical Data	CRSwNP (N=11)	CRSsNP (N=11)	NO-CRS (N=11)
Age, years	52.2±11.8	56.9±11.3	46.8±12.1
Sex, M/F	5/6	8/3	2/9
Asthma onset, years	31.9±13.7#	32.5±17.1#	16.8±12.5
Asthma duration, yeras	20.3±14.2	24.5±22.5	30.0±17.3
Atopy (yes/no)	8/3	5/6	7/4
Smokers• (yes/no)	2/9	6/5	1/10
BMI, Kg/m^2	25.3±5.6	27.5±3.9	28.5±6.7
Exacerbation/year	2.5±2.2	1.5±1.1	1.0±1.8
ICS dose (equivalent µg fluticasone)	579.5±465.3	675.0±399.2#	369.3±314.3
Step GINA 4	6/11 (54.5%)	4/11 (36.4%)	7/11 (63.6%)
Step GINA 5	3/11 (27.3%)	6/11 (54.5%)	2/11 (18.2%)
OCS	2/11 (18.2%)	2/11 (18.2%)	0/11 (0.0%)
Good/Poor control	5/3	7/1	8/1

•= Smokers: patients with a smoking history ≥10 pack/year

*=p<0,05 vs CRSnNP; #=p<0,05 vs NO-CRS

Table 2

Lung function data	CRSwNP (N=11)	CRSsNP (N=11)	NO-CRS (N=11)
FEV_1 (% pred.)	82.5±29.5	71.4±22.8	89.5±21.5
FVC (% pred.)	109.2±20.7	94.5±15.9	106.8±14.1
FEV_1/FVC (% pred.)	0.63±0.2	0.56±0.1##	0.73±0.1
FEV_1 post-BD (% pred.)	82.0±39.7	76.0±37.0	91.1±18.7
FVC post-BD (% pred.)	102.0±39.3	104.2±18.0	92.8±38.6
FEV_1/FVC post-BD	0.7±0.2	0.6±0.1#	0.7±0.1
RV (% pred.)	143.4±67.8#	145.6±35.3###	98.6±18.3
FRC (% pred.)	119.1±49.5	120.1±24.7##	90.3±15.8
RV/TLC (% pred.)	0.4±0.2	0.4±0.1	0.4±0.2

BD= bronchodilation *=p<0,05 vs CRSnNP; #=p<0,05 vs NO-CRS

Table 3

Biological data	CRSwNP (N=11)	CRSsNP (N=11)	NO-CRS (N=11)
FeNO (ppb)	34.6±21.4#	41.0±30.9#	23.1±29.9
Blood eosinophils (cell/µL)	498.2±208.5*#	261.8±199.1	225.5±190.8
Blood neutrophils (cell/µL)	3957±1732	4366±1184	3621±833.1
Blood monocytes (cell/µL)	583.6±271.4	668.9±179.9##	449.1±142.1
Serum IgE (KUI/L)	168.2±80.7*	97.4±95.5	299.2±430.4

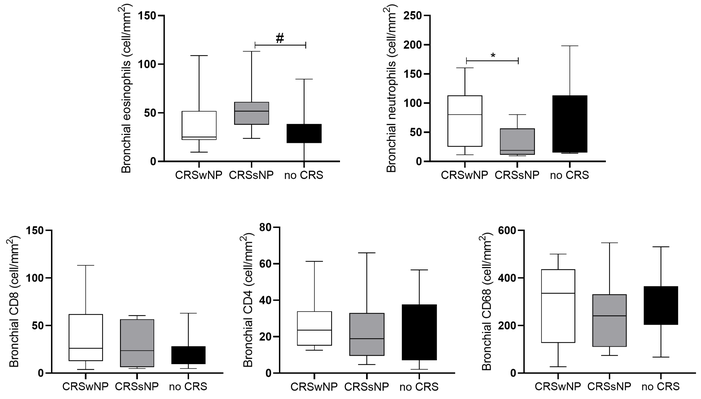
*=p<0,05 vs CRSnNP; #=p<0,05 vs NO-CRS

RESULTS

Both CRSwNP and CRSsNP had late asthma onset, higher RV% and FENO than no CRS. CRSsNP had lower FEV_1/FVC than no CRS; CRSwNP showed a higher blood eosinophilia than both CRSsNP and no CRS and a greater level of serum IgE than CRSsNP (Table 1,2 and 3).

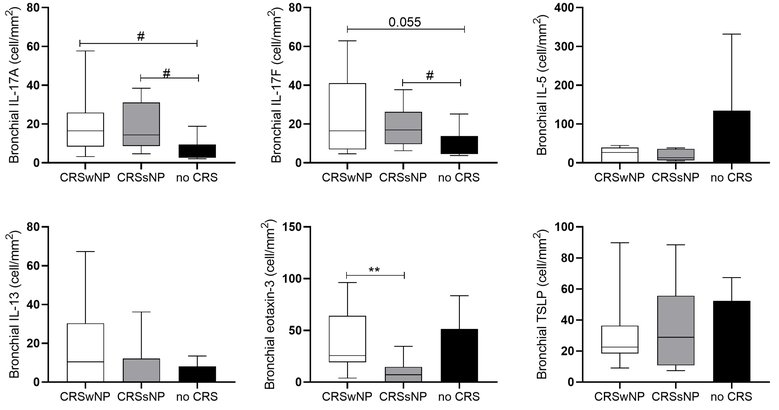
Immunohistochemistry of bronchial mucosa showed a higher number of eosinophils in CRSsNP compared to no CRS, higher neutrophil count and eotaxin3$^+$ cells in CRSwNP than CRSsNP, and a higher number of IL-17A$^+$ and F$^+$ cells in both CRS groups than no CRS.

Figure 1



*=p<0,05 vs CRSnNP; #=p<0,05 vs NO-CRS

Figure 2



*=p<0,05 vs CRSnNP; #=p<0,05 vs NO-CRS

CONCLUSIONS

Our results confirmed the presence of a T2 response in CRSwNP patients (F_ENO, IgE, blood eosinophils), but revealed a more complex condition when assessing the bronchial inflammatory status, suggesting a complex interplay of T2 and Th17-driven inflammatory pathways.

Conflict of Interests: All authors declare absence of any conflict of interest concerning this study