Serum periostin in asthma: a potential biomarker for stratification in severe treatment-resistant asthma

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Wessex Severe asthma cohort

Background

- Periostin is a highly inducible product of IL-4 or IL-13, signature cytokines of Th2-type immune responses
- Gene expression for periostin (POSTN) has been shown to be up regulated in bronchial epithelial cell brushings in asthma and to be down regulated by inhaled steroid therapy in steroid responsive asthmatics.
- In vitro studies indicate that periostin is basally excreted and its measure in the serum may reflect Th2 airway inflammation..
- Serum periostin has thus been proposed as a biomarker to direct anti IL-13 monoclonal antibody therapy in severe asthma

Aim

- To measure serum periostin in a large cohort of patients with severe asthma as well as in those with milder asthma and healthy controls, to gain insight into the value of this biomarker in asthma stratification
- To evaluate how serum periostin relates to other markers of eosinophilic airway inflammation

Wessex Severe Asthma Cohort

- A well characterised cohort of over 300 patients with severe treatment-resistant asthma who remain inadequately controlled despite management at step 4/5 of the BTS/SIGN asthma management guidelines.
- Milder subjects and healthy controls were also recruited for comparison
- Characterised with respect to history, ACQ, AQLQ, lung physiology pre and post b'dilator, small airways function, NO, atopic status, co-morbidities, nasal inflammation, lower airway inflammation in association with serum, DNA and urine biobank samples

Methods

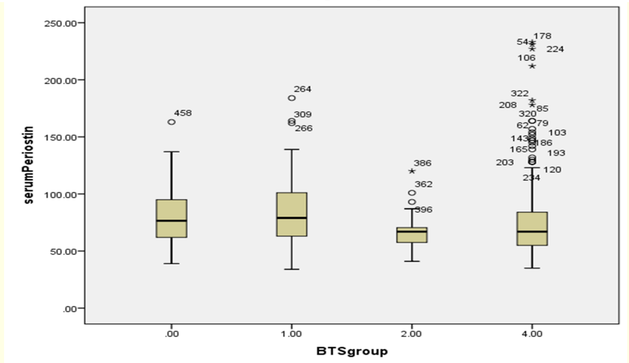
- Serum samples from 126 healthy non-asthmatic controls (HC), 93 non-steroid treated mild asthmatics (MA), 35 asthmatics on low dose corticosteroids +/- LABA (ModA) and 276 severe treatment-resistant asthmatics (SA) [78 oral steroid treated] were assayed for serum periostin by ELISA with SS18A*SS17B antibody (Shino-Test Corporation, Kanagawa, Japan) and the results related to physiological and inflammatory markers

Results

Table 1: Characteristics of subjects in the WSAC with serum periostin

* Mean † Median	Healthy	Mild	Mod	Severe
n	126	93	35	276
Age (yrs)*	36.9	30.5	37.7	49.2
BMI*	24.9	26.2	30.8	31.3
Gender (M/F)	28/50	37/56	16/19	88/185
FEV_1 % predicted*	104.5 ±12.2	93.8 ±14.0	90.8 ±20.0	70.6 ±24.9
Serum periostin†	76.5 (39-163)	79 (34-184)	67 (41-120)	67 (35-233)
FeNO (ppb)†	15.5 (5-93)	20.2 (8-162)	21.0 (5-64)	14.5 (2-179)
Sputum eosinophils%†	0.75 (0-5.5)	2.6 (0-5.6)	1.1 (0-11.1)	1.38 (0-87)
Peripheral eosinophils $X10^9/L$†	0.177 (0-0.7)	0.225 (0-0.7)	0.283 (0-0.7)	0.333 (0-2.6)

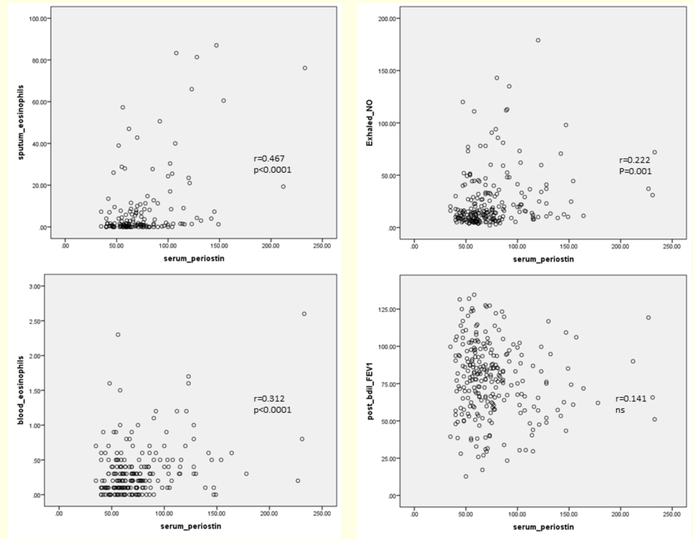
Figure 1: Boxplot showing serum periostin measures for each group



Results (cont)

- Group median serum periostin levels were significantly ($p<0.0001$) lower in both the steroid treated asthma groups (ModA and SA) than the HC or MA groups.
- There was greater spread in SA with 21% of values ± the normal range
- Tertile analysis of the SA serum periostin identified that those in the upper tertile (≥79 ng/ml) had significantly higher sputum eosinophils ($p=0.001$), peripheral blood eosinophilia ($p=0.002$), FeNO ($p=0.001$) and total IgE ($p=0.01$) as well as lower FEV_1 % predicted ($p=0.02$) than those in the lowest tertile (≤58ng/ml).
- In the severe asthma group serum periostin correlated significantly with sputum eosinophils, FeNO and peripheral blood eosinophils

Figure 2: biological and physiological correlations with serum periostin in severe asthma



Conclusions

- Serum periostin is not increased in severe asthma but there is considerable heterogeneity and those with high periostin levels (top tertile) have evidence of uncontrolled eosinophilic inflammation and poorer lung function