SYSTEMATIC CHARACTERISATION OF INFLAMMATION IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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Background

The pathogenesis of chronic thromboembolic pulmonary hypertension (CTEPH) is poorly understood. Idiopathic pulmonary arterial hypertension (IPAH) is associated with systemic and localised inflammation. Distal vasculopathy is seen in both IPAH and CTEPH (2 compartment model). Inflammation has also been proposed as a potential factor in CTEPH. We undertook a systematic assessment of immune cells in tissue and serum cytokines to understand the role of inflammation in CTEPH.

Methods

We examined distal tails of 26 pulmonary endarterectomy (PEA) specimens and explanted lungs (5 CTEPH, 11 IPAH). Formalin fixed samples were immunostained with anti human CD45 (inflammatory cell), CD79a (B cell), CD68 (macrophage) or CD3 (T cell) antibodies, labelled and examined by light microscopy. Cell counts were normalised to perivascular area (defined as area surrounding vessels bounded by airspace structures) for perivascular cell counts; to vessel area for media cell counts and per high powered field for lung parenchyma cell counts. Serum was collected from 16 patients pre and 6 months post PEA. Cytokines were measured using a multiplex array (pg/ml; mean±SD).

Results

CD3+ cells were less abundant in the media of small vessels (mean 0.03±0.01mm^2) in CTEPH compared to IPAH (p=0.02). Perivascular and parenchymal cell counts showed non-significant reductions of CD3+ cells in CTPEH (p=0.19 and 0.08 respectively). More CD68+ cells were seen in the parenchyma in CTEPH (p=0.03). Few CD20+ cells were seen in parenchyma with no difference.

Neovascularisation correlated to CD45+ cells in PEA specimens when normalised to specimen area (r=0.4, p=0.01).

Most cytokines were not significantly elevated (<2pg/ml) in preoperative samples. IL10 and TNFα were elevated pre PEA (27. 6±33.7 and 2.9±4.1) and fell post PEA (p=0.02 and 0.06 respectively).

Conclusion

In CTEPH, most serum cytokines were not elevated to be of biological significance or to suggest systemic inflammation is important in pathogenesis. The change in IL10 and TNFα are likely due to improvement in cardiac function post PEA as described previously. While, the relative lack of CD3+ T cells in the media of small arteries in

CTEPH suggests that localised inflammation is also less important. The significance of CD68+ cells in CTEPH lung parenchyma needs further assessment.

The correlation of CD45+ cells and neovascularisation in PEA specimens may suggest an association between inflammation and neovascularisation.

We suggest inflammatory signals are related to thrombus remodelling and cardiac dysfunction rather than to processes causing CTEPH. A lack of animal models hinders understanding. Further work carefully isolating these different processes is therefore required to expand on this descriptive study.