Mast Cells and Macrophages of Rats Lungs in an Acute Model of Fat Embolism

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Introduction

- Fat embolism (FE) by IV injection of Triolein (T) causes vasculitis, septal inflammation and fibrosis in rat lungs at 48 hours, which is mitigated by two drugs acting on the renin angiotensin system (RAS) Captopril and Losartan (1,2).
- An increase in mast cells is noted following administration of T, with an even higher increase by concomitant treatment with Captopril and significant reduction by Losartan (3).
- In this study we evaluated the the presence and number of macrophages in rat lungs after T treatment with or without addition of Captopril and Losartan.

Methodology

- Sprague Dawley rats (280-300g BW) received T (0.2 ml n=18) or saline n=4.
- The T treated rats, divided into 3 groups of 6 each, were IP injected one hour later either with 0.2 ml Saline, Captopril 50 mg/kg or Losartan 100 mg/kg.
- 48 hours later rats were killed under isoflurane anesthesia and the lungs stained with H&E, Trichrome for fibrosis, and CD68 for macrophages.
- 10 photographs at 400x of all slides were reviewed by two pathologists unaware of the slides' identity for macrophage count and histopathological evaluation.
- Slide photographs and mast cell count was performed by two other pathologists.

CD68 Stain

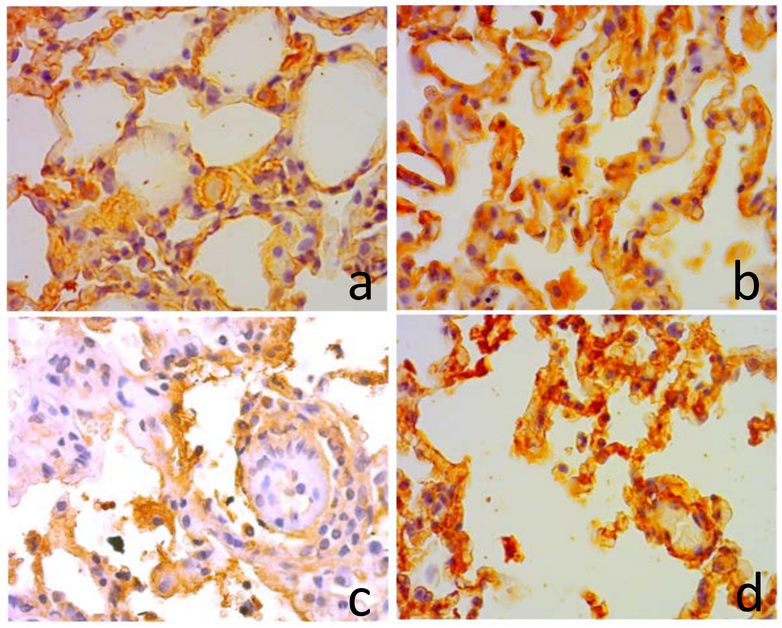

Figure 1. Representative photographs of lung sections. a) Saline + Saline b) Triolein + Saline c) Triolein + Captopril d) Triolein + Losartan.

Few macrophages, different in their size, are evident in these images.

References

- (1) McIff T. E. et al, J Orthoped Res 2010:28 (2):191-197.
- (2) McIff T. E. et al, J Trauma 2011:70 (5):1186-1191
- (3) Colson J.D. et al, FASEB J 2018 32.1, Suppl. 817.16
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Results

- As expected, T injection induced pulmonary vasculitis, septal inflammation and fibrosis which was markedly reduced by the RAS inhibitors Captopril and Losartan.
- Contrary to the statistically significant increase of mast cells after these 3 treatments, macrophage counts were only increased but minimally by T and T + Captopril and not by T + Losartan.
- The difference were not statistically significant.
- Two types of macrophages were observed: one composed of small cells with compact cytoplasm and nucleus, similar in their size to the size of the mast cells and a second type with a larger vacuolated cytoplasm.
- The number of cells of this second group was rather small, so that any increase of these cells was not likely to influence the macrophages total number.

Conclusion

- Both mast cells and macrophages play a determinant role in the pathogenesis of the inflammatory and fibrotic pulmonary damage after T fat embolism.
- A different response to the injury was observed between the numbers of these two series of cells in the earlier phase of the injuries.
- The difference also observed in mast cells versus macrophages number present following T + Captopril and T + Losartan administration, suggests a diversely regulated pharmacologic activity of the Renin Angiotensin System of the two drugs in the protection of the fat embolism mediated damage.