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The Pathogenic Potentials of Salmonella typhi specific Human and Lapin Cryoglobulins in a Lapin Model

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Abstract

A three doses of 5 mg\ml in foure days a part of human (Xenogenic) and rabbit (Allogenic) cryoglobulins were used for intravenous inoculation in two separated groups each of three. These dosage regmine were followed by seven days leave, then, sacrifice. A third group of three rabbits were receiving saline in same protocol. Pneumogenic effects were found as interstitial pneumonia and fibrinoid formation. Nephrogenic influence appeared as glomerular infiltrates of mononuclear cells (glomerulonephritis). While the splenic changes were found as lymphoid cells hyperplasia in the white pulp. Thus, both of the allogenic and xenogenic cryoglobulins induce Pneumogenic, nephrogenic as well as lymphogenic pathogenic potentials in rabbits. Control rabbits were showing normal tissue architecture of the test organs. These pathogenic potentials of cryoglobulins are basically of immune complex hypersensitivity in case of human cryoglobulins and pathologic autoimmune responses in case of rabbit cryoglobulins. Thus, S. typhi specific cryoglobulins pathogenic in a lapin model, a finding is not ever being reported in literatures and reported for the first time.

Keywords: Pathogenic, potentials, salmonella typhi, human, cryoglobulins, lapin model.

Introduction

Crystalline cryoglobulin preparations have found to be immunogenic and immunopathogenic (mediate tissue injuries[1]. Monoclonal cryoglobulin preparations were found immunopathogenic in laboratory animals[2-4]. The objective of the present work was an attempt to determine the possible immunopathogenic influence of allogenic and xenogenic cryoglobulins in a lapin model.

Material and Methods

Cryoglobulin preparations: In case of allogenic cryoglobulin, S.typhi O antigen in a density of billion cell / ml have been used in induction of allogenic rabbit cryoglobulin. The cryoglobulin was separated and characterized as in Shnawa and Jasim[5]. The solutions were ratified to 5 mg / ml. While, in case of xenogenic cryoglobulin, from an clinical cases of human typhoid, was separated and characterized as in Lynch[6]. The solutions were ratified to 5 mg / ml.

Inoculation Protocol: Inoculation of rabbits in 4 days apart followed by 7 days leave with allogenic and xenogenic cryoglobulins[7].

Group 1 of three rabbits inoculated with allogenic, group 2 of three rabbits inoculated with xenogenic and group 3 of three rabbits received saline.

Tissue responses: Using standard evisceration techniques, lung, liver, spleen and kidney were collected in 2 x 2 cm blocks . Tissue sections were made following standard sectioning and staining techniques[8].

Results and Discussion

Lungs: Lung tissue sections from both the human and lapin cryoglobulin inoculated rabbits were showing an interstitial inflammatory mononuclear cell infiltrates with fibrinoid formation figure 1.

Livers: Liver tissue sections from both of the human and lapin cryoglobulin inoculated rabbits were showing congestion in hepatic blood vessels figure 2.

Spleen: Splenic tissue sections from both of the human and lapin cryoglobulin inoculated rabbits were showing lymphoid cell hyperplasia in the white pulp and congestion in the red pulp zones figure 3.

Kidneys: Kidney tissue sections from both of the human and lapin cryoglobulin inoculated rabbits were showing mononuclear cell infiltrates in the glomeruli and congested glomerular capillaries as well as congestion of intertubular blood vessels figure 4.

Discussion: The noted pneumogenic effects of cryoglobulins figure 1 can be attributed to the flux of the inflammatory cell infiltrate of polymorphs.The inflammatory cell flux was assured through the activation of C5 in the alternative pathway which play a role in splitting C5 to C5a which attracts inflammatory cells leading to inflammation[9]. The hepatic tissue

changes were found as blood vessels congestion figure 2. Such congestion may be attributed to the deposits of cryoglobulin in this vessels leading to vascular damage which in turn reduce the blood flow and congestions[10-12]. The clearance of immune complexes also relies on phagocytic cells, mainly macrophages in the spleen and the liver[13]. The lesion consists of an admixture of lymphocyte and aggregates of macrophages, where they appeared as lymphocyte hyperplasia figure 3. Such hyperplasia is of a polyclonal increase in the number of lymphocytes[14]. Or it may be to a state of reactive lymphoid hyperplasia to cryoglobulin antigen[15]. The tissue changes in kidney figure 4, may be due to the inflammatory influences of the mixed cryoglobulin which forms immune complexes precipitated in small and medium sized vessels of the glomeruli[16]. The glomerular capillary walls were showing irregular membrane thickening induced by the endothelial cell swellings, accumulation of cryoglobulin in the subepithelial tissues, and or due to remodeling of capillary basement membrane[17]. Thus, the allogenic and xenogenic cryoglobulin have pneumogenic, nephritogenic and lymphogenic pathologic potentials. Such pathologic effects can be attributed to immune complex hypersensitivity in case of human cryoglobulin and pathologic autoimmune tissue responses in case of rabbit cryoglobulin[1-18].

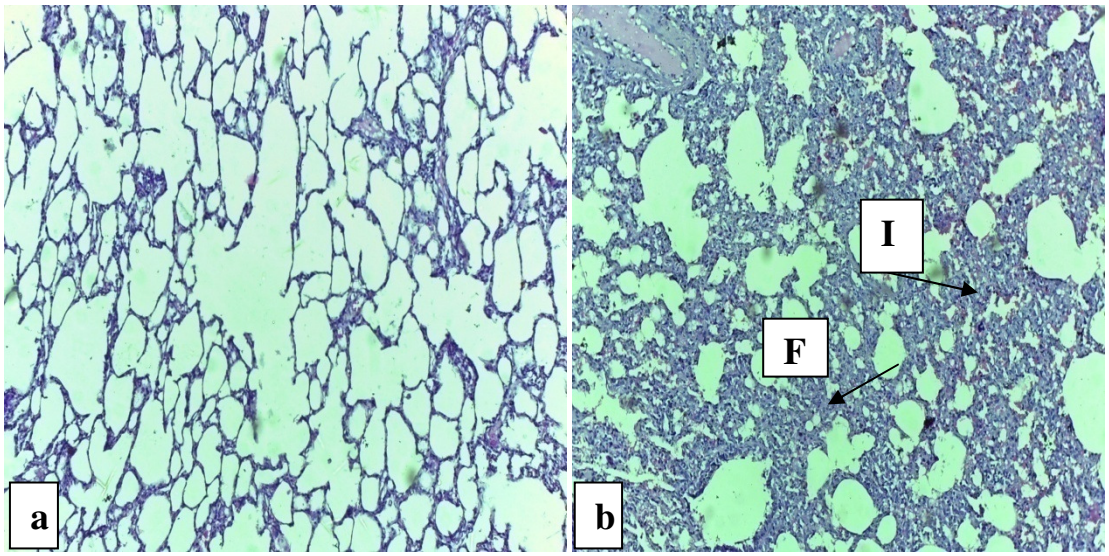

Figure-1
(a) cross section through lung tissue showing normal lung alveoli in negative control group . H & E . 40X . (b) cross section through lung tissue showing interstitial tissue infiltration by inflammatory cells (I) with fibrosis (F) in treatment group .H & E . 40X

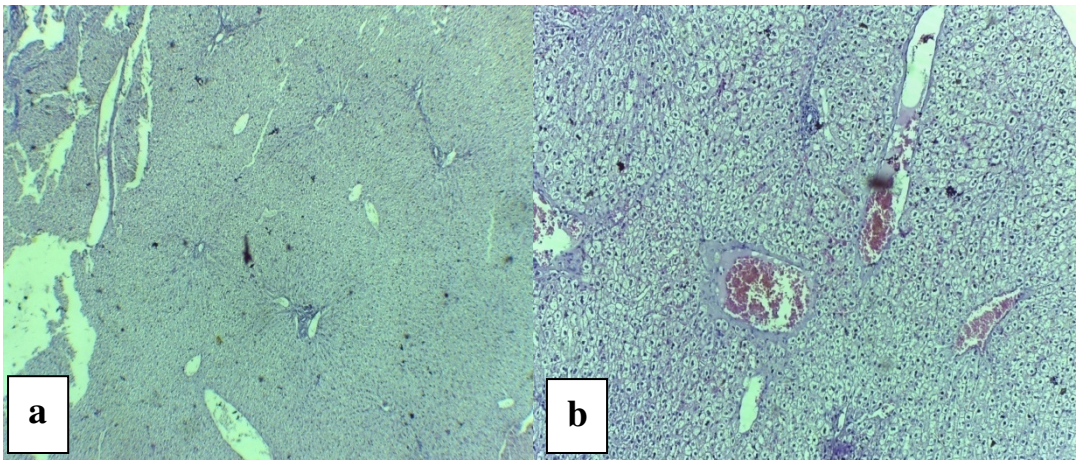

Figure-2
(a) cross section through liver tissue showing normal tissue in negative control group . H & E. 40X (b) cross section through liver tissue showing congested hepatic blood vessels in treatment group, H & E. 100X

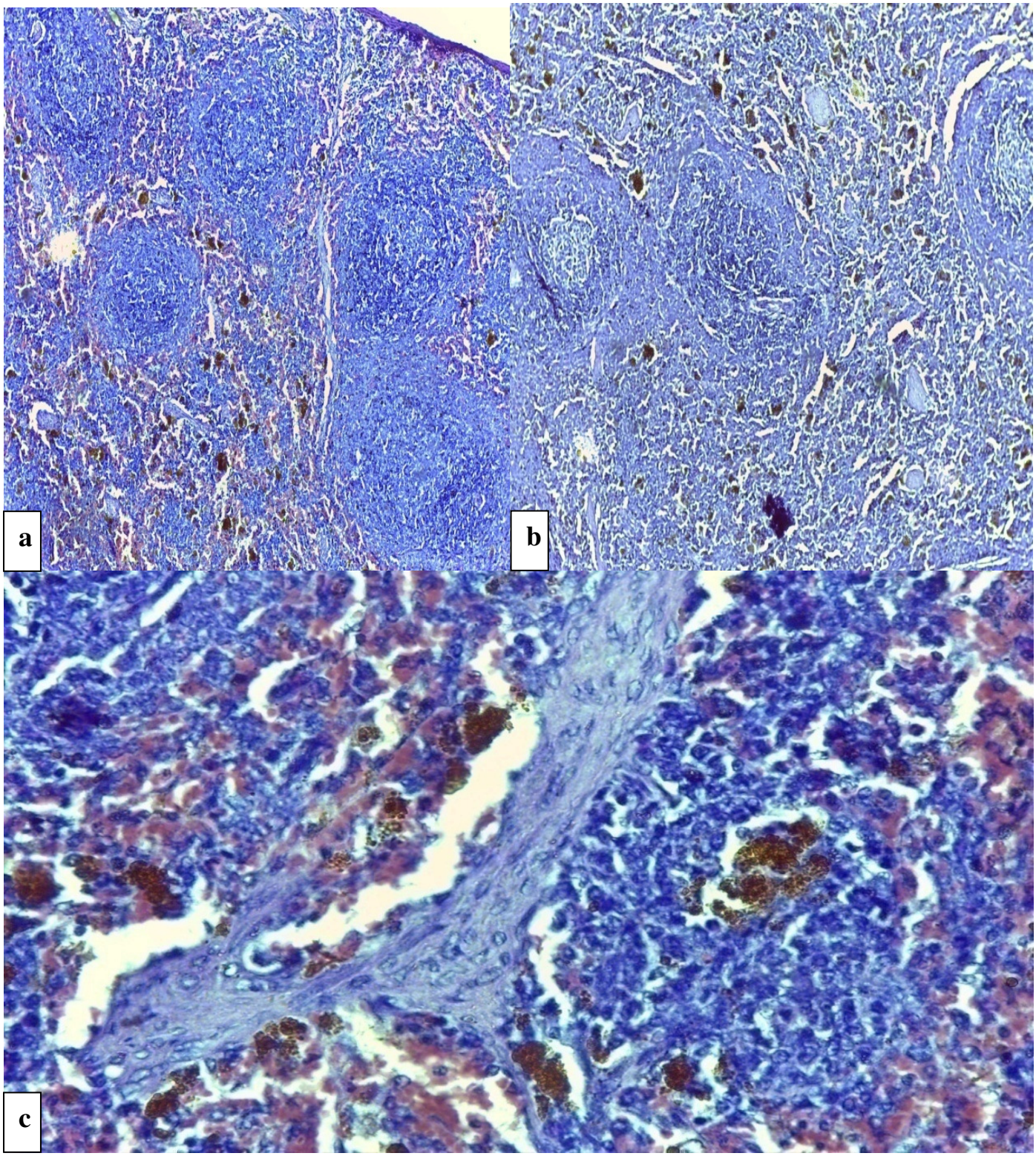

Figure-3
(a) cross section through normal splenic tissue in negative control group, H & E 40X (b) cross section through splenic tissue showing white pulp hyperplasia in treatment group . H & E . 40X . (c) cross section through splenic tissue showing congested red pulp in treatment group . H & E. 400X

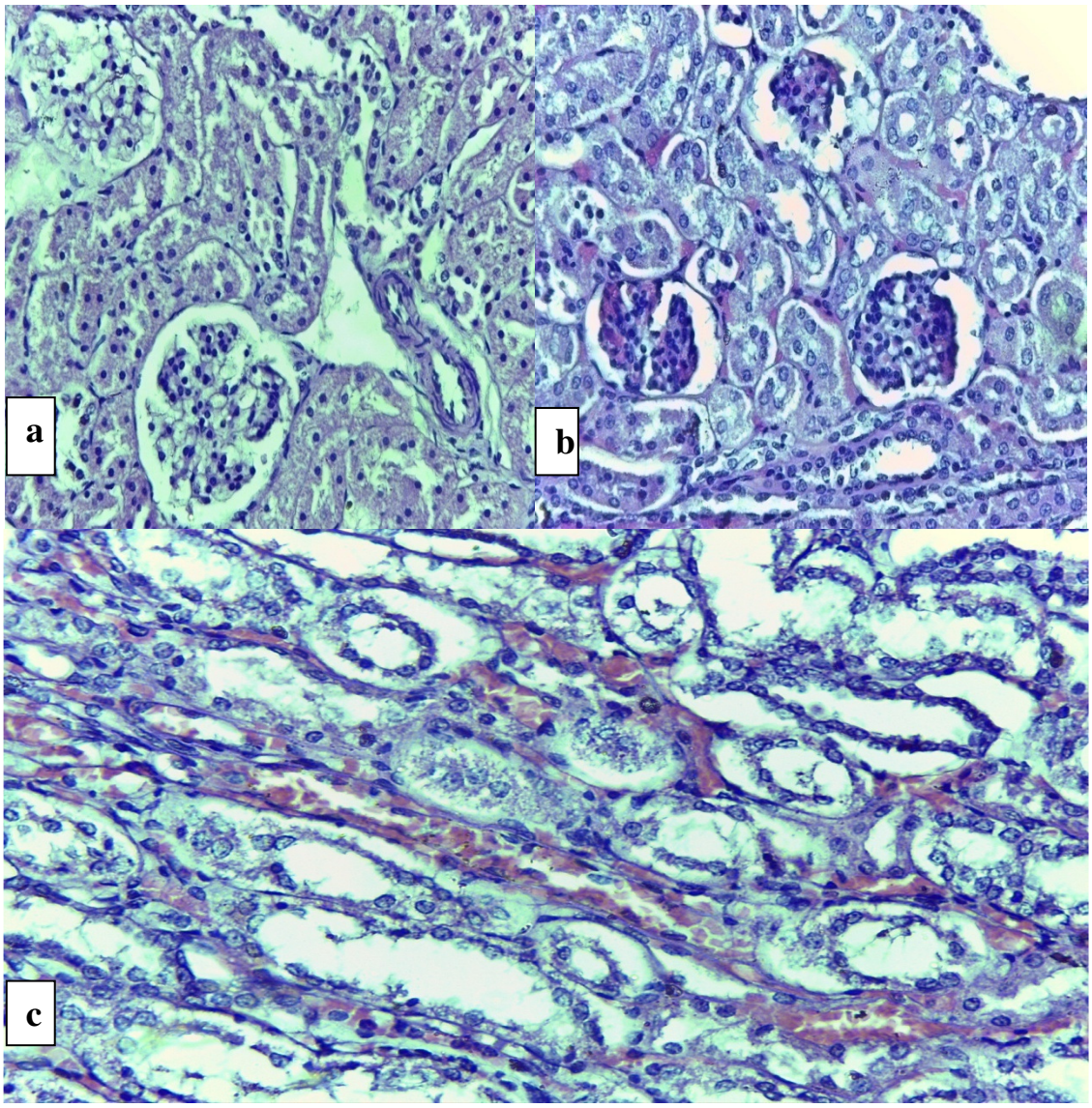

Figure-4

(a) cross section through renal tissue showing normal tissue in negative control group . H & E . 400X . (b) cross section through renal tissue showing glomeruli with increased inflammatory cells and congested glomerular capillaries in treatment group . H & E . 400X . (c) cross section through renal tissue showing congestion of intertubular blood vessels in treatment group H & E. 400X

Conclusion

S.typhi specific allogenic and xenogenic serum cryoglobulins are pathogenic in a lapin model causing pneumogenic, lymphogenic and nephritogenic effects.

References

1. Rengers J.U., Touchard G., Decourt C., Deret S., Michel H. and Cogne M., Heavy and light chains primary structure control IgG3 nephritogenicity in an experimental model for crycrystaloglobulinlemia, *Blood*, **95(1)**, 3467-3472 **(2000)**

2. Kikuchi S., Pastore Y., Fossati –Jimack L., Kuroki A., Yoshida H., Fulpius T., Araki K.,Takahashi S., Lemoine R., Reininger L. and Izui S.A transgenic mouse model of autoimmune glumerulonephritis and necrotizing artritis associated with cryoglobulinemia, *J.Immunol*, **169**, 4644-4650 **(2002)**

3. Spertini F., Gyotoku Y., Shibata T., Izui S. and Lambert P.H., Experimental model of murine cryoglobulinemia induced by monoclonal antibodies and modulation by anti-idiotypic antibodies, Springer semin, *Immunopathol*, **10**, 91-101 **(1988)**

4. Kowalewska I., Muhlfeld A.S., Hudlkins K.L.,Yeh M.M., Farr A.G., Ravetch J.V. and Alpers C.E., Thymic stromal lymphopoitin transgenic mice develop cryoglobulinemia and hepatitis with Similarities to Human Hepatitis C Liver Disease, *Am. J.Pathol*, **170,** 981-989 **(2007)**

5. Shnawa I.M. and Jassim Y.A., BCG & tuberculin induced experimental lapin secondary cryoglobulinemia, Q.M.J, **7(12),** 209-219 **(2011)**

6. Lynch PLM., Audit of Cryoglobulin Determination in Northern Ireland, Clinical Biochemistry Department, Altnagelvin Area Hospital, Londonderry, Full implementation of all new guidelines, 1-13 **(2006)**

7. Abd F.G., Khalifa K.A. and Shnawa I.M., Lapin Escherichiae coli K1 Vaginosis, Baby.Univ.J, **14(4),** 278-285 **(2007)**

8. Mohan H., Pathology Practical Book. 2nd ed. Medical publisher(P) LTD, New Delhi, 1-15 **(2007)**

9. Gorevic P.D., Rheumatoid factor, complement, and mixed cryoglobulinemia, *Clin. Dev. Immunol,* 2012, 1-6 **(2012)**

10. Liou Y.T., Huang J.L., Ou L.S., Lin Y.H., Yu K.H., Luo S.F., Ho H.H., Liou L.B. and Yeh K.W., Comparison of cryoglobulinemia in children and Adults, *J Microbiol Immunol Infect*, **46**, 59-64 **(2013)**

11. Lauletta G., Russi S., Conteduca V. and Sansonno L., Hepatitis C virus infection and mixed cryoglobulinemia, *Clin Dev Immunol*, 2012: 1-11 **(2012)**

12. Ferri C. and Mascia M.T., Cryoglobulinemic vasculitis, *Curr. Opin. Rheumatol*, **18,** 5-63 **(2006)**

13. Guo S., Mühlfeld A.S., Wietecha T.A., Peutz-Kootstra C.J., Kowalewska J., Yi K., Spencer M., Pichaiwong W., Nimmerjahn F., Hudkins K.L. and Alpers C.E., Deletion of activating Fcgamma receptors does not confer protection in murine cryoglobulinemia-associated membranoproliferative glomerulonephritis, *Am J Pathol*, **175(1)**, 107-118 **(2009)**

14. Suttie A.W., Histopathology of the Spleen, *Toxicol Pathol*, **34**, 466-503 **(2006)**

15. Male D., Brostoff J., Roth D.B. and Roitt I., Immunology 7th ed. Mosby, Elsevier, Canada, 461–463 **(2006)**

16. Sargur R., White P. and Egner W., Cryoglobulin evaluation: best practice, *Ann Clin Biochem*, **47**, 8–16 **(2010)**

17. Kowalewska J ., Cryoglobulinemic glomerulonephritis — lessons from animal models, *Folia Histochem Cytobiol*, **49(4),** 537–546 **(2011)**

18. Ruebush M., Immunology, In, Ruebush M. and Hawley L.(Eds).USMLE Step1 Immunology and Microbiology, Kaplan Medical, U.S.A , 141-158 **(2010)**