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Cardiomyocyte apoptosis contributes to the pathology of the septic shock heart

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Sir: With a research interest in myocardial injury [1], my attention was drawn to the article by Ammann et al. [2] concerning the increased blood levels of troponin I (cTnI) in sepsis and septic shock. Shock is the common pathway to death unless the latter comes so quickly that shock mechanisms have no time to develop. The authors [2] indicate that three of their septic patients died without shock. This is a surprising fact that deserves further explanation.

Septic shock manifests a sad privilege of high mortality. This outcome permits, however, a high number of deceased patients which may be autopsied and their clinical manifestations confronted with pathologic findings. One regrets that the results of five autopsies performed by the authors [2] were not documented by microphotographs of the heart.

With this documentation lacking, a perusal of the literature concerning the shock heart, i.e. the heart affected by a shock of all etiologies [3], yielded an unexpected result: one needs to go back two decades in order to find its comprehensive histopathologic description. Since that time, pathology has undergone a revolution with the discovery of apoptosis. It would be intriguing, therefore, to reevaluate some older findings concerning the shock heart from the viewpoint of the present knowledge.

Among other things, the shock heart manifests subepicardial and subendocardial hemorrhages [3]. Recently, it was proposed that cardiomyocyte apoptotic bodies were similar to red cells in histopathologic slides [1]. This brings to question whether red cell-like particles in the shock heart are red cells or apoptotic bodies. Using Cartesian coordinates and centimeters as units for exact localization, I have analyzed several shock hearts presented in the literature. Note in Fig. 3-24 [3] that (a) numerous alleged red cells are located inside cardiomyocytes: x=0.2, y=7.1; x=1.4, y=0.2; x=3.8, y=3.3; x=4–5, y=3–6; x=5.9–6.2, y=7.7–9.8; x=6.6–8, y=0.2–3; x=8–8.4, y=3.5–5 and (b) alleged red cells manifest irregular forms, heterogeneous composition and different diameters: x=4.4–5.2, y=7.6–8.5. In another shock heart [4, Fig. 8], notice two clearly recognizable myofibers fragmenting into red cell-like particles: x=7.5–8.5, y=5–8.4. All of these facts favor the apoptotic origin of a majority of red cell-like particles in the shock heart. Evidently, the apoptosis of cardiomyocytes must be accompanied by their disappearance. This is evidenced by widened interstitial spaces and damaged narrowed cardiomyocytes [3, 4].

The most inclusive study of the shock heart is that of McGovern and Tiller [5]. In their Fig. 13, there is an alleged extensive subendocardial hemorrhage. Surprisingly, the extravasated blood does not exercise any pressure on the surrounding myocardium, indicating that alleged red cells are located in large myocardial defects. These defects could not have been formed by cardiomyocyte accidental death and their phagocytosis by macrophages due to the shortness of time (48 h). Only cardiomyocyte apoptosis could be responsible for their formation [1]. Also, if the alleged hemorrhage in Fig. 13 had been genuine blood, it would have clotted in contact with connective tissue. We would have seen a hematoma containing not only red cell-like particles but also platelets and fibrin. Finally, one feels that the eosinophilic particles forming the "hemorrhage" are too small to be erythrocytes. Cardiomyocyte nuclei are about 4 μM large and 14 μM long. Having compared their dimensions with those of the alleged red cells in Fig. 13, one realizes that a majority of the red cell-like particles are only 2–3 μM in diameter. If one is not persuaded by this conclusion, an opportunity exists to make the same comparative measurements in Figs. 6 and 7b [5] in which nuclei and alleged red cells are more distinct. Once more, the measurements tell us that the diameter of a majority of red cell-like particles (2–3 μM) is not compatible with erythrocytes (a mean diameter 8 μM) but cardiomyocyte apoptotic bodies [1].

By writing this, I do not wish to refute the work of those investigators who have found that heart microcirculation is damaged in sepsis and that erythrocytes may egress into the interstitial space. It may happen, however, that two entirely different pathologic processes (interstitial hemorrhage and cardiomyocyte apoptosis) manifest their histopathologic features so similarly that they are identified as one phenomenon.

In an Editorial concerning the article by Annann et al. [2], Wu [6] has concluded that increased blood cardiac troponin levels are manifestations of both reversible and irreversible injuries. I agree with him entirely because cardiomyocytes undergoing apoptosis manifest an enormous power of regeneration and are able to reverse an incomplete apoptotic process (*apoptosis interrupta*) [7]. There is no doubt that cardiomyocyte apoptosis is present in the septic shock heart. Future research will show whether cardiomyocyte apoptosis is also responsible for increased blood troponin levels in patients with sepsis but not in shock.

References

1. Beranek JT (2001) Pathogenesis of transverse midventricular disruption. Int J Cardiol 81:289–290
2. Ammann P, Fehr T, Minder EI, Gunter C, Bertel O (2001) Elevation of troponin I in sepsis and septic shock. Intensive Care Med 27:965–969 DOI 10.1007/s001340100920
3. Robbins SL, Cotran RS, Kumar V (1984) Pathologic basis of disease. Saunders, Philadelphia, pp 112–117
4. Kleinman WM, Krause SM, Hess ML (1980) Differential subendocardial perfusion and injury during the course of Gram-negative endotoxemia. Adv Shock Res 4:139–152
5. McGovern VJ, Tiller DJ (1980) Shock. A clinicopathologic correlation. Masson, New York, pp 17–77
6. Wu AHB (2001) Increased troponin in patients with sepsis and septic shock: myocardial necrosis or reversible myocardial depression? Intensive Care Med 27:959–961 DOI 10.1007/s001340100970
7. Bowen FW, Hattori T, Narula N, Salgo IS, Plappert T, St. John Sutton MG, Edmunds LH Jr (2001) Reappearance of myocytes in ovine infarcts produced by six hours of complete ischemia followed by reperfusion. Ann Thorac Surg 71:1845–1855

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