

Perinatal cardiac failure from the eyes of the pathologist

Armando Faa¹, Theodoros Xanthos², Nicoletta Iacovidou³, Elvira Podda¹

¹Department of Surgical Sciences, Division of Pathology, University of Cagliari, Cagliari, Italy

²National and Kapodistrian University of Athens, Medical School, MSc “Cardiopulmonary Resuscitation”, Athens, Greece

³2nd Department of Obstetrics and Gynecology, Neonatal Division, National and Kapodistrian, University of Athens, Medical School, Greece

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The role of the clinical pathological dialogue in problem solving

Guest Editors: Gavino Faa, Vassilios Fanos, Peter Van Eyken

Abstract

Cardiac abnormalities in neonates are often underdiagnosed and require an high index of suspicion by the perinatal pathologist. Perinatal conditions, such as preterm birth, infection and asphyxia can affect newborn health and disease, and in particular may cause relevant pathological changes in the cardiovascular system. On the basis of our experience on the histological study of the neonatal heart, endothelial damage represents a diffuse pathological feature in the myocardial vessels of newborns subjected to perinatal hypoxia. Endothelial cell swelling, apoptosis, detachment and microthrombosis are the most frequent lesions observed in the neonatal heart. In cases of severe vascular changes associated with disseminated intravascular coagulation (DIC), cardiomyocyte apoptosis and coagulative necrosis represent the histological marker of cardiac pathology in the neonatal heart. A new and very sensitive early tool to identify cardiac changes in perinatal period is represented by immunoreactivity of cardiac cells for S100B protein. Immunostaining for S100B protein in the neonatal heart might indicate an early protective reaction of cardiomyocytes in newborns subjected to asphyxia, clearly indicating a chronic or sub-acute evolution of the clinical picture, and contrasting with the hypothesis of a sudden death. In conclusions, our data shows that the perinatal pathologist represents a pivotal figure in the early study and detection of cardiac changes in all neonates, particularly in newborns undergoing asphyxia in the perinatal period.

Keywords

Cardiac failure, fetus, newborn, pathology, heart, S100B protein.

Corresponding author

Armando Faa, Department of Surgical Sciences, Division of Pathology, University of Cagliari, Cagliari, Italy; email: armando.faa@hotmail.it.

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Introduction

Cardiac abnormalities in neonates are often underdiagnosed and require a high index of suspicion by the pathologist. The hypothesis of the fetal origin of adult heart disease identifies the relationship between impaired growth during intrauterine life and the risk of adult cardiovascular disease and death is still clear [1].

Perinatal conditions, such as preterm birth, also can affect adult health and disease, particularly the cardiovascular system. For example, neonatal hyperoxic stress affects myocardial structure, function, and expression of renin-angiotensin system components. Persistent hypoxia may also result in pulmonary hypertension with consequent right to left shunt across patent ductus arteriosus and foramen ovale, aggravating the clinical picture.

Perinatal inflammation and hyperoxia exposure after fetal development may determine early cardiac dysfunction, inducing discernible alterations in cardiomyocyte contractility due to calcium signalling dysfunction. Clinically transient myocardial ischemia (TMI) should be suspected in any newborn in the clinical settings of asphyxia, respiratory distress syndrome and poor pulses [2].

With the increasing rates of survival of preterm infants born at early gestational ages, the need of a correct diagnosis by the pathologist is more important. In recent works from our group, normocapnic hypoxia and reoxygenation in an animal neonatal model resulted in significant myocardial histological changes, suggesting that this newborn piglet hypoxia-reoxygenation model might be a reliable model for investigating human neonatal cardiac hypoxia-related injury.

In this experimental work, the finding of severe myocardial changes, including coagulative necrosis, strictly correlated with the time of recovery, suggesting a previously unreported individual susceptibility of myocardial cells to perinatal hypoxia [3].

Finding your way in the interpretation of the neonatal heart

Recent studies show that endothelial damage represents a diffuse pathological feature in the myocardial vessels of piglets subjected to normocapnic hypoxia and resuscitation. Endothelial cell swelling, apoptosis, detachment and microthrombosis are the most frequent lesions observed in the piglet heart following asphyxia and reoxygenation, leading to a possible role of hyperoxygenation in aggravating endothelial damage and the subsequent activation of the thrombotic cascade, ending with hypoperfusion and death of cardiomyocytes (**Fig. 1**) [4].

Taking together, these new findings suggest a new approach of the pathologist in the study of perinatal cardiac dysfunction, mainly focused on the detection of these new histologic pathological changes. On the basis of these findings, coagulative necrosis associated with endothelial cell damage and disseminated intravascular coagulation (DIC) appear nowadays the most interesting and useful features to discover perinatal cardiac abnormalities.

We searched for a very sensitive and early tool to identify cardiac changes in perinatal period. The detection of a high percentage of S100B-immunoreactive hearts in a perinatal animal model with a fast recovery, compared with a decreased immunoreactivity for S100B protein in animals with a slow and a very slow recovery, clearly indicates S100B protein as an early protective factor with a positive prognostic value in asphyxiated newborn piglets (**Fig. 2**) [5].

Conclusions

In conclusions, our recent data shows that the perinatal pathologist represents a pivotal figure in the early study and detection of cardiac changes in all neonates, particularly in newborns undergoing asphyxia in the perinatal period. On the basis of our study of cardiac pathology in a large series of newborns dead in the perinatal period, we suggest the necessity of focusing, in

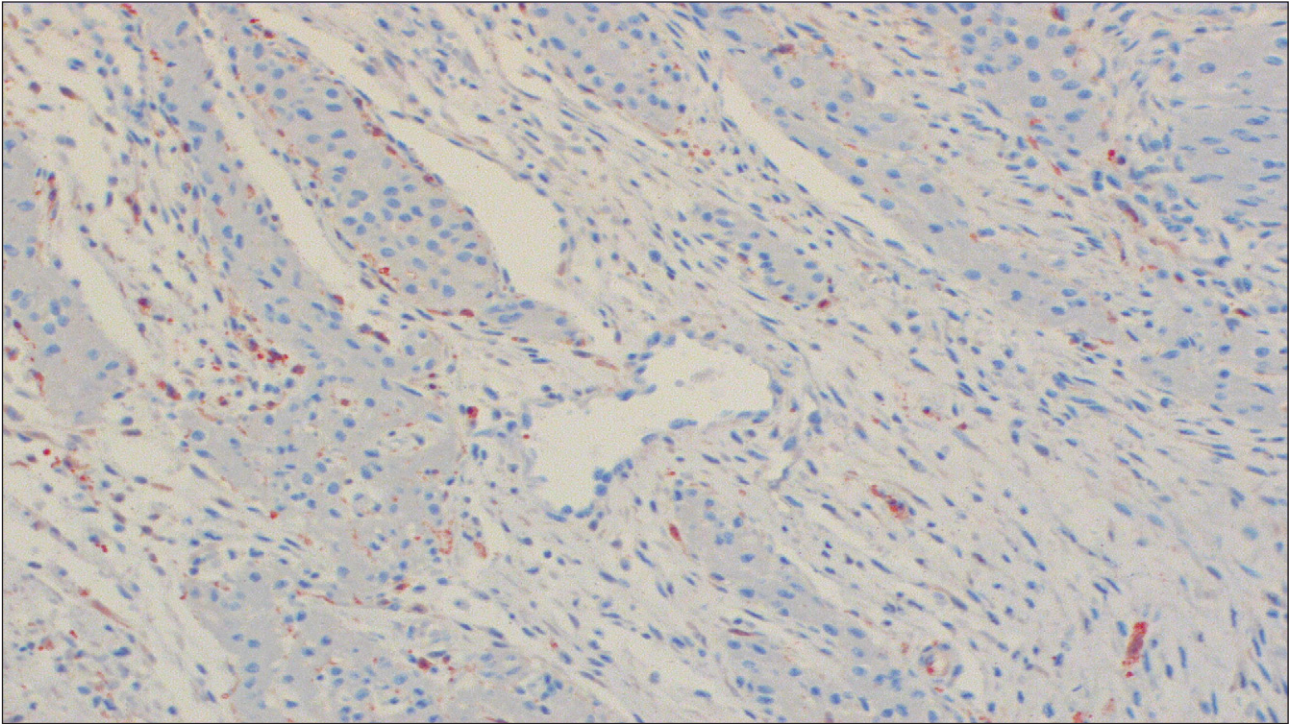


Figure 1. Endothelial damage, edema and hypoperfusion in heart vessels following asphyxia.

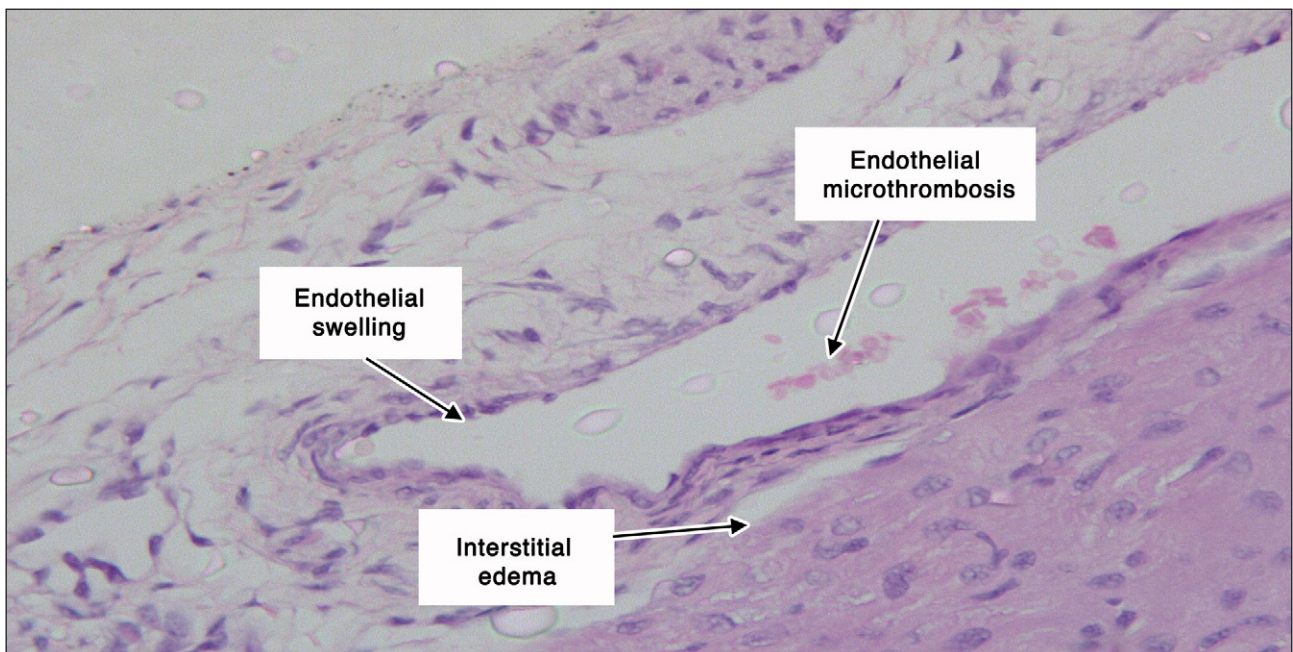


Figure 2. Diffuse S100B immunopositivity with cytoplasmic and intercardiomyocytes positivity.

the histological examination of the neonatal heart, on myocardial and endothelial morphological changes, endothelial damage and loss of the endothelial barrier representing the most frequent lesion responsible for cardiac failure in the majority of cases. Finally, the

immunohistochemical detection of S100B protein in cardiomyocytes as well as in the interstitial spaces appears a new useful tool for the reconstruction, at the histological level, of the cardiomyocyte reaction in the last moments of the neonatal life.

Declaration of interest

The Authors declare that there is no conflict of interest.

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