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Papillary Muscle Necrosis in Neonates and Infants

— Analysis of 209 Autopsies —

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A total of 209 consecutive neonate and infant autopsies were reviewed with special attention to papillary muscle necrosis (PMN) of the heart. Associated major pathological findings were analysed for the evaluation of significant pathological accompaniments of PMN. PMN was found in 52 cases among 171(30.4%) neonates and major pathological accompaniments were bronchopneumonia, hyaline membrane disease, hypoxic neuronal change, sepsis, subarachnoid hemorrhage, disseminated intravascular coagulation (DIC) and acute tubular necrosis, among which hypoxic neuronal change and ATN had a statistically significant higher incidence when compared with the control group. ($p<0.005$). PMN was found in 13 cases among 38(34.2%) infants and accompaniments were congenital heart disease, sepsis, bronchopneumonia, DIC and hypoxic neuronal change, all of which showed no difference from the control group in incidence. The results imply that PMN is a kind of organ damage in stressed subjects regardless of age, that it is not a special form of myocardial injury in any specific age group including the newborh period, and is possibly of different pathogenesis and significance.

Key Words: *Papillary muscle necrosis, Heart, Neonate, Infant, Autopsy*

INTRODUCTION

In our personal experience of pediatric autopsies, papillary muscle necrosis (PMN) of the heart, which seemed to be an interesting phenomenon, was not infrequently encountered but we could find neither constant nor specific pathological accompaniments suggesting the presence of PMN. Some authors performed a systematic and detailed review of its clinicopathological significance in recent years, but those studies were confined to newborn cases in perinatal distress and an analysis of associated clinical parameters or settings was their major point of interest (Donnelly et al., 1980; Setzer et al., 1980).
The facts led us to perform a histopathological survey of the actual prevalence of PMN in neonate and infant autopsies and the associated major pathological findings.

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MATERIALS AND METHODS

Routine hematoxylin-eosin stained slides of a total of 209 consecutive neonate (less than 4 weeks of age) and infant (less than 1 year of age) autopsies during the period of January, 1985 to December, 1990 along with their autopsy records were reviewed from the autopsy files of the Department of Pathology, Seoul National University Children's Hospital. Both stillborn and fetal death in utero cases were excluded.

Evaluation of papillary muscle necrosis of the heart was done with longitudinal sections of each anterior papillary muscle of both the mitral and tricuspid valves and its was regarded as PMN positive only if it was found in one of the sections. Classic coagulation necrosis, coagulative myocytolysis, contraction bands, cellular infiltration, fibrosis and calcification were the criteria for PMN. In each case, five major associated

pathological findings were assessed and processed by personal computer database system. The statistical significance of associated pathological findings was evaluated using chi square test with Yates correction.

All cases were divided into two groups according to their age; Group I (N=171) were neonates and Group II (N=38) were infant cases. In both groups, cases with or without PMN were subgrouped into a and b, respectively. The sex ratios of Group I and II were 1.34:1 and 1.71:1, respectively.

RESULTS

Incidence and Histological Patterns of PMN

In Group I, 52 cases had histologic evidence of PMN (30.4%; Group Ia) as did 13 cases in Group II (34.2%; Group IIa), thus revealing no significant difference in their incidence of PMN between Group I and Group II. In 17 and 4 cases of Group Ia and Group IIa, other foci of myocardial necrosis of the same nature were also observed in the involved ventricular myocardium. In 5 and 1 cases of Group Ia and Group IIa, fibrosis with or without calcification was observed in the areas of PMN. Inflammatory cell infiltrations were observed in 13 and 2 cases of Group Ia and Group IIa, respectively, but the infiltrates were rather sparse.

Major Associated Pathological Findings In Each Group

In Group Ia, neonates with PMN, bronchopneumonia (18/51), hyaline membrane disease (17/52), hypoxic neuronal change (13/52), sepsis (13/52), subarachnoid hemorrhage (8/52), disseminated intravascular coagulation (8/52), acute tubular necrosis (8/52), congenital heart disease (8/52), and germinal matrix hemorrhage (7/52) were the major associated pathological findings in order of frequency. In Group Ib, a control group of this period, congenital heart disease (35/119), hyaline membrane disease (32/119), bronchopneumonia (26/119), sepsis (25/119), subarachnoid hemorrhage (17/119), disseminated intravascular coagulation (10/119), and hypoxic neuronal change (8/119) were the frequent findings. Among these, only acute tubular necrosis and hypoxic neuronal change in Group Ia had a significantly higher incidence when compared with Group Ib. ($p<0.005$)

In Group IIa, congenital heart disease (7/13), bronchopneumonia (4/13), sepsis (4/13), disseminated in-

Table 1. Comparison of Incidence of Associated Pathological Findings in Group I.

Neonates with IPMN (Group Ia, n=52)		Neonates without IPMN (Group Ib, n=119)	
	No.		No.
Bronchopneumonia	18	Congenital heart disease	35
Hyaline membrane disease	17	Hyaline membrane disease	32
Sepsis	13	Bronchopneumonia	26
Hypoxic neuronal change*	13	Sepsis	25
Subarachnoid hemorrhage	10	Subarachnoid hemorrhage	17
Acute tubular necrosis*	8	DIC	10
DIC	8	Germinal matrix hemorrhage	9
Congenital heart disease	8	Hypoxic neuronal change	8

*: statistically significant, $p<0.005$.

Table 2. Comparison of Incidence of Associated Pathological Findings in Group II.

Infants with IPMN (Group IIa, n=13)		Infants without IPMN (Group IIb, n=25)	
	No.		No.
Congenital heart disease	7	Bronchopneumonia	7
Bronchopneumonia	4	Congenital heart disease	7
Sepsis	4	Sepsis	4
DIC	3	Hypoxic neuronal change	2
CMV infection	3	CMV infection	2
Hypoxic neuronal change	3	Acute tubular necrosis	2

travascular coagulation (3/13) were major findings and in the control group, Group IIb, bronchopneumonia (7/25), congenital heart disease (7/25), sepsis (7/25), cytomegalic inclusion disease (2/13), acute tubular necrosis (2/13), and hypoxic neuronal change (2/13) were observed in order of frequency. There was no significant difference between Group IIa and IIb in the frequency of associated pathological findings. Major associated pathological findings the Group I and Group II are summarized in Tables 1 and Table 2.

The proportion of low birth weight and smallness for gestational age in each group was as follows; low birth weight population was 36/52 in Group Ia, 64/119 in Group Ib, 3/13 in Group IIa, and 3/25 in Group IIb; smallness for gestational age population was 6/52 in Group Ia, 9/119 in Group Ib, 5/13 in Group IIa, and 9/25 in Group IIb, respectively.

DISCUSSION

While analyzing pediatric autopsies, we encountered papillary muscle necrosis (PMN) as a frequent finding, but we could not find any specific pathological condition in other viscera foretelling the presence of PMN of the heart. These facts led us to design this study. A histopathological reappraisal of the significance of PMN was its main purpose.

The ventricular subendocardium, especially the papillary muscle, locates at the terminal portion of coronary circulation and thus is more susceptible to damage induced by tissue hypoxia or ischemia due to hypoperfusion (Nishimura et al., 1983). In this respect, papillary muscle necrosis due to ischemia (ischemic papillary muscle necrosis: IPMN) is thought to be a common and major type of PMN, and Donnelly et al performed an impressive study on the clinicopathological aspects of IPMN in the 82 neonatal autopsies with documented perinatal stress (Donnelly et al., 1980). Their criterion for IPMN was classic coagulation necrosis and other types of injury were not included. But in our experience, definite distinction of the specific type of myocardial necrosis is complicated in some cases with light microscopic examination alone and to decide whether a myocardial necrosis was induced by ischemia or not isn't an easy problem in individual cases, thus we prefer the broad term PMN in the study by Setzer et al. (1980). They reviewed a broad range of papillary muscle necrosis in a neonatal autopsy population. But these previous studies were mainly concentrated on the detailed clinical parameters associated with PMN and were confined to only those who died in the immediate neonatal period. In this study therefore, documentation of the possible presence of any other specific histopathological change that is related with PMN was the major point of interest and infant cases were included to evaluate the incidence of PMN in this age and furthermore to know whether only neonates in immediate postnatal period are prone to PMN of the heart.

The results can be summarized as follows; (1) PMN was not infrequently observed in both neonates (30.4%) and infants (34.2%) and its incidence was not different between the two groups, (2) In neonates with PMN, bronchopneumonia, hyaline membrane disease, hypoxic neuronal change, sepsis, subarachnoid hemorrhage, disseminated intravascular coagulation, and acute tubular necrosis were frequent findings, but only hypoxic neuronal change and acute tubular necrosis had a significantly higher incidence compared with the control group in the same period, (3) In infants with PMN, congenital heart disease, sepsis, bronchopneumonia, disseminated intravascular coagulation, and hypoxic neuronal change were frequently observed, but they showed no difference in incidence compared with the control group.

Based on the above results, PMN does not seem to be a frequent phenomenon confined to the neonatal period as in previous reports and this coincides well with the result of the study by Berry (1967). He examined myocardia of necropsy specimens from 135 consecutive autopsies in infancy and childhood and found ischemic myocardial necrosis with increased fuchsinophilia in 96 cases, i.e. in more than half. Though acid fuchsin staining was not performed in each case of our study, the presence of myocardial necrosis in a high proportion of Berry's study strongly supports our results because PMN is also a form of myocardial necrosis. In adults, PMN has been described to be present in 20 ~ 58% in the postmortem studies of acute myocardial infarction and the findings are identical to those of PMN observed in neonates of previous studies (Brand et al., 1960; Coma-Canella et al., 1989). We believe that PMN is possible not only in stressed neonates but in any age group and it mainly results from an identical pathogenetic mechanism, a compromised coronary circulation. We also have some childhood autopsy cases with PMN of the heart though they were excluded in the present study due to the limited number of cases.

As aforementioned, ischemia would be a cause of PMN in many cases but a pathogenetically different type of myocardial necrosis is also possible. Baroldi reviewed different types of myocardial necrosis in coronary heart disease with their pathophysiologic sig-

nificance (Baroldi, 1975). He described 'coagulative myocytolysis' as a different process from classic 'ischemic coagulation necrosis' showing subsequent polymorphonuclear leukocytic infiltration, granulation tissue, and scar formation. He mentioned that the pathogenesis of coagulative myocytolysis is a tetanic death of myofibers in hypercontracted state due to catecholamine release and this was not correlated with the degree of coronary occlusion. It was characterized by an absence of leukocytic infiltration during evolution and was also found in control subjects dying by accident besides cases with acute cardiac infarctions. It was also mentioned that the cause of coagulative myocytolysis is a metabolic problem rather than a vascular one. Considering the relative lack of leukocytic infiltration in the areas of PMN in the present study, the results of his study strongly suggest a possibility that some or a significant proportion of PMN observed by us was a result of coagulative myocytolysis rather than ischemic coagulation necrosis though the exact evaluation is deferred. Systemic metabolic derangement may have been feasible in the autopsied subjects. Cardiogenic shock is also a known cause of myocardial injury (Page et al., 1971) and it occurs in preterm infants with perinatal asphyxia (Cabal et al., 1980).

Although papillary muscle dysfunction was demonstrated in the stressed neonates and adults with acute myocardial infarction and was thought to cause a fatal hemodynamic derangement that may lead the subject to death (Coma-Canella et al., 1989), fibrosis and calcification observed in the foci of PMN suggest that some cases have tolerated the PMN for a significant period. The significantly higher incidence of acute tubular necrosis and hypoxic neuronal change in Group Ia raise a strong possibility that a larger proportion of PMN in this period is a manifestation of acute systemic organ injury of which the major constitution is the kidney, the central nervous system, and the heart (Perlman et al., 1989).

As a final discussion, there seem to be no specific accompaniments of PMN of the heart least histopathologically in the present study though congenital heart disease, which is known to be associated with PMN, was rather frequent in Group Ia and Ib. We did not examine the coronary branches but the contribution of obstructive coronary heart disease in PMN seems to be minimal (Bor, 1969).

The results imply that PMN of the heart may cover a broad range of myocardial injury due mainly to a compromised coronary circulation and partly to other causes such as catecholamine release and that it may occur in any stressed neonates and infants and possibly in older subjects though there may be differences in their resistance to that kind of injury. We believe that PMN would be encountered not so infrequently in pediatric autopsies. Thus, giving a serious significance to them in all cases in inappropriate (Setzer et al., 1980).

REFERENCES

Baroldi G: *Different types of myocardial necrosis in coronary heart disease: A pathophysiologic review of the functional significance. Am Heart J 89:742-752, 1975.*

Berry CL. Myocardial ischemia in infancy and childhood: *J Clin Path 20:38-41, 1967.*

Bor I, Myocardial infarction and ischemic heart disease in infants and children: *Analysis of 29 cases and review of the literature. Arch Dis Child 44:268-281, 1969.*

Brand FR, Brown AL, Berge KG: *Hitology of papillary muscles of the left ventricle in myocardial infarction. Am Heart J 77:26-32, 1969.*

Cabal LA, Devaskar U, Siassi B, Hodgman JE, Emmanouilides G: *Cardiogenic shock associated with perinatal asphyxia in preterm infants. J Pediatr 96:705-710, 1980.*

Coma-Canella I, Gamallo C, Onsurbe PM, Jadraque PM: *Anatomic findings in acute papillary muscle necrosis. Am Heart J 118: 1188-1192, 1989.*

Donnelly WH, Bucciarelli RL, Nelson RM: *Ischemic papillary muscle necrosis in stressed newborn infants. J Pediatr 96:295-300, 1980.*

Nishimura RA, Schaff HV, Shub C, Gersh BJ, Edwards WD, Tajik AJ. Papillary muscle rupture complicating acute myocardial infarction: *Analysis of 17 patients. Am J Cardiol 51:373-377, 1983.*

Page DL, Caufield JB, Kastor JA, DeSanctis RW, Sanders CA: *Myocardial changes associated with cardiogenic shock. N Engl J Med 285:133-137, 1971.*

Perlman JM, Tack ED, Martin T, Shackelford G, Amon E: *Acute systemic organ injury in term infants after asphyxia. AJDC 143:617-620, 1989.*

Setzer E, Ermocilla R, Tonkin I, John E, Sansa M, Cassady G: *Papillary muscle necrosis in a neonatal autopsy population: Incidence and associated clinical manifestations. J Pediatr 96:289-294, 1980.*