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Immunohistochemistry in the Recognition of Early Myocardial Infarction

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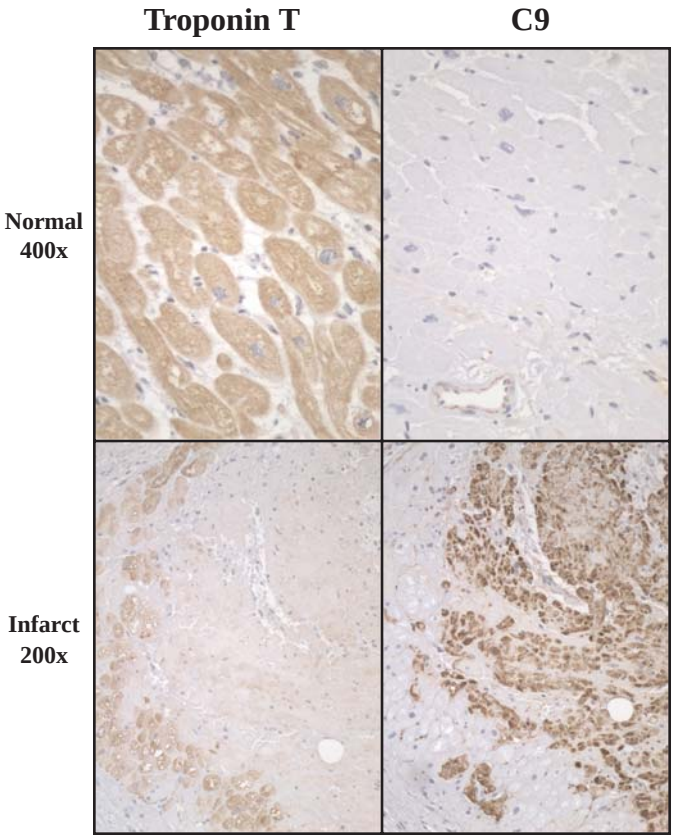
by Rodney T. Miller, M.D., Director of Immunohistochemistry

Myocardial infarction (MI) remains one of the most common causes of death in the US, so identification of MI as a contributing cause of death is fairly common in patients coming to autopsy. The morphologic changes associated with MI are well described, and with knowledge of these changes, pathologists are often able to estimate fairly accurately when the actual infarct occurred. However, there remains a period of time early after the inciting event (typically within the first 12 hours) where diagnostic morphological changes can absent or too subtle to be confidently recognized. Over the years, a number of different staining techniques have been employed to assist in the identification of these early infarcts that are not yet recognizable on H&E. This month, we briefly review the utility of immunostains for complement component C9 and Troponin T to address this problem.



Immunostains for complement component C9 have been shown by a number of investigators to be a reliable and sensitive method for detecting early myocardial hypoxia. Normal (non-hypoxic) cardiac muscle lacks staining with C9, but hypoxic myocardium demonstrates positive immunostaining for this marker. In a 1996 study from England, Doran and associates studied 25 autopsy cases of suspected or known MI, and 25 cases without appreciable morphological evidence of MI. 24 of the 25 cases of known MI showed positive C9 immunostaining, but upon review, the one case that did not stain was eventually thought in reality to not have any evidence of infarction. 16 of these cases had detectable changes on H&E (all with MI >24 hours premortem), and the other 8 hearts had clinical evidence of infarction less than 24 hours old. The 25 control hearts showed no H&E changes of infarction, but 3 were stained positively for C9. Each of these 3 positively-staining cases were from patients with sepsis or those who had another reason for myocardial damage. The authors also compared C9 immunostains with a histochemical method (nitroblue tetrazolium/phenazine methosuphate) in a smaller group of 8 infarction cases, and found that the histochemical method detected infarction in 5 hearts, but the C9 immunostain detected infarction in 7 hearts. Furthermore, the authors noted that the histochemical method required fresh tissue (unlike the C9 immunostains), and the histochemical method results were more difficult to interpret.

In a 2001 study from France, Piercecchi-Marti et al studied 121 heart heart specimens, including 33 cases with histologically evident ischemic change, 20 cases in patients who died with EKG evidence of ischemia but no H&E changes of infarct, 35 cases with severe coronary

disease but unknown cause of death, and 33 control patients. The patients in the first group of 33 cases with histologically evident ischemic damage all showed positive C9 immunostains. 17 of the 20 patients who died with EKG evidence of ischemia demonstrated positive C9 immunostains, and the three that were negative were noted to have pain that began less than one hour before death. 6 of the 35 cases with severe coronary artery disease but unknown cause of death demonstrated positive C9 immunostaining, and all 33 control cases were negative for C9 immunostaining. The authors concluded that C9 immunostaining was 100% specific and 85% sensitive for infarction.

In a 2003 study, Fishbein and colleagues studied the utility of immunostains for troponins T and I in an experimental model of myocardial infarction. They evaluated 50 hearts from dogs, pigs, and rats, including 34 animals that had permanent coronary artery occlusion for 0.5 to 6 hours before death, and also a group of 16 that had occlusion of between 0.75 to 6 hours, followed by reperfusion. They found that normal myocardium stained with antibodies to troponin, and necrotic myocardium showed a loss of immunostaining, which in some cases was identifiable as early as 30 minutes after coronary occlusion. There was some degree of non-uniformity of loss of Toponin T immunostaining, as the periphery of the infarcts tended to show greater loss than the central regions. In general, the findings noted with troponin T were more impressive than those noted with troponin I.

In summary, in cases where MI is suspected but typical histologic changes are not apparent, immunostains for complement component C9 and troponin T can be very useful in documenting the presence of myocardial ischemia in specimens that are obtained too early after the hypoxic event to show appreciable morphological changes on H&E. Both of these antibodies are available at ProPath for those pathologists who are faced with this problem.

	Troponin T	**C9**
Normal Myocardium	Positive	Negative
Infarcted Myocardium	Decreased	Positive

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Rodney T. Miller, M.D.
Director of Immunohistochemistry
214-237-1631 • Fax 214-237-1770
rmiller@propathlab.com

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PROPATH
8267 Elmbrook Dr, Ste 100 • Dallas, Texas 75247-4009
(214) 638-2000 • Fax: (214) 905-3457
www.propathlab.com