CLINICOPATHOLOGIC CORRELATIONS

De Subitaneis Mortibus

VII. Disseminated Intravascular Coagulation and Paroxysmal Atrial Tachycardia

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SUMMARY

Disseminated intravascular coagulation was the cause of death of a 19-year-old woman with a lifelong history of paroxysmal atrial tachycardia. Her final illness began with a bout of tachycardia during her second trimester of pregnancy and was then characterized by sustained tachycardia with hypotension, oliguria, and renal failure, with a steadily falling hematocrit in the absence of significant bleeding externally. At necropsy there were numerous platelet and fibrin emboli throughout the heart. Small arteries in both the sinus node and in the atrioventricular (A-V) node and His bundle were involved. The sinus node was virtually destroyed by recent infarction. Structural variation in the A-V node and His bundle, probably congenital in nature, provided an anatomic substrate for re-entrant loops which may have been the basis for the paroxysmal atrial tachycardia.

Additional Indexing Words:

Pregnancy Platelets Atroioventricular node Cardiac anatomy Sinus node Fibrin Vasopressor drugs

SOME HAVE SAID that the real mystery is not why our blood clots but what keeps it from clotting under normal circumstances. Under certain abnormal circumstances things can and do go awry with the result of disastrous clotting and bleeding at the same time. The hemorrhagic state which accompanies disseminated intravascular coagulation is now widely recognized to occur as the consequence of a remarkable array of diseases and conditions.1-31 Although distinct abnormalities of coagulation have been described in patients with several forms of heart disease,4-8 relatively little attention has been given to the subject of disseminated intravascular coagulation in the cardiological literature. The purpose of the present report is to describe a case in which a young woman with a lifelong history of paroxysmal tachycardia died with disseminated intravascular coagulation.

Case Description

A 19-year-old woman had recurring episodes of rapid cardiac action throughout most of her life, her mother specifically remembering them since the patient was six years old. Two episodes several months before the final illness had been successfully treated with metaraminol. Except for the bouts of tachycardia, she had always been healthy. The terminal illness began with an episode of tachycardia in the sixth month of pregnancy. Although the tachycardia (figs. 1-3) again responded to metaraminol, shortly thereafter she began to vomit and cough and became cyanotic and ashen in color. There were moist rales in both lung bases. Respirations were labored at 44/min. Treatment with digitalis, diuretics, and oxygen was begun, but the tachycardia very soon recurred and thereafter resisted any subsequent attempt at conversion to sinus rhythm. A tracheostomy was performed. An indwelling catheter was placed in the superior vena cava via the right subclavian vein. During the week of her terminal illness, she received antibiotics, corticosteroids, heparin, diphenylhydantoin sodium, quinidine, and propranolol. Repeated attempts at cardioversion with DC shocks did not alter the tachycardia significantly. Blood pressure could not be maintained with various pressor agents or blood

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transfusions and she gradually developed oliguria and renal failure. A stillborn baby girl was delivered near the midpoint of this week of terminal illness. The last day she had a series of cardiac arrests, following one of which all resuscitative efforts failed.

Throughout the terminal illness she remained febrile although all cultures were persistently negative. There was also a progressively decreasing hematocrit level (48% on admission, 44% later that day, 31% the fourth day and 21% the seventh day) without external evidence of excessive blood loss. Partial thromboplastin time was 30 sec the day of admission and 61 sec on the day of death.

At necropsy there was mild endometritis from the recent delivery, acute renal tubular necrosis, and central necrosis in the liver. Scattered capillary glomerular thromboses were present (fig. 4). In the lungs there was bilateral pulmonary edema and congestion, extensive interstitial pneumonitis and hyaline membrane formation. Numerous thrombi were present in small and medium sized pulmonary arteries, some being very recent and others undergoing organization. A thrombus which occluded the right subclavian vein also extended through the superior vena cava into the right atrium (fig. 5). Nonbacterial endocarditis involved both the mitral and tricuspid...
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valves. Throughout the myocardium of all four cardiac chambers many small arteries were occluded by varying admixtures of platelets and fibrin (figs. 6-9). Micro-infarcts were diffusely present in the myocardium with and without contracture bands, but there was no grossly visible myocardial infarction. Because of the lifelong history of paroxysmal tachycardia, the conduction system was especially studied.

The regions of the sinus node and of the A-V (atrioventricular) node with His bundle were cut into ten equally spaced blocks approximately two millimeters thick. Each of the twenty blocks was embedded in paraffin and then at least ten screening sections (about 7 microns thick) were prepared from each block. After the initial study, some blocks were serially sectioned, a total of 543 slides eventually being studied from the conduction system. Tissue was also sampled from the wall of each of the four cardiac chambers for comparison with vascular and other changes found in the conduction system. The major coronary arteries were free of disease and the nutrient vessels of the sinus node and of the A-V node arose from the right coronary artery at usual sites.12

The thrombus in the superior vena cava was attached directly beneath the sinus node (fig. 5). There was a small thrombus attached to the endothelium of

Figure 4

These are photomicrographs of lung (A) and kidney (B and C). In one pulmonary artery there are both platelet (P) and fibrin (F) masses. Capillary thrombi in a glomerulus are seen in B, and fibrin free in Bowman’s space is shown in C (arrow). Magnifications are as indicated. These and all other photomicrographs are from preparations with the Goldner trichrome stain.

Figure 5

The thrombus in the superior vena cava (SVC) was directly beneath the sinus node (SN). In the lower photomicrograph a thrombus beneath the tricuspid valve (TV) is shown.

Figure 6

Platelet aggregates were present in many small arteries in the left ventricle.
the sinus node artery (fig. 8) and both platelet and mixed platelet-fibrin thrombi were present within many terminal branches of the sinus node artery (fig. 9). Virtually the entire substance of the sinus node was infarcted but there was no cellular infiltrate (fig. 10).

The A-V node contained long fronds of cells extending into the central fibrous body, some spurring into blind pockets and others returning back to the main body of the node to form loop connections (fig. 11). The His bundle did not have the usual smooth outline on cross section seen in normal adult hearts but exhibited fragmentation and outpocketings, although it was not at any point discontinuous. At its anterior margin the His bundle had some focal degeneration and edema, with similar lesions near the origin of both the right and left bundle branches (fig. 12). As in the sinus node artery, the main A-V node artery contained a small mural thrombus and some of its terminal branches were occluded (fig. 7).

Discussion

Disseminated intravascular coagulation is a catastrophic process for which little can be done in its later stages. Yet its early manifestations may be subtle and protean, being associated with or following such a wide spectrum of causative diseases and conditions, that the diagnosis is seldom made at the onset. Warnings and reviews concerning this clinical dilemma are available in several recent presentations, and we will focus our attention on particular features of the present case.

One is struck by the dramatic onset of the terminal illness, beginning with sudden vomiting, coughing, cyanosis, and vascular collapse. All of these appeared very shortly after the conversion of the paroxysmal atrial tachycardia by the administration of metaraminol, a treatment which had been consistently successful in the past in the same patient. Whatever caused the disseminated intravascular coagulation, there is no question of the increased susceptibility of patients with pregnancy, and the fact that the patient was pregnant must have been a jeopardy. However, since she was not initially in any obstetrical distress or having any obstetrical treatment, the pregnancy could at most have been a contributory factor at the outset. When the miscarriage occurred several days later, this may have compounded the problem.

Figure 7

In the A-V node there was a small platelet mass attached to the endothelium of the main A-V node artery (shown at two magnifications), as well as platelet-fibrin masses occluding some of its terminal branches (lower right).

Figure 8

A mural thrombus of platelets was present in the main sinus node artery (shown at two magnifications) and resembled that in the A-V node artery (fig. 7).
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Two other possible etiological factors in the initial period are some aspiration from vomiting, and generalized tissue hypoxia from intense vasoconstriction secondary to the use of a pressor amine. By the time of necropsy there was extensive pneumonia and hyaline membrane formation, and these may have been initiated by an earlier aspiration of vomitus although none was later identified. Conversely, the multiple small pulmonary emboli must have compounded the other disease in the lung. A second possible cause for disseminated intravascular coagulation may have been the use of a pressor agent (metaraminol) in a pregnant woman. Hardaway \(^4\) has emphasized the essentiality of stagnant, acid capillary blood flow in the production of disseminated intravascular coagulation. In retrospect, some other form of treatment for the paroxysmal atrial tachycardia may have been preferable, especially during pregnancy, even though metaraminol had consistently been effective and safe in the same patient on previous occasions.

Paroxysmal atrial tachycardia is now generally considered to be a re-entrant mechanism occurring within or near the A-V node. For such an explanation many diagrams have been published illustrating a hypothetical loop or circuit within a schematic A-V node. In this patient there were actual anatomic loops as well as long fronds of A-V nodal tissue extending away from the node into the central fibrous body. These may have served as true anatomic counterparts to the hypothetical diagrams, permitting periodic recycling of sinus beats as they arrived within the A-V node. With focal ischemia and damage subsequent to the widespread microembolization, there may have been further effective partitioning of conduction within the A-V node, permitting re-entry to occur still more readily. Finally, with uneven arterial perfusion in the A-V node, its various cells would additionally be expected to have differing levels of excitability even in the absence of visible damage, further facilitating the likelihood of re-entry.

Although the His bundle is not usually considered as a site for re-entrant mechanisms, both anatomic \(^5\) and experimental pharmacologic \(^6\) evidence has recently been presented suggesting that longitudinal dissociation of conduction normally occurs within the

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**Figure 9**

Masses containing varying mixtures of platelets and fibrin were found occluding multiple terminal branches of the sinus node artery, with three examples shown here from the crista terminalis adjacent to the sinus node. All are at the same magnification.

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**Figure 10**

Virtually the entire sinus node was infarcted, with varying degrees of contraction of myofibrils. These two photomicrographs are from the midportion of sinus node and are representative of its over-all appearance.
His bundle. In the present case there was furthermore visible fraying of the His bundle, providing still another potential anatomic site for re-entry to occur. This too would have been further aggravated by uneven local arterial perfusion caused by multiple local thrombo-emboli. Actual damage at the origin of both the right and the left bundle branches and in the distal portion of the His bundle itself almost certainly accounts for the distortion of the QRS complex and A-V block seen later in the terminal illness.

Extensive destruction of the sinus node was present, but it all appeared to be very recent. Possible abnormal sinus node function early in the terminal illness could hardly be attributed to the widespread degeneration of the sinus node seen a week later, without cellular infiltrate being present. On the other hand, if mural thrombi repeatedly formed in the sinus node artery and acted as a source for recurring showers of platelets into branches of the artery, many of these platelet emboli later disaggregating, then the sinus node may have repeatedly failed early. The later extensive destruction seen fits more closely in time with the recurring bouts of cardiac arrest which comprised the final series of events. The presence of a large mural venous thrombus in the superior vena cava directly underlying the sinus node is difficult to relate to malfunction of the node, since it usually has multiple available routes of thebesian venous drainage, and since there was no apparent venous congestion within the sinus node.

There was also thrombosis beneath the tricuspid valve near the A-V node, but for the same reasons cited above it seems unlikely that this caused local ischemic or other malfunction of the A-V node. Both the subvalvular thrombus and that in the superior vena cava are attributable to local injury from the indwelling venous catheter, particularly with the hyper-coagulable state present. The verrucae on both atrioventricular valves have been repeatedly described by others as one of the features of disseminated intravascular coagulation, as well as of the closely related state of thrombotic thrombocytopenic purpura. Focal damage within the cardiac conduction system likewise occurs in both conditions.

Of the various organs containing multiple platelet and fibrin emboli, the heart was most extensively affected, the lungs less so — although the variety of ages of emboli there was broader — and the kidneys least. As emphasized by Deykin, disseminated intravascular coagulation is a complex process in which
fibrinogen is attacked simultaneously by both thrombin and plasmin. In the present case, as in so many others reported in which heroic therapeutic measures failed, some of the complications and final findings are in part a consequence of the treatment. The hyaline membranes in the lung and renal tubular necrosis are two examples, as are some of the micro-infarcts in the heart, all of which must have been worsened by the recurring severe hypoxia and hypotension and by the continued use of vasopressor substances.

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