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July 23, 1985

Mr. W. C. Bachtel
B.F. Goodrich
500 South Main Street
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Dear Mr. Bachtel:

Attached is a copy of the article which identifies the Swan-Ganz catheter constructed of polyvinylchloride as being thrombogenic and increasing platelet consumption.

My colleagues and I would appreciate you receiving this information and giving us your thoughts and expertise on the matter.

Sincerely,

Patricia F. Johnson

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Nonbacterial Thrombotic Endocarditis Associated with Severe Preeclampsia and Pulmonary Artery Catheterization

A Case Report

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A pulmonary artery catheter was placed in a parturient whose 33-week gestation was complicated by severe preeclampsia and pulmonary edema. Cesarean delivery was performed for both maternal and fetal indications. During the second postoperative day the patient developed disseminated intravascular coagulation; subsequently she experienced sudden cardiopulmonary arrest and died. Autopsy revealed multiple pulmonary thromboemboli and trivalvular nonbacterial thrombotic endocarditis.

Introduction

There is increasing enthusiasm for the use of invasive cardiac monitoring in critically ill obstetric patients.[1-7] Serious complications from a pulmonary artery catheter are infrequent but include arrhythmia, catheter knotting, pulmonary infarction, pulmonary arterial rupture, sepsis and both septic and aseptic thrombotic endocardial vegetation.[8] Below we report on the death of a pregnant patient with severe preeclampsia and an indwelling pulmonary artery catheter. Autopsy confirmed the presence of multiple pulmonary thromboemboli and nonbacterial thrombotic endocarditis, a finding previously unreported in an obstetric patient.

Case Report

A 26-year-old, obese, white woman, gravida 3, para 0, ab 2, presented to her obstetrician at 33 weeks' gestation with a three-day history of symptoms of an upper respiratory tract infection. Despite treatment with oral erythromycin for two days, she developed a worsening cough associated with fever to 38.1 C. After admission to her community hospital the initial blood pressures were 150–170/110–120 mm Hg but were subsequently 100–140/60–90. The physical examination was described as consistent with upper respiratory tract infection. The hematocrit was 41.7, and the white blood cell count was 20,800. Urinalysis revealed 3+ proteinuria. The patient was treated with intravenous ampicillin. The following day a chest X ray revealed bilateral lower lung field consolidation. Late that afternoon the patient became severely tachypneic; the room air arterial blood P_{O_2} was 49 mm Hg, P_{CO_2} was 27 mm Hg, and pH was 7.42. Persistent respiratory distress prompted a transfer to Duke University Medical Center. A blood pressure of 160/110 mm Hg was noted immediately prior to transfer.

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On admission the patient appeared severely distressed, with a respiratory rate of 70. Her blood pressure was 160/115 mm Hg, pulse was 136, and temperature was 37.5 C. No cardiac murmur was heard; breath sounds were shallow at the apices and absent at the bases. Arterial blood gas on 80% oxygen by mask included a P_{O_2} of 63 mm Hg, P_{CO_2} of 34 mm Hg and pH of 7.30. Nasotracheal intubation was performed, and mechanical ventilation with 14-cm H_2O-positive end-expiratory pressure was begun and continued until death. Foley catheter placement confirmed severe oliguria and 4+ proteinuria. A diagnosis of severe preeclampsia was made, and intravenous magnesium sulfate was begun. The hematocrit was 41; white blood cell and platelet counts were 28,300 and 493,000, respectively. BUN was 18 mg/dl, and serum creatinine was 1.6 mg/dl. SGOT and SGPT were 329 U/liter and 225 U/liter, respectively. Chest X ray revealed diffuse bilateral alveolar consolidation.

Three hours after admission a Swan-Ganz catheter was placed via the right internal jugular vein. Initial pulmonary artery pressure was 55/32 mm Hg; pulmonary capillary wedge pressure (PCWP) was 27 mm Hg, and central venous pressure was 12 mm Hg. Cardiac output was 4.8 liter/min (body weight, 115 kg), and calculated systemic vascular resistance was 1,910 dyne·cm·sec^{-5}. Following small doses of intravenous nitroglycerin, diastolic blood pressure was 100 mm Hg, PCWP was 14 mm Hg, and cardiac output was 7-8 liter/min. Urine output improved to 30-50 ml/hr.

Despite maintenance of left uterine displacement, external fetal heart rate monitoring revealed a baseline rate of 120, absent variability and spontaneous decelerations with a slow return to baseline, suggestive of fetal distress. Meanwhile, urine output decreased to 10 ml/hr. Thirteen hours after admission a low transverse cesarean delivery under general anesthesia resulted in the birth of a 2,170-gm male with Apgar scores of 1, 5 and 8 at one, five and ten minutes, respectively. Umbilical venous blood pH was 6.93. The infant was subsequently discharged in good condition.

Thirty-one hours after admission the hemodynamic parameters were essentially unchanged. With an F_iO_2 of 0.4, the arterial blood P_{O_2} was 75-85 mm Hg, but the chest X ray was improved. Fifty-five hours after admission the patient's temperature was 39 C. PCWP was 20 mm Hg, and urine output was 30 ml/hr. Hematocrit was 30, and platelet count was 81,000. Prothrombin time ratio was 1.4. Serum fibrinogen was 55 mg%, fibrin split products were positive at a dilution of 1:1,000, and fibrin monomer was present. Chest X ray revealed almost complete clearing of the alveolar consolidation. One hour later the patient abruptly developed bradycardia followed immediately by ventricular fibrillation. Aggressive cardiopulmonary resuscitation, including attempts at electrical defibrillation and transthoracic pacing, was unsuccessful.

Figure 1
Photograph of tricuspid valve at autopsy, demonstrating verrucous vegetation on the valve leaflets.

Autopsy revealed nonbacterial thrombotic endocarditis with verrucous vegetation on the tricuspid, pulmonic and mitral valves (Figure 1). In addition there was cardiomegaly; the mitral valve was scarred and its chordae tendineae fused and thickened, consistent with old rheumatic heart disease. There were multiple thromboemboli of the lungs and kidneys as well as thrombi of the uterine veins. All antemortem blood, sputum and urine cultures were negative. Postmortem blood culture was positive for *Staphylococcus*, coagulase negative. All valvular histologic specimens revealed the absence of an inflammatory response and organisms.

Discussion

It is unclear whether pneumonia, respiratory failure and hypoxemia preceded the onset of preeclampsia in this patient or whether severe preeclampsia was the primary illness, resulting in acute pulmonary edema. Regardless, the criteria for the diagnosis of severe preeclampsia and pulmonary edema were fulfilled.

Nonbacterial thrombotic endocarditis (NBTE) is the deposition of various-sized fibrin-platelet thrombi upon the surface of one or more cardiac valves. The microscopic hallmark of these lesions is the

absence of an inflammatory cell response, thus distinguishing these lesions from those accompanying acute and subacute bacterial endocarditis.[9] The valves and vegetation are generally sterile, though the thrombi may act as filters to entrap blood-borne bacteria, resulting in occasional secondary infection.[10]

The incidence of NBTE has varied from 0.4% to 1.6% in large, general autopsy series.[9,11-13] For many years NBTE was regarded primarily as a pathologic curiosity noted at autopsy in elderly, debilitated patients, many of whom had widespread malignancy.[9,12-15] In addition, the presence of old rheumatic heart disease has been associated with the development of left-sided NBTE.[9,13] To our knowledge this is the first reported case of NBTE in an obstetric patient.

In 1957 MacDonald and Robbins first reported the occurrence of multiple embolic infarctions in patients with NBTE. Subsequently Biller et al reported that 62 of their 99 cases were associated with distal emboli, most commonly involving the brain and kidneys. The three leading causes of death in their series, however, included pulmonary thromboemboli.[13]

Our patient developed a coagulopathy, a known complication of preeclampsia. Disorders of coagulation have been implicated in the pathogenesis of NBTE. Sugiura et al reviewed 64 autopsy cases with documented disseminated intravascular coagulation (DIC) and noted NBTE in 17.[14] Kim et al reported morphologic evidence of DIC in 18 of 36 patients with NBTE.[12] Young and Zalneraitis reported a 100% incidence of coagulopathy in seven children and young adults with NBTE.[16]

There is both experimental and clinical evidence to implicate the pulmonary artery catheter as an etiologic agent in the pathogenesis of NBTE. Gutschik and Christensen reported the consistent establishment of sterile endocarditis within three days of insertion of a polyethylene cathether into the hearts of rabbits.[17] The Swan-Ganz catheter is constructed of polyvinylchloride, which is also thrombogenic.[18,19] The pulmonary artery catheter has also been demonstrated to result in increased platelet consumption and subsequent thrombocytopenia in both healthy dogs[19] and surgical patients.[20]

Clinically there has been a significant increase in the incidence of right-sided NBTE since the introduction of the Swan-Ganz catheter in 1970. In the 1957 series of MacDonald and Robbins, 97% of the vegetation occurred on the valves in the left side of the heart.[9] Greene et al reported only one case of endocarditis involving the right side among 493 autopsies during the 30-month period prior to the introduction of the pulmonary artery catheter at their hospital, but they noted endocarditis of the right side of the heart in 10 of 438 autopsies performed during the subsequent 30 months after introduction of the pulmonary artery catheter. Five of these cases were associated with an indwelling pulmonary artery catheter, and four were associated with a central venous pressure catheter.[21] Pace and Horton also reported a significantly greater incidence of right-sided NBTE in patients with Swan-Ganz catheters than in other patients.[22]

NBTE is seldom diagnosed in living patients.[11,12,16] A murmur has not been heard in the majority of reported cases.[11,13] A sudden change in the cardiovascular or neurologic status may be the most frequent, albeit late, clinical manifestation of NBTE.[13,15] Echocardiographic diagnosis of NBTE in a patient with repeated embolic episodes has led to subsequent successful mitral valve replacement.[23] Anticoagulation therapy has been suggested,[15] but there has been no documented experience with the treatment of NBTE with anticoagulation or antiplatelet agents.

Attempts to reduce the duration of pulmonary artery catheterization may be one of the most practical means of reducing the incidence and minimizing the clinical sequelae of NBTE. Ford and Manley recently reviewed 100 consecutive autopsies of hospital inpatients.[10] Not only did all five cases of NBTE occur in the 24 patients with intracardiac catheters, but major endocardial lesions were discovered in all patients in whom a Swan-Ganz catheter was present for longer than 48 hours, whereas no patient with a Swan-Ganz catheter present for less than 48 hours had a major endocardial lesion. The authors admitted that these findings might have reflected the severity of the underlying illness as well as the prolonged endocardial trauma secondary to the catheter. However, there is at least experimental evidence to support the utility of removing the pulmonary artery catheter even after the discovery of NBTE. In a study in rabbits cited above, catheter withdrawal resulted in a rapid decrease in the size of the vegetation, with its almost-complete disappearance within ten days.[17] Such a spontaneous disappearance of NBTE has not been documented in humans.

We suspect that parturients may be at greater risk of developing NBTE than previously recognized. Pregnancy is normally associated with a hyperdynamic circulation, which may be exaggerated in the preeclamptic patient.[1,5-7] The constant contraction of

the heart against an indwelling catheter may predispose to endocardial trauma,[24] which, when occurring in patients with disorders of coagulation, may result in NBTE. Such an association of NBTE with hyperdynamic circulation and hypercoagulability has been reported in burn patients monitored with an indwelling pulmonary artery catheter.[25]

It is not the purpose of this report to discourage obstetricians from utilizing the pulmonary artery catheter. The available evidence continues to support the selected use of the Swan-Ganz catheter when cardiac or respiratory failure complicates pregnancy.[18] After placing a pulmonary artery catheter, however, the physician must continually weigh the benefits versus risks of continued monitoring. Serial echocardiography should be considered if it is deemed necessary for the catheter to remain *in situ* beyond 48 hours, if there is a sudden change in the neurologic status, or if there is other evidence of embolic phenomena. The development of coagulopathy should also alert the physician to the increased risk of NBTE development.

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bcc: J. Tanzilli
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August 22, 1985

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Dear Ms. Johnson:

Thank you for your letter of July 23, 1985 and the interesting article "Nonbacterial Thrombotic Endocarditis Associated with Severe Preeclampsia and Pulmonary Artery Catheterization" by Chestnut, D.H. et al. In the particular case cited, it is difficult to assign the total effects seen to the catheter alone. This particular patient had multiple diseases which could have been related to the nonbacterial thrombotic endocarditis (NBTE). However, as noted in the article, this is not an isolated instance of NBTE associated with the Swan-Ganz catheter, or as a matter of fact, other catheters.

It may be helpful to give you some very brief background information pertaining to polyvinyl chloride (PVC) and polyvinyl chloride products. The BFGoodrich Company produces PVC resin and some formulated PVC compounds. We are a raw material supplier of this material, rather than a finished article supplier. Due to the enormous versatility of PVC and the myriad applications for this substance, we are often not cognizant of each and every end use and the peculiarities of such uses. Most people are unaware that PVC plastics are formulated products; they do not represent a single entity. PVC resin by itself is a rigid substance and, to be made into useful products, must be formulated with other substances. In flexible PVC articles, PVC resin itself represents only about 50-70% of the formulation. The remaining 30-50% is composed of substances such as plasticizers (imparts flexibility), lubricants, heat stabilizers, colorants, etc., any one or all of which may have a more profound effect on the toxicological effects and bio-compatability than the PVC resin itself.

Without knowing the specific formulation used in the Swan-Ganz catheter, it is difficult to comment on any effects such ingredients may have. However, there does not appear to be any evidence to implicate the catheter chemically. Rather, it appears that such complications are the result of a foreign body type relationship.

After reviewing various articles, it is apparent that many of the hematological effects noted are not peculiar to the Swan-Ganz catheter, but occur in varying degrees with other types of catheters. Reduction in platelet count and thrombogenicity are probably related in part to surface area. Hence, the size and configuration of the Swan-Ganz catheter probably has an effect on these parameters.

Patricia F. Johnson, R.N., MSN
Reading Hospital

Surface properties appear to have some effects on biomaterials. R.E. Baier[1] has discussed at length the role of surface energy in thrombogenesis. He proposes that the critical surface tension is related to the physical bio-compatability of various biomaterials. He notes that platelet adhesion to various surfaces can be correlated with the critical surface tension of a material. For short contact times there is an apparent direct relationship between critical surface tension and the average number of adherent platelets. There also seems to be an inverse relationship of critical surface tension to clotting time, i.e. when the critical surface tension is high, the clotting time is shortened. He has shown in some experiments that exposure of some materials to fresh flowing blood for as little as five seconds will result in a coating of proteinaceous film (most likely fibrinogen) and that a typical thrombus mass grows on such surfaces. For thrombo resistance, the critical surface tension is in the range of 20 to 30 dynes/cm. Most polymers, however, are in the range of 30 to 40 dynes/cm. PVC has been reported to be 39 dynes/cm. I am not sure how representative this value is of all PVC formulations.

Without knowing details of the formulation and the surface characteristics of the Swan-Ganz catheter, I can only speculate as to the cause of the observed effects. It would seem the reported thromocytopenia and thromogenic properties associated with the Swan-Ganz catheter are related to foreign body surface phenomena related to surface tension. This physical effect induces platelet activation, resulting in platelet deposition and increased phagocytosis by the reticuloendothelial system. These effects could account for thrombus formation and decrease in platelet count. These physical effects may be intensified by the hematological state of the patients in which these catheters are employed. And since the catheter is positioned through the right ventricle in use, it follows that physical effects in this area would be noted.

I hope this discussion and speculation may be useful to you. If you wish further information, I suggest you contact Edwards Laboratories, Santa Ana, California. They are likely to have more specific data and information on adverse reactions associated with these catheters than we have.

Sincerely,

W. C. Bachtel
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The BFGoodrich Company

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[1]The Role of Surface Energy in Thrombogenesis, R.E.Baier, Ph.D. Bull. N.Y. Acad. of Med. pg. 257-72, Vol. 48, No. 2, Feb. 1972.