CASE REPORT

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Myocardial Infarction in Pregnancy

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ABSTRACT: Myocardial infarction occurring during pregnancy or the puerperium is a rare condition, occurring in about 1 per 10 000 deliveries, and carries a mortality of approximately 30%. As a consequence of its rarity, symptoms of impending infarction may be easily mistaken by physicians for much more common and innocuous conditions, especially those (such as gastroesophageal reflux) typically associated with pregnancy. Two cases of infarction in pregnant women are presented, with a discussion of risk factors which may predispose towards development of coronary artery disease or thrombosis in this population. Other, more uncommon, causes of myocardial infarction during pregnancy are also addressed.

KEYWORDS: pathology and biology, pregnancy, myocardial infarction, cardiovascular system

Although atherosclerotic vascular disease is a leading cause of death among industrialized nations, it is generally recognized that women in the reproductive years have a far lesser risk of coronary occlusive disease, and thus myocardial infarction, than males of the same age. After menopause, the incidence of myocardial infarction dramatically rises to parallel that of men, implying that some sort of protective factor is lost during the development of ovarian hormonal senescence. Many possible reasons for the relative protection from atherosclerotic disease in premenopausal women have been explored, including estrogens, hematocrit disparities, blood lipid differences, decreased incidence of cigarette smoking, and a so-called "sheltered mode of life" [*1*]; none of these have yielded conclusive information of statistical validity.

As may be expected, myocardial infarction is extremely uncommon in pregnant women, and it is thus not widely recognized that atherosclerotic vascular disease which is serious enough to cause infarction (or death) may manifest itself during pregnancy. Several well-known (and relatively more common) conditions may cause sudden death in a pregnant woman, including ruptured tubal pregnancy, pulmonary thromboembolism, and amniotic fluid embolism. Most of these entities manifest distinctive premortem symptomatology or

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should be detected with little difficulty at the postmortem examination. However, the rarity of coronary vascular disease during pregnancy may render accurate detection difficult, both by the clinician and the pathologist. The myriad of clinical symptoms that much more commonly may accompany a growing intrauterine pregnancy, such as heartburn as a result of gastroesophageal reflux or cholecystitis exacerbating preexisting cholelithiasis, can simulate the symptoms of angina or an impending infarction. As a consequence, this potentially fatal condition may be misinterpreted by even the most experienced physician because its presentation in a pregnant woman is somewhat out of the usual context. Similarly, a cursory examination of the coronary arteries in a sudden maternal death may cause the pathologist to miss a subtle yet fatal stenotic or thrombotic lesion.

The following are two cases which are illustrative of myocardial infarction during pregnancy.

Case Reports

Case 1

A 37-year-old X-ray technician, Gravida I, Para O, experienced a bout of substernal chest pain during the late evening, while in her 12th week of pregnancy. Although a heavy smoker and moderately overweight 67.5 in. [171.5 cm] in height and 180 lbs [81 kg], she had no family history of heart disease. The pain subsided spontaneously after about 30 min. The next day, while at work in the hospital, she had an electrocardiogram performed, which was interpreted as normal. Fifteen minutes later, she was found collapsed and unresponsive in the radiology department. Intensive resuscitative efforts were unsuccessful.

At autopsy, an intrauterine pregnancy of approximately twelve weeks gestation was found. Significant pathologic findings were limited to the heart. The left anterior descending coronary artery bifurcated early in its course and continued as two parallel branches, a smaller and a larger. The larger branch had eccentric, focally calcific atherosclerosis which narrowed the slit-like remnant of the lumen approximately 80%. The smaller branch had 90% stenosis by atherosclerosis, and the remainder of the lumen was occluded by fresh thrombus (Fig. 1). In the adjacent myocardium of the left ventricular free wall were focal interstitial infiltrations of polymorphonuclear leukocytes, and wavy fiber change of the myocytes, indicative of an acute infarction of about 12 to 24 h duration.

Case 2

The patient was a 26-year-old woman who had been an insulin-dependent diabetic for 22 years. She had delivered her first pregnancy in 1982 via Cesarean section. Following this, she had an episode of retrosternal chest pain lasting several days, which was diagnosed as "viral myocarditis." She was advised not to have further children, but 2 years later, she again became pregnant. One month before death, in her twelfth week of gestation, she had an episode of chest pain with electrocardiographic stress changes. Her physician urged hospitalization, but she refused admission. On the night of her death, she awoke feeling ill. Fearing an insulin reaction, her husband administered an unknown amount of Glucagon, and they rushed to the hospital. A flat tire halted their progress, and her husband went to a nearby tavern. By the time an ambulance was called and help arrived, she was dead.

Autopsy examination of the heart (which weighed 290 g) revealed marked concentric thickening of the left anterior descending coronary artery, with a 98% stenosis (Fig. 2). The right and circumflex coronary arteries were also affected by atherosclerotic narrowing, but to a lesser degree. The anterior leaflet of the mitral valve had atherosclerotic plaque and thickening. The papillary muscles of the left ventricle were fibrotic, with most severe involvement of the anterior papillary muscle. Multiple areas of old, fibrotic infarction were scattered

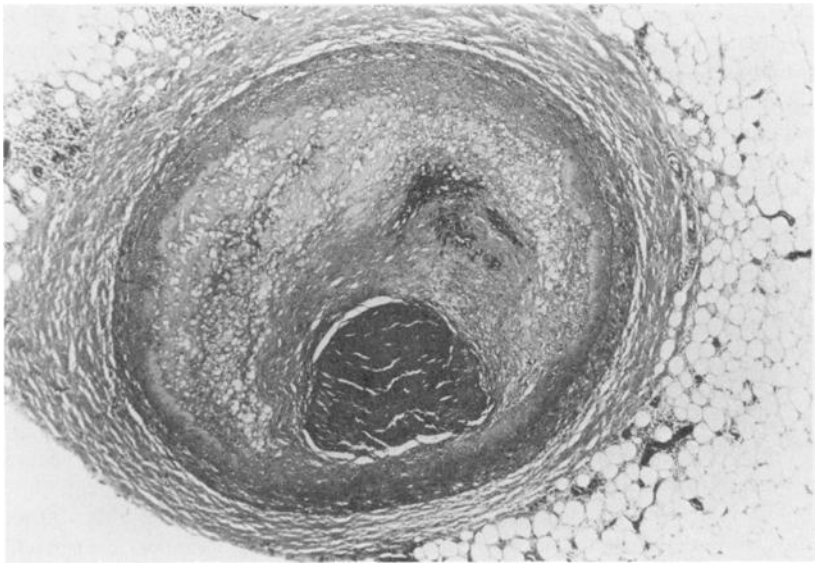

FIG. 1—*Case 1: Approximately 90% atherosclerotic narrowing of smaller branch of left anterior descending coronary, with complete occlusion of lumenal remnant by fresh thrombus (×55).*

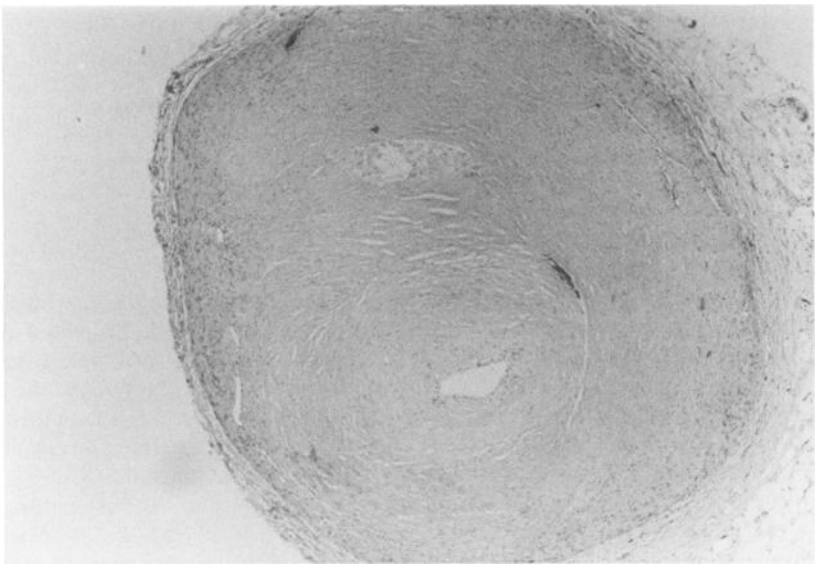

FIG. 2—*Case 2: Extremely severe atherosclerotic stenosis of the left anterior descending coronary artery (×28).*

throughout the left ventricular myocardium, with diffuse subendocardial scarring. The interventricular septum likewise had multifocal areas of fibrosis. Microscopically, multiple stellate foci of fibrosis with a diffuse lymphocytic infiltrate were distributed throughout the myocardium (Fig. 3). The papillary muscles had extensive fibrosis and coagulation necrosis. These findings were consistent with a chronic ischemic cardiomyopathy, with foci of recent and old myocardial infarction.

Kidney sections exhibited severe sclerosis of small arteries and arterioles, with diffuse glomerular sclerosis, and focal nodular, Kimmelstiel-Wilson changes. An intrauterine pregnancy of 16 weeks gestation was present, which was grossly and microscopically unremarkable.

Discussion

The estimated frequency of myocardial infarction during pregnancy has been calculated at approximately 1 per 10 000 deliveries [*2,3*]. It is quite probable that a significant number of infarctions are clinically missed, especially in survivors where symptoms of chest pain may be misinterpreted as the much more prevalent entities of pulmonary thromboembolism, cholecystitis, indigestion, or of chest wall origin.

Husaini [*4*] reviewed 43 cases of infarction during pregnancy, finding an overall mortality of 30%; thus, the mortality from this condition is about 1 in 30 000 deliveries. In his series, the mortality appeared to peak in the second trimester and puerperium, and was 4 to 5 times higher in patients under 35 years of age. The reasons for this are obscure; as maternal mortality from all causes increases with age [*5*], it would be expected that older patients would tend to do worse, but the reverse appears to be the case in the specific consideration of myocardial infarction.

In terms of risk factors, the most common increased risk is associated with hypertension; 16 of 45 cases (36%) in Husaini's series were hypertensive, the majority with accompanying

FIG. 3—*Case 2: Advanced chronic ischemic fibrosis and scarring of myocardium, with accompanying diffuse lymphocytic infiltrate (×280).*

manifestations of eclampsia or preeclampsia. Mann et al. [6] identified specific risk factors for myocardial infarction in younger women to include heavy cigarette smoking, reported treatment for preeclampsia, Type II hyperlipoproteinemia, hypertension, and diabetes mellitus. A combination of any 3 of these factors had a synergistic effect, increasing the risk of development of myocardial infarction 128-fold.

Hibbard [7] reviewed maternal deaths in California over a 9-year period, and found 77 of 1362 (6%) a result of cardiac disease; of these, 9 (12%, or 0.6% of the total) were due to coronary artery disease. Only 1 of the 9 patients was under 36 years of age; 1 other was a juvenile onset diabetic.

Several recent individual case reports [8-11] have concerned young women who develop symptoms and signs of myocardial infarction, with enzymatic and electrocardiographic documentation, but were found subsequently to have normal coronary angiography. A number of causes have been suspected for this [1], including valvular disease, polycythemia, cardiomyopathy, syphilis, and trauma. In each case, known diseases were eliminated, and a physiologic mechanism was hypothesized, based upon transient coronary artery narrowing by uterine renin release and angiotensin production. Conversely, Ciraulo and Markovitz [12] studied a 36-year-old multigravid woman who developed an infarction five months postpartum and found a thrombus-like filling defect with coronary angiography. They believed that the known hypercoagulable states that occur around the time of delivery [13,14] may, in some way, contribute to the formation of coronary thrombi, and that thrombolysis results in subsequent "normal" angiographic visualization.

Only rarely does treatment with ergot derivatives cause spasm of the coronary arteries. As these drugs are routinely used in some postpartum hemorrhagic conditions, it is possible that such treatment may inadvertently cause coronary spasm. Salem et al. [15] described a case of a 30-year-old woman with a myocardial infarction and normal coronary angiography, and postulated ergonovine provocation as the inciting factor.

A few other isolated conditions have been reported to be associated with myocardial infarction during pregnancy. Diro et al. [16] described an infarct, with subsequent ventricular aneurysm formation, following an incident of coronary arteritis as a result of an idiosyncratic reaction to imipramine hydrochloride. Lewis [17] delineated an infarction which resulted from *Bacteroides* infection of the myocardium, with subtotal thrombosis of the left anterior descending coronary artery.

The 2 cases reviewed here illustrate several of the patterns seen in myocardial infarction during pregnancy. In Case 1, the decedent was above the age of 35, the average of all previously reported cases, and exhibited severe atherosclerotic involvement of her coronary arteries. This finding is in keeping with the data of Hibbard [7], who found that the older age group of pregnant women who suffer myocardial infarctions do so almost always on the basis of atherosclerotic coronary vascular disease. Although there was no family history of coronary artery disease, she was overweight and a heavy smoker, and this probably contributed to her underlying condition and death. Interestingly, Restrepo et al. [18] studied coronary arteries and aortas from pregnant and nonpregnant women killed in accidents. They found that pregnant women in the 35- to 44-year age group had significantly less fatty streaks in the left anterior descending coronary artery than the nonpregnant group. It is clear that the interrelationships between the myriad factors that culminate in development of coronary artery atherosclerosis are poorly understood.

In the second case, the decedent's long history of diabetes mellitus certainly accelerated her coronary atherosclerosis. It is doubtful that the episode of "myocarditis" two years before her death was truly a virally mediated inflammatory process, and it is more likely that she had sustained a small infarct or was suffering from an acute exacerbation of her ongoing chronic ischemic cardiomyopathy. Microscopically, the postmortem myocardium exhibited a pattern characteristic of old infarction and profound chronic ischemia, with superimposed progressive hypoxic changes.

Conclusions

Myocardial infarction during pregnancy is a rare phenomenon, occurring in approximately 1 per 10 000 deliveries, with a mortality of 30%. In women over the age of 35, atherosclerosis is the predominant cause. In younger women, there is a higher likelihood of finding normal coronary arteries, with widely patent lumina. In sudden deaths such as these, the discovery of essentially normal coronary arteries during an autopsy still requires a detailed examination of the myocardium to search for evidence of infarction if other causes of death have been eliminated. The mortality rate among pregnant women who suffer myocardial infarctions is 4 to 5 times greater in those who are under the age of 35 years, as compared with the older age group; there is no evidence that satisfactorily explains this unexpected reversal. Elements of the patient background, such as the smoking history, personal and family medical history, and presence of hypertension or preeclampsia all aid in suggesting that a sudden maternal death may have occurred as a consequence of a myocardial infarction.

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