

Pregnancy and PXE

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Introduction

Pseudoxanthoma elasticum (PXE) is a hereditary disorder which is characterized by: 1) yellowish papules and plaques in the skin of the neck and flexural areas ("pseudoxanthomas"), 2) angioid streaks in the retina, resulting from breaks in Bruch's membrane of the choroid, and 3) cardiovascular and gastrointestinal complications related to abnormal elastic tissue in arterial walls. Bulletins, available from PXE International, entitled "PXE and the Primary Care Physician" or "PXE and the Dermatologist" offer detailed information about the disease.

The Effect of PXE on Pregnancy

A small number of published series have looked at pregnancy in women with PXE.

Berde *et al*¹ reviewed 24 pregnancies in nine women, published in five previous articles. In 20 pregnancies, five women accounted for eight instances of gastrointestinal hemorrhage due to abnormal blood vessels. Neldner² reported that 54 women noted significant worsening of skin, eye, and cardiovascular manifestations during pregnancy, but detailed corroborating analysis of obstetrical records is not available.

Viljoen *et al*³ did a retrospective analysis of 54 pregnancies in 20 South African women with PXE. In their series, no episodes of gastrointestinal hemorrhage were noted. Seven out of 54 patients were found to have hypertension and it was managed by traditional means (bed rest, diuretics, antihypertensives).

No ocular or other cardiovascular problems were reported, but there appeared to be a slightly higher incidence of first-trimester miscarriage (12/54). Labor and vaginal delivery were uncomplicated. In this series as in previous reports, cosmetic worsening of abdominal skin laxity and striae appeared to be proportional to parity and weight gain during pregnancy (as one would expect even in non-PXE pregnancies). Flexural skin appeared to remain stable.

Bercovitch *et al*⁴ studied 795 pregnancies in 306 women with PXE. 83% of pregnancies ended in live births. The incidence of miscarriage was 11%. Gastric bleeding was reported in about 1% of PXE-related pregnancies. Worsening of skin lesions was reported in 12.5% of pregnancies. Subretinal hemorrhages occurred in 0.5% of pregnancies. No thromboembolic complications were reported. Hypertension during pregnancy was reported by 10% of women. Of the 306 women surveyed, 17 had been advised by their physician not to become pregnant and 11 had decided on their own not to become pregnant due to PXE. The authors concluded that the incidence of PXE-related complications in pregnancy appears to be low, and pregnancy outcomes in PXE appear to be similar to the general population and that there was no basis for advising women with PXE to avoid pregnancy.

It appears, therefore, that based on the largest series in which obstetrical records were available, that fertility is normal, and the majority of women with PXE have a normal pregnancy, labor, delivery, and post-partum

period. The incidence of upper gastrointestinal hemorrhage during pregnancy in PXE appears to be much less than previously reported in small series and textbooks. It is recommended hypertension and pre-eclampsia be vigorously managed. Caesarean section should be considered for women who have choroidal neovascularization during the pregnancy.

Effect of PXE on the Fetus

In Viljoen's series³, the rate of premature delivery was in the expected range, and only 1/40 babies was born with a congenital malformation. In Berde's series¹, 20/22 infants were born in "good condition", one was stillborn following late trimester GI hemorrhage, and one died of congenital rubella syndrome. Two of three placentas showed calcifications of unknown cause.

In one study of the ultrastructure of the placenta in PXE⁵, there was no significant difference between the gross and light microscopic appearance of the placenta between PXE and controls, but by electron microscopy, an increase in mineral deposits associated with "matrix" type fibrinoid and collagen fibrils on the maternal side and the absence of mineralization of elastic fibers in either controls or PXE were noted. The changes were not felt to have significant physiologic consequences for the fetus.

In Bercovitch's series⁴, the incidence of stillbirth was about 1%, but only one stillbirth was suspected to be the result of a PXE-related complication (GI hemorrhage). The rest were the result of fetal causes or unknown factors. The incidence of prematurity (6%) and low birth weight was within the range expected in the normal population. In summary, except for the consequences of severe maternal hemorrhage, which appears to be uncommon, PXE has no known significant effect on the fetus. At this time, although genetic testing for PXE exists, it has not been used for prenatal diagnosis, and clinical manifestations of the disease are not visible at birth.

Effect of Pregnancy on PXE

In the series of Bercovitch *et al*⁴, there was no statistically significant effect of gravidity on the severity of skin, eye, cardiac, or peripheral vascular manifestations of PXE in women over 40. In addition, women over 40 with PXE who had ever been pregnant did not have more severe skin, cardiac, ocular, or vascular manifestations of PXE than those who had never been pregnant.

Gynecological Aspects of PXE

In Viljoen's series³, menarche occurred at the usual age, menstrual cycles were normal, and menorrhagia occurred with the expected frequency. No complications of oral contraceptive use were reported. Gynecologic and gynecologic surgical histories appeared unremarkable in their series. Viljoen raised the issue of whether other means of contraception should be considered because of the risk of thromboembolic complications in oral contraceptive users, but no data exist to support this concern in young women with PXE.

Genetic Counseling for Women with PXE

Women of childbearing age with PXE or family history of PXE should be offered genetic counseling. PXE is inherited as an autosomal recessive condition. There is no conclusive evidence that autosomal dominant inheritance occurs and all known cases of PXE occurring in parent and offspring which have been studied by mutation screening have been shown to result from pseudodominance (in which one parent is an affected individual carrying two mutations and the other is a heterozygous carrier). Genetic counseling will be greatly facilitated by availability of a FDA approved test kit for mutation detection in PXE in late 2006 or early 2007.

References

1. Berde C, Willis DC, Sandberg EC. Pregnancy in women with pseudoxanthoma elasticum. *Obstet Gynecol Surv* 1983; 38: 339-44.
2. Neldner KH. Pseudoxanthoma elasticum. *Clin Dermatol* 1988; 6: 1-159.
3. Viljoen DL, Beatty S, Beighton P. The obstetrical and gynaecological implications of pseudoxanthoma elasticum. *Brit J Obstet Gynaecol* 1987; 94:884-8.
4. Bercovitch L, Leroux T, Terry S, Weinstock MA. Pregnancy and obstetrical outcomes in pseudoxanthoma elasticum. *Br J Dermatol* 2004; 151:1011-18.
5. Gheduzzi D, Taparelli F, Quaglino D Jr, DiRico C, Bercovitch L, Terry S, Singer DB, Pasquali-Ronchetti I. The placenta in pseudoxanthoma elasticum: clinical, structural, and immunochemical study. *Placenta* 2001; 22:580-90.

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