Case Report

Placental Calcification in Pseudoxanthoma Elasticum

Wei Ching Tan,[1] *MBBS, MRCOG*, Charles H Rodeck,[2] *DSc, FRCOG, FRCPath*

Abstract

Introduction: Pseudoxanthoma elasticum (PXE) is an inherited multisystem disorder of the elastic tissue and the objective of this case report is to correlate ultrasonographic and histological appearances of placental calcification in PXE. Clinical Picture: We report a case of a 37-year-old white woman with PXE, whose antenatal imaging showed a markedly echogenic placenta due to extensive calcification confirmed on postpartum placental histology. Outcome: There were no maternal or fetal complications in the antenatal period. A healthy baby of appropriate maturity and weight was delivered via Caesarean section and remained well at 6 months. Conclusion: The majority of cases of PXE is caused by mutations in the ABCC6 gene. Serious complications in pregnancy can include gastrointestinal haemorrhage, congestive heart failure and cardiac arrhythmia but has not been shown to be associated with markedly increased fetal loss or adverse reproductive outcomes as reported in previous literature. Apart from the cosmetic deterioration of the abdominal skin, there were few serious complications and most have normal pregnancies. Obstetric prognosis is dependent on the vascular damage caused by the illness. There is no basis for advising women with PXE to avoid becoming pregnant, and most pregnancies in PXE are uncomplicated.

Ann Acad Med Singapore 2008;37:598-600

Key words: Angioid streaks, Echogenic placenta, Gastrointestinal haemorrhage

Introduction

Pseudoxanthoma elasticum (PXE) is an inherited multisystem disorder of the elastic tissue leading to skin disease as well as ocular and cardiovascular complications. Although earlier literature on pregnancy in PXE contained reports of severe complications, most patients show no serious complications during pregnancy. Some pregnancies were associated with worsening of skin manifestations but more recent reports showed no maternal or fetal complications in the perinatal period. We report a case of a 37-year-old white woman with PXE, whose antenatal imaging showed a markedly echogenic placenta due to extensive calcification known to be associated with PXE.

Clinical Picture

We report a case of a 37-year-old white woman with PXE, who delivered a healthy infant at the 38th week by Caesarean section following an uncomplicated antenatal period.

The onset of non-specific skin lesions was first noted at the age of 20 and skin biopsies then were inconclusive. A clinical diagnosis was subsequently made at the age of 26 in the presence of yellowish grouped papules with angioid streaks characteristic of PXE.

In this pregnancy, the 37-year-old primigravida was referred at 24 weeks' gestation for maternal PXE. A detailed scan showed fetal measurements to be appropriate for gestation with normal amniotic fluid volume and uterine artery Dopplers. The placental appearance was normal. A repeat scan at 34 weeks showed constant fetal growth velocity and normal uterine artery and umbilical artery Dopplers. The placental appearance was markedly echogenic due to extensive calcification (Fig. 1) which is known to be associated with PXE.[1]

The mother remained well in the antenatal period and did not complain of aggravation of skin lesions, symptoms of hypertension or gastrointestinal bleeding. She did not notice any significant changes in abdominal skin quality nor excessive striae gravidarum.

Treatment

She underwent an elective Caesarean section at 38 weeks for a non-reassuring fetal cardiotocograph. A baby boy weighing 3040 g with normal Apgar scores was delivered.

[1] Department of Obsterics and Gynaecology, Singapore General Hospital, Singapore
[2] Fetal Medicine Unit, Elizabeth Garrett Anderson & Obstetric Hospital, University College Hospital, London
Address for Correspondence: Dr Tan Wei Ching, Department of Obsterics and Gynaecology, Singapore General Hospital, Outram Road, Singapore 169608.
Email: aileen_tan2000@yahoo.com.sg

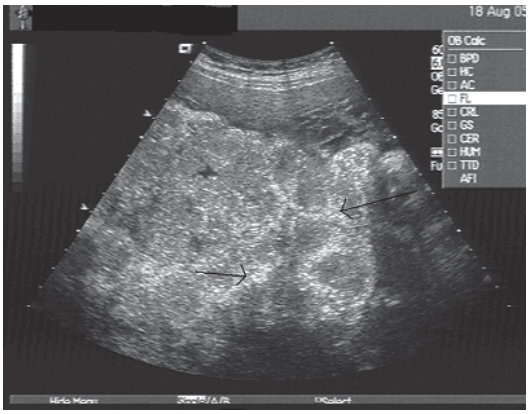

Fig. 1. Prenatal sonographic image of the placenta of a patient with pseudoxanthoma elasticum showing extensive calcification.

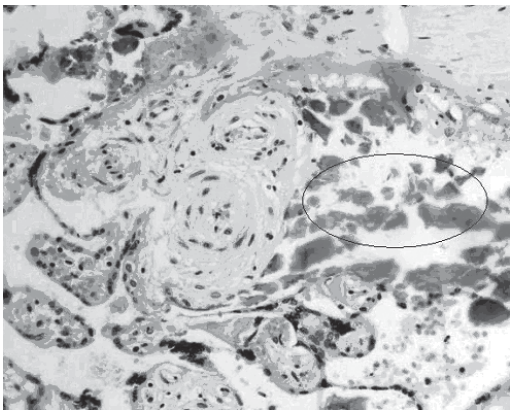

Fig. 2. Histology slide showing patchy and non-specific coarse calcification within the parenchyma.

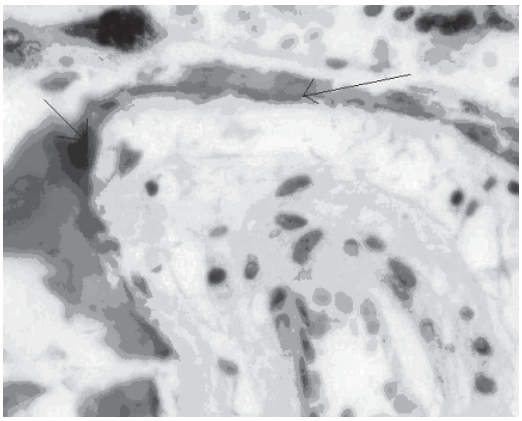

Fig. 3. Histology slide showing calcification in the basement membrane.

Postnatal recovery was uneventful and there was good wound healing with no aggravation of the angoid streaks. Both mother and baby were discharged well on post-operative day 5.

Placental histology showed patchy and non-specific coarse calcifications within the stroma (Fig. 2) and along the maternal surface without any discrete lesions. High power magnification showed calcium deposits in the basement membrane (Fig. 3). The fetal surface of the placenta was unremarkable and there was no evidence of villitis.

The male infant did not show any characteristic skin lesions at birth and remained well at 6 months of age.

Discussion

PXE demonstrates both autosomal recessive (the usual) and autosomal dominant (rare) modes of inheritance.[2] The assessment of inheritance is complicated by clinical heterogeneity and variable age of onset. The overwhelming majority of cases of PXE is caused by mutations in the ABCC6 gene. Autosomal dominant PXE, which may be phenotypically indistinguishable from the autosomal recessive form, is caused by heterozygosity for mutation in the same gene. There are 4 clinical forms which correspond to 4 different genetic types (I or II, dominant or recessive).[3]

PXE is characterised by calcified dystrophic elastic fibres in skin, retina and arteries. Although infrequent, complications during pregnancy in women affected by PXE have been reported. Much of the earlier literature on pregnancy in PXE[4] contained reports of severe complications, leading some healthcare providers to advise women with PXE against becoming pregnant.

Some serious complications in pregnancy that have been described include gastrointestinal haemorrhage, congestive heart failure and cardiac arrhythmia antenatally, and in 1 case a fatal attack of cardiac arrhythmia postpartum.[1,5]

The true risks of serious complications during pregnancy, however, may be overstated.[6] A study[7] analysing obstetrical implications of PXE showed the eye, blood vessels and other organ systems involved in PXE to be unaffected by pregnancy. Apart from the cosmetic deterioration of the abdominal skin, there were few serious complications and most have normal pregnancies.

Obstetric prognosis is dependent on the vascular damage caused by the illness. In a series of 15 cases and 14 controls,[8] the investigators compared the structural features of placentae at term from normal and PXE-affected women, to better understand how matrix accumulation might affect placental function in PXE. In all cases, pregnancy, fetal growth and delivery were normal. Both gross and light microscopic examination did not reveal any significant differences in weight, dimensions, infarcts, thrombi or presence of inflammatory lesions between placentae of normal and PXE-affected patients. The only difference was necrotic changes and mineralisation appeared statistically more pronounced in PXE. Electron microscopy showed a significantly higher deposition of calcium among

collagen fibrils, especially on the maternal side in PXE-affected patients and immunocytochemistry revealed the presence of vitronectin and fibronectin. There is a paucity of ultrasound descriptions of the placenta of PXE-affected women and there is no evidence that fetal disease correlates with the extent of placental calcification.

Elejalde et al[9] found that the placental cotyledons were small and more numerous in a PXE-affected patient than normal. One third of the placenta was hypoplastic or atrophic, with focal calcification in septa, stroma, villi, and decidua, and increased deposition of fibrin around villi. The most striking change was the increased number of septa and the abnormal elastic tissue.

PXE is not associated with markedly increased fetal loss or adverse reproductive outcomes.[2] Fertility in PXE patients is normal and the frequency of miscarriage is not above that of the general population. The incidence of gastric bleeding, although probably higher than in the unaffected population, is much lower than previously reported. Retinal complications are uncommon although aggravation of the skin symptoms in pregnancy has been reported.[10,11] For the pregnancies associated with worsening of skin manifestations, there was no correlation of either gravidity or ever having been pregnant with ultimate severity of skin, ocular or cardiovascular manifestations. In our patient, no observable aggravation of the patient's pre-existing skin lesions was noted.

Conclusion

Nearly all deliveries were spontaneous with only a few exceptions, and no maternal or fetal complications in the perinatal period were reported recently. Literature on the effects of PXE on the fetus is sparse.[12] Reports of complications of PXE occurring during pregnancy have dissuaded some women with the disorder from attempting to conceive for fear of exacerbating the disease. Based on recent reports and our findings, there is no basis for advising women with PXE to avoid becoming pregnant, and most pregnancies in PXE are uncomplicated.

Acknowledgements

The authors want to thank Dr Rosemary Scott from the Department of Histopathology, University College Hospital for her help in the preparation of the histology slides.

REFERENCES

1. Xiromeritis P, Valembois B. Pseudoxanthoma elasticum and pregnancy. Arch Gynecol Obstet 2005;30:1-2.
2. Neldner KH. Pseudoxanthoma elasticum. Clin Derm 1988;6:83-92.
3. Viljoen DL, Beatty S, Beighton P. The obstetric and gynaecological implications of pseudoxanthoma elasticum. Br 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;151:1011-8.
5. Berde C, Willis DC, Sandberg EC. Pregnancy in women with pseudoxanthoma elasticum. Obstet Gynecol Surv 1983;38:339-44.
6. Yoles A, Phelps R, Lebwohl M. Pseudoxanthoma elasticum and pregnancy. Cutis 1996;58:161-4.
7. Baratte I, Schaal JP, Laurent R. Pseudoxanthoma elasticum in pregnancy. Rev Fr Gynecol Obstet 1991;86:243-5.
8. Gheduzzi D, Taparelli F, Quaglino D Jr, Di Rico C, Bercovitch L, Terry S, et al. The placenta in pseudoxanthoma elasticum: clinical, structural and immunochemical study. Placenta 2001;22:580-90.
9. Elejalde BR, de Elejalde MM, Samter T, Burgess J, Lombardi J, Gilbert EF. Manifestations of pseudoxanthoma elasticum during pregnancy: a case report and review of the literature. Am J Med Genet 1984;18: 755-62.
10. Valenzano M, Corticelli A, Podesta M, Nicoletti L, Saffioti S, Derchi L. Pseudoxanthoma elasticum and pregnancy: a case report. Clin Exp Obstet Gynecol 2000;27:215-7.
11. Mansat-Krzyzanowska E, Sagot P, Le Neel N, Stalder JF. Pseudoxanthoma elasticum and pregnancy. Ann Dermatol Venereol 1993;120:391-4.
12. Bork K. Pseudoxanthoma elasticum in pregnancy: effects on mother and child. Hautarzt 1983;34:77-80.