

EPILEPSY RISK AND SPONTANEOUS ABORTION

Risk of Epilepsy in Offspring of Affected Women: Association with Maternal Spontaneous Abortion

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BACKGROUND: Previously, the authors found that risk of spontaneous abortion was increased in the pregnancies of women with epilepsy compared with their same-sex siblings, which could have implications for risk of epilepsy in their offspring. An association between a history of spontaneous abortion in the mother and risk of epilepsy in her live-born offspring may arise through selective loss of fetuses with a genetic susceptibility to epilepsy or through intrauterine environmental factors that may predispose the mother to a spontaneous abortion and to epilepsy in her live-born children.

METHOD: The authors examined the relation of a history of spontaneous abortion to the risk of idiopathic or cryptogenic epilepsy in 791 live-born offspring of 385 women with cryptogenic localization-related epilepsy (probands) ascertained from voluntary organizations. A semistructured telephone interview with probands and additional family informants, supplemented by medical record review, was used to obtain information on seizures and other risk factors in probands and relatives.

RESULTS: Live-born offspring of women with a history of spontaneous abortion were four or five times as likely to develop epilepsy as were children of women without (12.8% versus 4.7%; rate ratio = 4.6, 95% CI: 2.3–9.0). Cumulative incidence of epilepsy was 21.9% in offspring of women with a history of spontaneous abortion and a family history of epilepsy, compared with 4.7% in offspring of women with neither risk factor.

CONCLUSIONS: These results suggest that a history of spontaneous abortion is associated with increased risk of epilepsy in live-born offspring and may be a marker for genetic susceptibility for epilepsy in the mother.

COMMENTARY

The risk of epilepsy for the children of mothers with epilepsy is an issue faced by every physician caring for women with epilepsy. The article by Schupf and Ottman adds an important piece of information about that risk, with their report that maternal spontaneous abortion imparts an increased risk of epilepsy to the offspring of mothers with idiopathic or cryptogenic epilepsy.

The authors make a strong case, based on the evaluation of historical factors such as family history of epilepsy, that spontaneous abortion in mothers with epilepsy is a marker for genetic susceptibility to epilepsy. The findings also suggest that there is an increased risk of epilepsy in the offspring whose mothers had the onset of epilepsy after their birth, with the risk enhanced where there is a history of spontaneous abortion. This again points toward a genetically imparted epilepsy risk, as other potential factors by definition did not occur, such as intrauterine exposure to antiepileptic drugs or to maternal seizures in utero.

The authors confirm their earlier report (1) that maternal seizures during pregnancy themselves increase the risk of epilepsy in the offspring; this does not intuitively fit into a genetic susceptibility model, except that mothers having seizures during pregnancy may have very severe epilepsy and this provides the genetic “weight.” Additionally, the low level compared with the high level of maternal education associating with an increased risk of epilepsy in the offspring definitely suggests an environmental, not a genetic, risk factor, or at least a combination of environmental and neurobiologic factors. However, a history of spontaneous abortion increased the risk of epilepsy in the offspring in all of these subanalyses.

This article provides further evidence that the search for genetic factors influencing the expression of epilepsy should continue with full effort. Combining epidemiologic evidence with molecular research will surely lead toward some answers for our questions regarding who will develop epilepsy.

References

1. Ottman R, Annegers JF, Hauser WA, Kurland LT. Higher risk of seizures in offspring of mothers than of fathers with epilepsy. *Am J Hum Genet* 1988;43:257–264.

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