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Familial Ovarian Dermoid Cysts

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ABSTRACT

A family consisting of a mother and her two daughters with ovarian dermoid cysts showed an increased frequency of aneuploidy and chromosomal breakage indicating chromosomal instability.

INTRODUCTION

There are several reports on familial occurrence of dermoid cysts of the ovary: (2,3,4,5,8,10,11). These reports plus other characteristics of dermoids, such as high percentage of bilaterality and low age of occurrence, point to genetical causes in some of the cases of the disease. No cytogenetic studies of familial cases seem to have been done. This report describes a family consisting of a mother and two daughters with ovarian dermoid cysts who were subjected to chromosomal investigations. The mother and one daugther showed signs of chromosomal instability.

CASE REPORTS

Patient 1: (I:1 in the pedigree), is a 54-year-old, 2-gravidae woman. She was operated on for a perforated appendicitis at 26 years of age, as nulli-gravidae woman because of intermittent abdominal pain. At operation, an ovary the size of a small orange partly embedded in adhesions was found. An ophorectomy was performed. The left ovary was normal and histological examination of the right ovary revealed a corpus luteum cyst in addition to a plum-sized dermoid cyst that was without histological signs of malignancy.

Patient 2: (II:2 in the pedigree), a 24-year-old nulligravidae woman previously healthy, who had been taking contraceptive pills during the 18 months preceeding the operation. A right-sided ovarian lump had been found on routine examination. At operation a dermoid cyst the size of a small orange involving the right ovary was found and removed. The left ovary was normal. Histological examination revealed a dermoid cyst without signs of malignancy.

Patient 3: (II:3 in the pedigree), a 22-year-old nulligravidae woman previously healthy, who had been taking contraceptive pills during the 24 months preceeding the operation. On routine examination a left-sided ovarian lump had been found. At operation, a dermoid the size of a small orange involving the left ovary was found and removed. The right ovary was normal. Histological examination revealed a dermoid cyst without signs of malignancy.

METHODS

On each of the three patients blood samples were taken on two separate occasions for cytogenetical investigations. After conventional cell culture procedure and

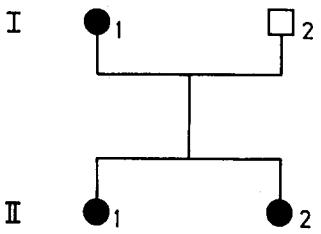

Fig. 1
Pedigree of the affected family.

□ Normal
● Ovarian dermoid cyst

Giemsa-banding, 100 metaphases were analysed from each patient. Chromosome breakage analysis was performed on 100 metaphases of Giemsa-stained air-dried slides from each patient. Analysis of sister-chromatid exchanges after BrdU-labelling were performed on cultured lymphocytes from the patients, as described by Alvest & Jonasson (1).

RESULTS

The results of the chromosomal investigations are shown in Table 1.

The three patients all had a normal female chromosomal constitution. There was an increased frequency of aneuploidy (4-20%) and chromosomal breakage in patients 1 and 3 as compared with controls. The frequency of sister chromatid exchanges was not increased.

DISCUSSION

Most ovarian teratomas have a normal 46,XX karyotype, suggesting that ovarian teratomas arise from germ cells and most often through parthogenesis (7). The present study as well as other investigations (2,4,5,8,10,11) have clearly demonstrated the existence of familial forms of ovarian dermoid cysts. Our study demonstrated an increase in the number of aneuploid cells and chromosomal breakage in lymphocyte cultures of the mother and one of her daughters. These findings support the theory that genetic factors are of importance in the development of ovarian dermoid cysts. The significance of the association between the ovarian teratomas, which are probably dominantly inherited, and the forementioned cytogenetical findings in cultured cells is uncertain. It is possible, however, that the increased frequency of aneuploidy and chromosomal breakage are signs of chromosomal instability typically seen in some distinct genetic disorders with a propensity to develop neoplasia, such as Fanconi's anemia, Bloom's syndrome, ataxia telangietasia, xeroderma pigmentosum and Gardner's syndrome, considered to be expression of the underlying gene defect (9), and that the increased frequency of aneuploid cells in cultured lymphocytes from our familial cases reflects a disturbance of the mitotic and meiotic processes, which might be of pathogenetic importance. Such a disturbance of the mitotic and meiotic process in our familial cases could be related to an underlying gene defect or due to metabolic and/or hormonal influences. It should be of interest to perform further studies and compare non-familial with familial cases. We have thus started a prospective study of consecutively operated cases of ovarian teratomas in the Uppsala Hospital Region, Sweden, including chromosomal analyses and DNA analytical procedures of blood and dermoid tissue. We have also started a retrospective study in order to find out the frequency of familial cases of the disease.

Table 1. Cytogenetic findings in cultured lymphocytes from the three relatives with ovarian teratomas

Patient	Karyotype (No. of cells)	Aberrations per cell				SCE (mean per cell)	Fragile sites (In No. of cells of 100 examined cells)
		Chromatid and iso-chromatid breakages	gaps	fragments	total		
Patient 1 (I:1)							
1st culture	46,XX(17) 47,XXX(1) 48,XXXX(1) 45,X(1)	0.15	0.01	0.03	0.19	0	-
2nd culture	46,XX(40) 47,XX,+8(1) 45,X(1) 45,XX,-4(1) 45,XX-12(1) 44,XX,-1,-1(1) 44,X,-3,-18(1)	0.08	0.03	0.03	0.14	8.5	0
Patient 2 (II:1)							
1st culture	46,XX(20) 45,XX,-11(1) 45,XX,-21(1)	0.01	0	0	0.01	7.6	-
2nd culture	46,XX((49) 45,XX,-10(1)	0.03	0	0	0.03	-	3p13(2)
Patient 3 (II:2)							
1st culture	46,XX(19) 47,XX,+21(1)	0.30	0.18	0.08	0.56	0	-
2nd culture	46,XX(43) 47,XX,+5(1)	0.04	0.04	0.01	0.09	5.7	0
Controls	46,XX Aneuploidy <2%	0.02	0.05	0.002	0.072	11.4	

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