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Ovarian Dysgerminoma in Three Generations?

STEWART M. JACKSON

From Christie Hospital and Holt Radium Institute, Withington, Manchester

Dysgerminoma of the ovary is a rare disease representing about 1% of malignant ovarian tumours (Sjövall, 1943). Some 650 cases have been recorded in the world literature, but there have been no reports of a family history of the disease.

This paper describes patients in three generations of a Jamaican family with ovarian tumours, two of whom were known to have had dysgerminomas.

Case Reports

The three patients under review were a maternal grandmother, mother, and daughter, and they will be referred to as such (Figure).

The grandmother (I. 2) died in Jamaica in 1940, and unfortunately there are no medical records available regarding her illness. However, from interviews with surviving relatives and friends, it is known that she died of an ovarian cancer. She had an abdominal tumour with ascites, the relatives being told that this was a result of ovarian malignancy. There is no information regarding the pathology of this tumour.

The mother (II. 15) has already been documented by Liebert and Stent (1960). She is one of the few recorded patients with a mixed chorionepithelioma and dysgerminoma. During her sixth pregnancy at 26 weeks she developed pain in the left loin and was found to have a mass in the left flank; at laparotomy a large haemorrhagic left ovarian tumour adherent to the omentum was removed. It was found to contain two distinct areas of tumour, a larger haemorrhagic area consisting of chorionepithelioma tissue which was separated by a fibrous band from solid pale dysgerminoma tissue. Three weeks later a caesarean section and salpingo-oophorectomy were carried out and a secondary deposit on the descending colon excised. Nine days later she was referred to the Christie Hospital. In view of the strong possibility of residual malignancy, irradiation to the whole of the abdomen was begun. A week later the patient complained of vaginal bleeding and she was found to have a haemorrhagic nodule at the urethral orifice. The *x*-ray fields were lengthened to include the urethral orifice and the course of abdominal irradiation was completed. A biopsy of the nodule confirmed an infected, haemorrhagic subepithelial deposit of chorioncarcinoma. At the end of her *x*-ray treatment the nodule had shown no signs of regression and a small radon seed was implanted beneath the nodule. The patient then returned to the Withington Hospital. Unfortunately she developed signs of pulmonary metastases, and, despite methotrexate therapy, her disease progressed rapidly to death five months later. Necropsy revealed multiple deposits of chorionepithelioma tissue in the breast, lungs, liver, spleen, kidneys, omentum, and brain, but there was no evidence of tumour in the vagina or at the urethral orifice. Histological examination of all deposits revealed no evidence of dysgerminoma tissue.

The daughter (III. 3) was born in 1951, six years before her mother's illness. At the age of 12, in May 1963, she developed intermittent abdominal pain and in August 1963 she became aware of an abdominal mass. She had one episode of vaginal bleeding in August. She was referred to hospital in September and found to have a large tender irregular mass in the epigastrium and left hypochondrium. An *x*-ray film of her abdomen revealed a large abdominal mass which contained a small amount of calcium. An intravenous pyelogram and chest *x*-ray film were normal. Laparotomy revealed a large left ovarian tumour, approximately 18 × 10 cm. in diameter, which was easily removed. A frozen section of this tumour was reported as showing a dysgerminoma and the right ovary was, therefore, also removed. At subsequent histological examination both ovaries were shown to contain dysgerminoma tissue. The specimens were later circulated to the Children's Tumour Registry Pathologists Panel, and all the members of the Panel agreed that this was a dysgerminoma. Two weeks later the child was referred to the Christie Hospital. There was no clinical evidence of residual disease and she was in good general condition. Because of the known family history, chromosome studies were made on the child, but no abnormalities were discovered. Buccal smears and blood samples produced cells with the normal XX 46 chromosomes. In view of the bilateral ovarian involvement, it was considered advisable to irradiate the entire abdomen but with the kidneys shielded. This treatment was carried out during a period of 28 days in October 1963. She withstood the treatment easily and has remained well for the past three years.

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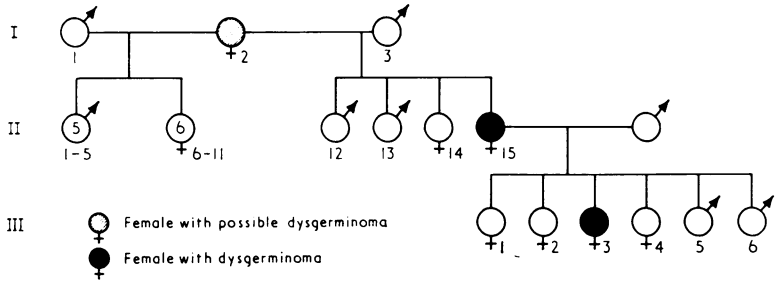

FIG. Pedigree of Jamaican dysgerminoma family

Discussion

A family history of ovarian cancer is not unusual. Lynch (1936) studied 110 patients, of whom two had mothers and one a sister with the same disease. Liber (1950) described a family in which the mother and five daughters all developed papillary adenocarcinoma of the ovary. Reported here are three generations of a family with ovarian cancer, the two younger members having dysgerminomas. Since the grandmother died 26 years ago in Jamaica it has proved impossible to determine the exact nature of her disease. It is unlikely that she had a dysgerminoma since the tumour is rare. Nevertheless, the possibility exists that she represented the first in a line of three generations developing the disease, and that in her case it was the result of a dominant gene mutation. The mother had six children in all, but none of her three other daughters, nor any other member of the family as far as can be ascertained, has shown any evidence of ovarian disease. It is unlikely that chromosome abnormalities would be demonstrated in this family and the only patient available for study, the affected daughter, has a normal complement of 46/XX chromosomes.

It is possible to calculate the probability of the association of dysgerminoma of the ovary occurring in three generations of the same family. Based on the Liverpool Cancer Registry figures, the probability of a female developing cancer of the ovary is $1{\cdot}506 \times 10^{-4}$, and assuming the incidence of dysgerminoma to be 1% of ovarian cancer, the probability of a female developing dysgerminoma is $1{\cdot}506 \times 10^{-6}$. The probability of a female and her daughter both having dysgerminoma is $2{\cdot}3 \times 10^{-12}$, and of a female, her daughter, and granddaughter all having the disease is $3{\cdot}4 \times 10^{-18}$. If it is assumed that the grandmother had ovarian cancer, but not dysgerminoma, then the probability of her daughter and grand-daughter having dysgerminoma of the ovary would be $3{\cdot}4 \times 10^{-16}$. If the female population of the world is taken as 10^9, then using the probability figures the association of a grandmother, daughter, and granddaughter all having dysgerminoma of the ovary may be expected to occur by chance once every 300 million years. The association of a grandmother with ovarian cancer and her daughter and grand-daughter with dysgerminoma may be expected by chance once every 3 million years. Even the chance association of a mother and daughter with dysgerminoma is rare and might occur only once every 450 years.

Summary

A Jamaican family with members of three generations developing ovarian tumours, two of whom were known to have had dysgerminomas, is reported. The possibility of this being a random association is discussed.

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