Gonadoblastoma and fertility

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Abstract

Most patients with gonadoblastoma have dysgenetic gonads. This rare tumour has been described in three pregnant women. A fourth case in a 26 year old pregnant woman who presented with gonadoblastoma and dysgerminoma, is reported. She had a normal term pregnancy, 46XX chromosomes, normal genitalia, no history of menstrual irregularities and no signs of hyperandrogenism, thereby differing from the other reported cases. The germ cell component of this patient's tumour had undergone rapid overgrowth, most of the tumour comprising pure dysgerminoma.

It is suggested that gonadoblastoma may occur in functionally and morphologically normal gonads more often than previous case reports imply.

Gonadoblastoma has a distinctive histological appearance, which distinguishes it from any other gonadal neoplasm, and was first described by Scully in 1953. The tumour is composed of germ cells but also contains sex cord stromal derivatives, resembling granulosa and Sertoli cells.¹ Sometimes these tumours contain stromal elements indistinguishable from lutein or Leydig cells.¹ This basic histology of gonadoblastoma may be altered and distorted by hyalinisation, calcification (81%), and overgrowth by dysgerminoma (50%).^{1,2}

Although most patients with gonadoblastomas are either virilised or non-virilised phenotypic females with dysgenetic gonads, are chromatin negative, and have 46XY karyotype or various forms of mosaicism,^{3,4} gonadoblastoma has been described in three pregnant women.⁵⁻⁷ Insofar as we can determine, the following case is the fourth pregnant woman with gonadoblastoma to be reported.

Case report

A 26 year old normal woman, para I, gravida II, was admitted to the Ege University Hospital on 30 January 1989. Her physician noted a large, rapidly growing right adnexial mass on physical examination. Her last period had occurred on 10 May 1988.

Menses had begun when she was 13 years of age, and she had regular menses every 28 days lasting for about 10 days. Her karyotype was 46XX. There was nothing relevant in her personal and family history.

On 6 February 1989 she was delivered, by

caesarean section, of a healthy baby boy weighing 2900 g. When the abdomen was inspected it was seen that the right ovary had been replaced by a large encapsulated tumour. The uterus and the contralateral ovary were normal in appearance, and there were no ascites or adhesions, but para-aortic lymph nodes were slightly enlarged in palpation. Total hysterectomy and bilateral salpingo-oophorectomy were performed.

The tumour was a partially lobulated large mass measuring 20 cm in maximum diameter, with a smooth surface, and grey-white in colour.

Microscopically most of the tumour was composed of pure dysgerminoma where there were nests or trabecular formations comprising large, uniform, round or oval cells with slightly granular, eosinophilic, or clear cytoplasm. The cytoplasm contained glycogen which stained with periodic acid Schiff. The nuclei were round or oval and had distinctive nuclear membranes and fine granular chromatin. The connective tissue stroma between these cells was small in amount and infiltrated by lymphocytes. Serial sections showed microscopic infiltration of the tumour capsule and large amounts of tumour cells in the blood vessels and lymphatics of the tumour stroma.

There were two separate gonadoblastic foci composed of cellular nests, surrounded by connective tissue containing Leydig or lutein-like cells. These cellular nests were composed of germ cells and relatively smaller sex cord derivatives. In some parts hyaline Call-Exner-like structures were observed. There was no microscopic or macroscopic calcification.

The patient received combination chemotherapy following surgery. She was alive without recurrence two years and nine months after diagnosis.

Discussion

Almost 200 cases of gonadoblastoma have been reported, but the incidence of this tumour in fertile women continues to be extremely rare. We analysed recent literature to uncover all the cases of gonadoblastoma seen in fertile women.

To date, only three pregnant women with gonadoblastoma have been reported. In one of these reported by De Bacalao *et al* in 1969, chromosome analysis indicated no abnormality, and following the excision of a dysgerminoma containing a small focus of gonadoblastoma, the patient had two normal pregnancies.⁵ The second patient, reported by

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Pratt-Thomas *et al*, had gonadoblastoma in association with an ectopic pregnancy but cytogenetic evaluation showed 46XX-45XO mosaicism.⁷ The third patient was a normal woman and had a gonadoblastoma associated with ectopic pregnancy.⁶

Gonadoblastoma has been observed in four true hermaphrodites, two of whom had the 46XX karyotype. One of these, reported by McDonough and associates in 1976,⁸ was a 13 year old male with severely malformed external and internal genitalia: he was obviously infertile. The case reported by Talerman and associates in 1981 is also interesting.⁹ She was 27 years old and had regular menses, a uterus measuring 7 × 3 × 2.2 cm, a normal cervix, a uterine cavity, and ovaries containing several corpora albicantia, corpora lutea, and primordial and graafian follicles in various stages of development. In addition to normal-looking ovarian tissue, a nodule of testicular tissue was present from which the gonadoblastoma appeared to originate. The patient elected to be a male but it is possible that if he had chosen to be a female, it might have been possible for him to have been a fertile woman after the excision of the testicular tissue and the focus of gonadoblastoma.

We are also aware of a report from India about a normal fertile woman who had a unilateral gonadoblastoma and dysgerminoma, and a woman with two normal children from Japan who had a similar tumour.^{3 10} Chromosomal analyses of these two women were not done.

Our case, having a normal term pregnancy, 46XX chromosomes, normal external and internal genitalia, no signs of hyperandrogenism when the tumour was first diagnosed, and no history of menstrual irregularities, is unique in these aspects among the three pregnant subjects with gonadoblastoma. She differs from De Bacalao's case who had only three spontaneous periods in 17 years between

menarche and her first pregnancy and showed slight hirsutism.⁵

It has been reported that dysgerminomas rapidly grow during pregnancy.^{11 12} This explains why the germ cell component of our patient's tumour had undergone a rapid overgrowth and why most of the tumour was composed of pure dysgerminoma. However, the focus of gonadoblastoma showed all of the characteristics defined by Scully, except calcification.

In conclusion, this case makes us think that the occurrence of gonadoblastoma in abnormal gonads may not be an absolute rule. As more cases are reported more detailed evidence of the prevalence of gonadoblastomas in functionally and morphologically normal gonads may become available which will clarify this.

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