

# Bilateral pure gonadoblastoma in a 46 XY individual – a case report

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## Abstract

We report here a rare case of bilateral pure gonadoblastoma which accounts for only 0.2% of all ovarian tumours seen at Universiti Kebangsaan Malaysia from 1980 to 1987. This tumour occurred in an 18 year old Chinese "female" who presented with primary amenorrhoea. Examination showed a phenotypic female with poorly developed external genitalia. Exploratory laparotomy revealed a hypoplastic uterus, rudimentary fallopian tubes and streak gonads. Histological examination of the gonads showed a mixed tumour comprising large germ cells and smaller sex cord derivatives arranged in characteristic nests or islands containing hyaline material.

*Key words* : bilateral, pure gonadoblastoma, karyotype.

## Introduction

Gonadoblastoma was first identified by Scully (1953) because he found gonadal components in this tumour recapitulating early stages of embryogenesis<sup>1</sup>. It is a mixed germ cell sex cord-stromal tumour of the ovary and is classified separately by the World Health Organisation (WHO)<sup>2</sup>.

Gonadoblastomas are seen in young patients, being encountered most frequently during the second decade and less frequently during the third and first decade, in that order<sup>3</sup>. Patients with a gonadoblastoma usually present with primary amenorrhoea, virilization and abnormal genitalia<sup>3,4</sup>. The majority are phenotypic females with the most common karyotype being 46 XY<sup>4,5</sup>. Bilateral involvement occurs in about 50% of the cases<sup>3</sup>.

The exact incidence of gonadoblastoma is not known but only about 200 cases have been reported<sup>3</sup>. We report this rare tumour seen at the Faculty of Medicine, Universiti Kebangsaan Malaysia, Kuala Lumpur.

## Case Report

The patient presented at 18 years of age with primary amenorrhoea. There were no other complaints. There was no significant past medical, surgical or drug history. Her mother attained menarche at 15 years of age. She has 2 other sisters, both of whom attained menarche at 16 years of age.

Physical examination revealed a patient of average build (150 cm. tall and weighing 44 kg). She had the external appearance of a female. There were no features of Turner's syndrome. Breast tissue was poorly developed and axillary hair was absent. Abdominal examination was unremarkable. Examination of the external genitalia revealed scanty pubic hair with poorly developed labia majora and minora. The clitoris was not enlarged. The hymen was not imperforate and the proximal vagina appeared normal. On rectal examination, the cervix and uterus could not be felt.

The following investigations were done: follicle stimulating hormone (FSH) 40 IU/L (normal range: 1 - 6), luteinizing hormone (LH) = 47.6 IU/L (normal range: 2 - 17), prolactin (PRL) = 182 MU/L (normal range: 117 - 468), serum testosterone = 0.9 nmol/L (normal range = 0.9 - 2.8), and serum estradiol (E2) < 46 pmol/L (normal range = 60 - 1000). The uterus was not visualised on an abdominal ultrasound and no adnexal masses were seen. Chromosomal analysis showed a 46 XY karyotype. Unfortunately, serum human chorionic gonadotrophin and alpha fetoprotein levels were not measured.

Exploratory laparotomy revealed a hypoplastic uterus with rudimentary fallopian tubes and streak gonads. All these structures were removed. Postoperative recovery was uneventful. She is presently on Tab. Premarin 0.625 mg daily and is well to date (4 years).

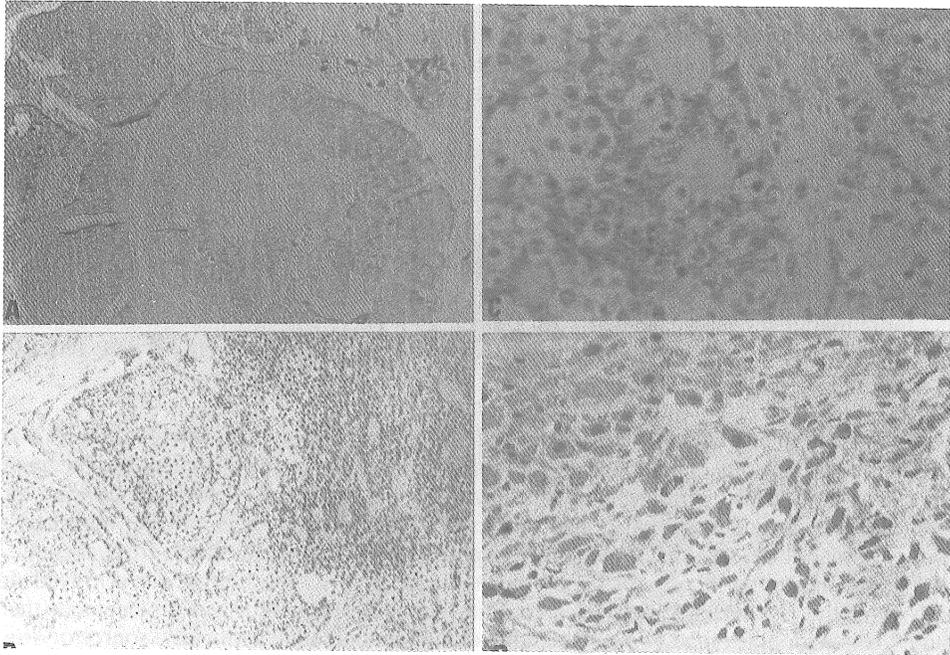
## Pathological findings

The specimen consisted of a hypoplastic uterus measuring 4.0 cm from fundus to cervix and 2.5 cm across, two fallopian tubes each measuring 4.0 cm. in length and two tiny, whitish firm gonads each measuring 1.0 cm. by 0.4 cm. The bilateral tumours were only detected on microscopic examination. The histological appearances of both tumours were typical. The tumours consisted of multiple cellular nests surrounded by a connective tissue stroma (Fig. 1A & B). The cellular nests are composed of large germ cells with clear cytoplasm and round vesicular nuclei, and the smaller sex cord derivatives with ovoid or elongated nuclei (Fig. 1C). These cells surround small round hyaline bodies (Fig. 1B & C). Calcification is seen microscopically within the cellular nests (Fig. 1A & C). The surrounding dense connective tissue stroma contained clumps of cells of Leydig or lutein type, with eosinophilic cytoplasm and round nuclei (Fig. 1D). The pseudocapsule of the tumour was composed of spindle-celled collagenous tissue resembling that of ovarian cortex; no definitive ovarian elements (i.e. follicles or their derivatives) were identifiable. There was no evidence of dysgerminoma or other neoplastic germ cell elements and a diagnosis of bilateral pure gonadoblastoma was made.

## Discussion

Gonadoblastomas are rare and account for only 0.2% of all ovarian tumours seen at the Universiti Kebangsaan Malaysia (1980-1987)<sup>6</sup>. They are seen most frequently during the second decade of life and in adults, the commonest presenting complaint is primary amenorrhoea. Although some patients may have sporadic episodes of spontaneous cyclical menstrual bleeding, the great majority present with primary amenorrhoea<sup>3,5</sup>. Our patient typifies this clinical presentation.

Most patients (80%) with a gonadoblastoma are phenotypic females and the remaining 20% are phenotypic males<sup>3,5</sup>. Of the phenotypic females with a gonadoblastoma, the majority (60%) are



**Fig. 1** Pathological features of gonadoblastoma. Nests composed of germ cells (arrowhead, C) and smaller sex cord derivative (smaller arrow, C) contain rounded hyaline bodies (\*B, C). Note foci of calcification (larger arrow, A, C). Cells of Leydig or lutein type are present in the stroma (D). Haematoxylin & Eosin, A x 40 : B x 100 : C x 400 : D x 400.

virilized. Although the remaining 40% appear normal, most of these exhibit poor genital development. Breast development is also frequently poor even among the non-virilized phenotypic female<sup>5</sup>. This patient is a phenotypic female albeit with poorly developed breasts and external genitalia. She did not however exhibit any features of virilisation.

The most common karyotype observed is 46 XY (50%) as was the case in this patient. This is followed by 45 X/46 XY mosaicism (25%), while the remainder consist of various other forms of mosaicism<sup>3,5</sup>. Although the majority of patients with a gonadoblastoma have a karyotype containing a Y chromosome, the absence of a Y chromosome does not exclude the presence of the lesion and its malignant potential<sup>4</sup>.

The presence of hormonal abnormalities in patients with a gonadoblastoma was first noted by Scully (1953)<sup>1</sup>. He reported the presence of virilization in one of his cases and considered that the tumour was capable of steroid hormone production. Elevation of the gonadotrophins was considered an important diagnostic criterion. Plasma testosterone was increased in half of the cases. The gonadotrophin levels were elevated in this patient while the testosterone levels were within normal limits. The actual source of the steroid hormone production is still a matter of debate and controversy: the Leydig-like or lutein cells have long been considered to be responsible for the steroid synthesis, but a stromal reaction has also been implicated<sup>3</sup>. It appears reasonable to consider that both types of cells are capable of steroid hormone production and may be involved in the steroid synthesis associated with gonadoblastomas<sup>3</sup>.

Gonadoblastomas are frequently bilateral. Although the reported incidence is about 38% subsequent experience indicates the presence of bilateral involvement in at least 50% of cases<sup>3</sup>. This case

illustrates such a bilateral involvement and emphasizes the need for a careful search for the presence of a lesion in the contralateral gonad. Pure gonadoblastoma is commonly a small lesion varying in size from microscopic up to 8 cm. in the largest diameter. Most of the macroscopically apparent lesions measure between 1 and 2 cm. and tend to be round or oval with a smooth or slightly lobulated surface. The consistency may vary from soft and fleshy to firm or even hard due to calcific granule. Calcification can be detected on microscopic examination in 80% of the cases<sup>3,4,5</sup>. In this case, the tumour was only diagnosed on microscopic examination. The histological appearance was typical with calcification.

A gonadoblastoma is frequently overgrown by a neoplastic germ cell element, this being observed in more than 60% of cases<sup>5</sup>. In at least 50% of cases this is a dysgerminoma and in the remaining 10% by other more malignant neoplastic germ cell elements<sup>3,5</sup>. There was no evidence of dysgerminoma or other neoplastic germ cell elements in our patient thus making this case a rare one of pure gonadoblastoma.

Because of the malignant potential of a gonadoblastoma, gonads harbouring such tumours are a danger to the patient. Furthermore, these gonads do not function normally as in this patient and the treatment of choice is excision. It is imperative that both gonads be excised and not only the gonad which appears abnormal because the contralateral gonad, however normal looking it might be, may harbour a microscopic gonadoblastoma. In this patient, both gonads were removed as they were dysgenetic. The bilateral gonadoblastoma were only diagnosed microscopically. The uterus was removed due to concern about the risk of endometrial carcinoma with long term estrogen replacement therapy. Although the gonadoblastoma has a considerable malignant potential, acting as a source of origin of malignant germ cell tumours, patients with a pure gonadoblastoma have an excellent prognosis provided both gonads are excised. This good prognosis holds true even when gonadoblastoma is associated with a dysgerminoma. When it is associated with other malignant germ cell elements however, the prognosis is poor.

In the case reported here, the clinical presentation is fairly typical of gonadoblastomas. The interesting feature is that unlike most gonadoblastoma, there was no evidence of other malignant germ cell elements - hence the term "pure" gonadoblastoma. Both the gonads, and the uterus with fallopian tubes were removed and she has to date remained well on estrogen replacement therapy.

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