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Prophylactic bilateral salpingo-oopherectomy in a 17-year-old with Frasier syndrome reveals gonadoblastoma and seminoma: a case report

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Abstract Mutations in the Wilms' tumor gene are present in children with Frasier syndrome, Denys-Drash syndrome, WAGR syndrome, and some cases of Wilms' tumor. The Wilms' tumor gene product, WT1, is necessary for normal urogenital development. Frasier syndrome is an association between focal segmental glomerulosclerosis, beginning in the second and third decade, male to female sex reversal, and dysgenetic gonads.

We report a case of Frasier syndrome in a 17-year-old adolescent girl with renal failure, kidney transplant, and dysgenetic gonads, with development of gonadoblastoma and dysgerminoma (seminoma). The diagnosis of Frasier syndrome was based on nephrotic syndrome with diffuse mesangial sclerosis leading to chronic renal failure, dysgenetic gonads, 46 XY karyotype in a phenotypic female, and a mutation in the Wilms' tumor gene. Prophylactic laparoscopic bilateral salpingo-oopherectomy revealed gonadoblastoma and seminoma in opposite atrophic ovaries as well as a hypoplastic uterus.

Early prophylactic resection of dysgenetic gonads is indicated in children with Frasier syndrome to prevent the development of germ cell malignancy.

Mutations of the Wilms' tumor gene (WT1) are present in children with Frasier syndrome, Denys-Drash syndrome, WAGR (Wilms' tumor, Aniridia, Genitourinary abnormalities, and mental Retardation) syndrome, and a minority of patients with Wilms' tumor [1]. Frasier syndrome was first described by Frasier et al [2] in 1964 as an association between glomerulosclerosis, male to female sex reversal, and dysgenetic gonads in a pair of monozygotic twins. Further reports have described this syndrome and the risk of dysgenetic gonads predisposing to gonadoblastoma [3-6]. Polymerase chain reaction amplification testing can confirm the diagnosis by demonstrating mutation in the WT1 gene [7]. We report a case of Frasier syndrome in a child with renal failure, kidney transplant, male to female sex reversal, and dysgenetic gonads with development of gonadoblastoma and dysgerminoma (seminoma).

1. Case report

A 17-year-old girl with Frasier syndrome was referred for bilateral prophylactic salpingo-oopherectomy. At the age of 10 years, she developed nephrotic syndrome and progressive renal failure. A renal biopsy specimen revealed diffuse

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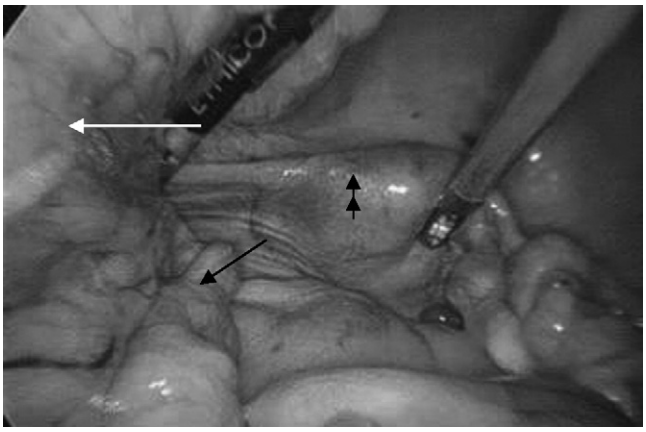

Fig. 1 Laparoscopic image demonstrating atrophic left ovary and fallopian tube (black arrow), hypoplastic uterus (double black arrow), and extraperitoneal transplanted kidney (white arrow).

mesangial sclerosis and moderate chronic active tubulointerstitial nephritis. Nephropathy progressed to end-stage renal disease by the age of 14 years. She subsequently underwent bilateral nephrectomy and a living-related renal transplant. At the age of 16 years, she presented with primary amenorrhea. Serum testing revealed elevated gonadotropins (follicle-stimulating hormone, 133.9 IU/L; luteinizing hormone, 76.9 IU/L) with low concentrations of estradiol (13 pg/mL) and normal levels of testosterone (36 ng/dL). Thyroid function was normal, and there was no pituitary lesion on head computed tomography. Chromosomal analysis showed SRY sequences consistent with XY genotype. A trans-abdominal pelvic ultrasound demonstrated a small uterus, and adnexae were not identified. Magnetic resonance imaging showed a hypoplastic uterus, compared to the child's stated age, and ovaries were not visualized. DNA analysis was completed which showed a mutation in the WT1 gene consistent with Frasier syndrome. The child received oral hormone replacement. Physical examination was consistent with Tanner 3 development.

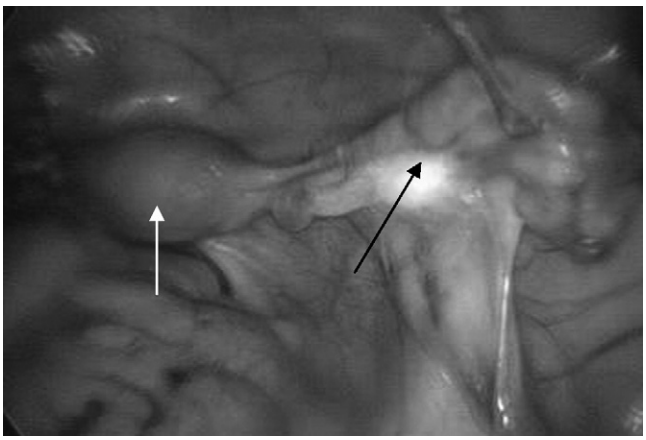

Fig. 2 Laparoscopic image demonstrating atrophic right ovary and fallopian tube (black arrow) and hypoplastic uterus (white arrow).

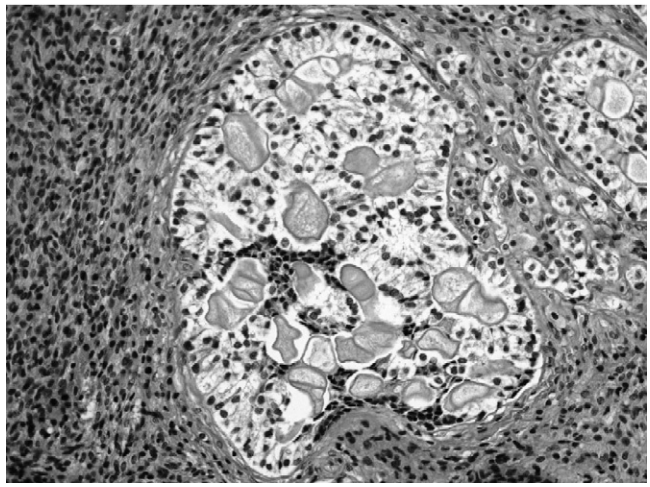

Fig. 3 Photomicrograph demonstrating gonadoblastoma in the left ovary. This tumor consists of cellular nests with uniform, round nuclei and abundant granular cytoplasm, surrounded by connective tissue stroma. Within the nests are acellular globules of hyaline material (hematoxylin and eosin, original magnification ×200).

Laparoscopic exploration revealed a hypoplastic uterus, long slender fallopian tubes, and approximately 1.5- to 2-cm ovoid white gonads bilaterally (Figs. 1 and 2).

Bilateral salpingo-oopherectomy was performed. There was no sign of ascites or peritoneal tumor spread. Histologic examination revealed a small left ovary with a gonadoblastoma measuring 0.4 cm and a small fibrotic right ovary with dysgerminoma (seminoma) measuring 0.8 cm (Figs. 3 and 4). A postoperative abdomen and pelvis computed tomography showed no suspicious adenopathy. Empiric adjuvant chemotherapy with 3 cycles of cisplatin, etoposide, and bleomycin was administered.

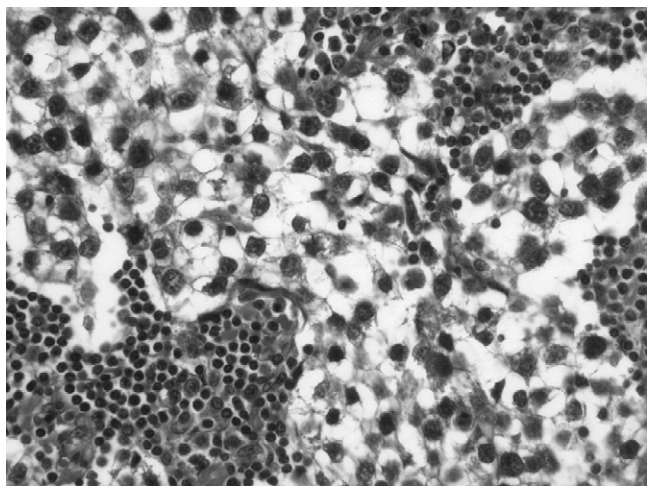

Fig. 4 Photomicrograph demonstrating dysgerminoma (seminoma) in the right ovary. Tumor cells show hyperchromatic, polygonal nuclei with irregular chromatin distribution and abundant pale cytoplasm. Mitotic figures are variable (hematoxylin and eosin, original magnification ×400).