

A Case of Klinefelter Syndrome with Retroperitoneal Teratoma

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Abstract

Klinefelter syndrome (KS) is often associated with various neoplasms, especially germ cell tumors. Mediastinum is the most favored site of extragonadal germ cell tumors with KS, which is somewhat different from those without KS. The retroperitoneal germ cell tumor in KS is very rare. A five-month-old boy with an abdominal mass was found to have a retroperitoneal tumor. After surgical removal, he was diagnosed to have mature cystic teratoma. Cytogenetic study of his peripheral lymphocytes revealed that his karyotype was consistent with KS. This case suggests that patients with KS might be at risk of having germ cell tumors in sites other than mediastinum. It also suggests that all cases with these tumors should be screened for the presence of karyotypic abnormalities, and it might help to assess the exact correlation between germ cell tumors and KS, and to treat them accordingly.

Key Words: Klinefelter syndrome, germ cell tumor, teratoma, retroperitoneal

INTRODUCTION

Klinefelter syndrome (KS) is the most common form in male hypogonadism.¹ It is characterized by small and firm testes, azoospermia, gynecomastia, and elevated levels of plasma gonadotropins in men with two or more X chromosomes. The common karyotype is either 47,XXY chromosomal pattern or 46,XY/47,XXY mosaicism.²

Klinefelter syndrome predisposes to developing germinal tumors in particular sites, mostly the mediastinum.³ We report a case of KS with retroperitoneal teratoma in an infant. This is the first case reported in Korea, and the third in the world.^{1,4}

CASE REPORT

A 5-month-old boy was admitted with palpable abdominal mass. His medical history showed no specific relevant findings. He was healthy and his

physical examination was normal except for the abdominal mass. He showed no other clinical features of KS.

Ultrasonograph and abdominal computerized tomogram showed a 5 × 5 × 4 cm – sized well demarcated retroperitoneal mass with heterogeneous echogenicity. Preoperative laboratory tests showed no evidence of a neuroblastoma: vanillylmandelic acid (VMA), ferritin, and lactic dehydrogenase values were normal. Alpha-fetoprotein and beta human chorionic gonadotropin values were also normal. Serum testosterone, LH, and FSH were not tested. Testicular biopsy was not performed. At laparotomy, the tumor was totally removed. Histologic examination showed a variety of tissue components, which contained skin, hair, and sebaceous glands (Fig. 1A), gastrointestinal tract tissues (Fig. 1B), and bone. Those were all compatible with mature cystic teratoma.

Chromosome analysis of blood lymphocytes showed 47,XXY karyotype in all cells of metaphase (Fig. 2).

DISCUSSION

KS was first described by Klinefelter in 1942. It is relatively common, being found in 0.1% of the male population. The frequency increases among azoospermic infertile males (10%) and in males in

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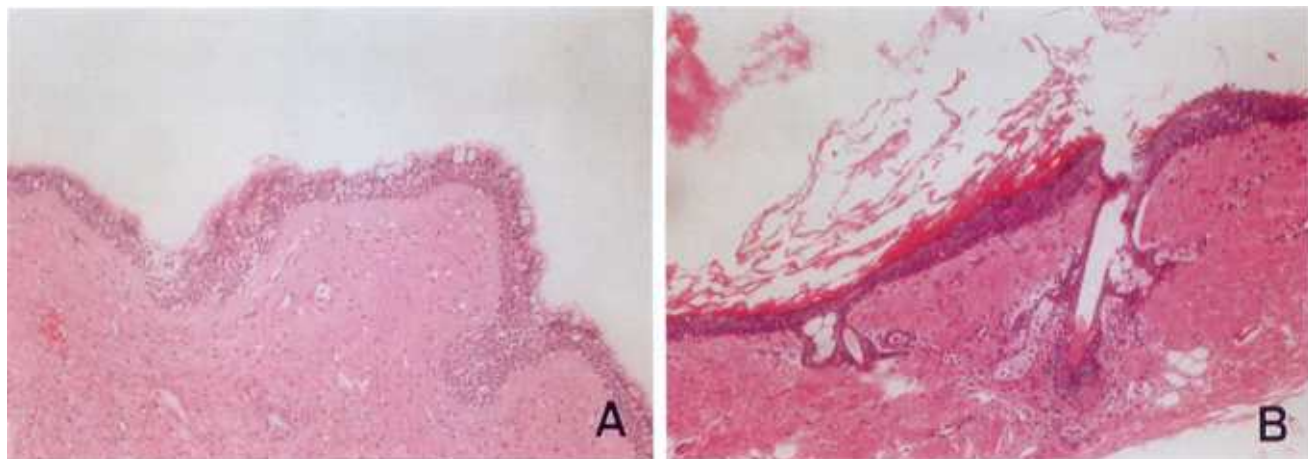


Fig. 1. Histologic findings of the tumor; Alimentary tract tissues (A $\times 200$); Keratinized squamous epithelium (B $\times 200$).

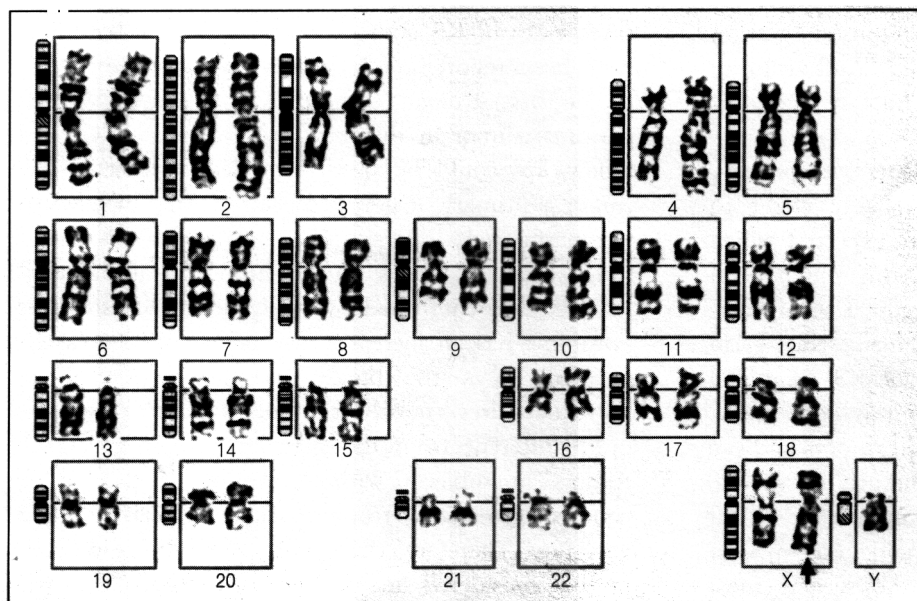


Fig. 2. Karyotype of this patient shows 47,XXY.

institutions for the mentally handicapped (1%).⁵ It is characterized by the 47,XXY genotype and clinical signs; for example, testicular atrophy, hyalinization of the seminiferous tubules; azoospermia or oligospermia, gynecomastia, eunuchoidism, longer legs, and mental retardation. As well, decreased serum testosterone, increased serum LH, and FSH are characteristic laboratory findings. Mean plasma estradiol levels are elevated. The result is a variable degree of feminization and virilization. The feminization, including gynecomastia, depends on the ratio of circulating estrogen to androgen (relative or absolute), while individuals with lower plasma test-

osterone and higher plasma estradiol levels are more likely to develop gynecomastia. The diagnosis of this syndrome is usually made after puberty due to secondary sexual characteristics.² The presence of KS may be overlooked because beta human chorionic gonadotropin-producing tumors per se may induce gynecomastia,⁶ but it should be suggested by the presence of small testes.⁷ Supplemental androgen, surgical treatment of gynecomastia, and in vitro fertilization could be applied to these patients.²

The frequent association of KS with various malignancies is well documented. Breast cancer has been most highly associated with KS.⁸ In 1979, Sogge

et al. published a report on two cases of KS associated with extragonadal germ cell tumors of the mediastinum.⁹ Klinefelter patients have been considered to be predisposed to developing malignant neoplasms of extragonadal germ cell origin.^{8,10}

The prevalent site of primary germ cell tumor in Klinefelter patients is the mediastinum, which is different from those without KS, testis or ovary.^{3,10} Dexeus and Gohji reported that the frequencies of mediastinal involvement by extragonadal primary germ cell tumor with KS are 73% and 91%, respectively.^{11,12} Determinations of serum tumor markers, alpha-fetoprotein and beta human chorionic gonadotropin are of particular importance in the diagnosis and follow-up of mediastinal germ cell tumors. Patients with benign teratomas are serum tumor marker-negative with elevations of alpha-fetoprotein and beta human chorionic gonadotropin, suggesting a malignant component of the tumor.¹³ And virilizing syndrome can result from beta human chorionic gonadotropin-secreting tumors.¹⁴

The frequency of KS in male patients with primary mediastinal germ cell tumor is probably closer to 20%, which is much greater than expected when compared to the prevalence of KS in the general population.⁷ These observations suggest a strong correlation between this syndrome and mediastinal germ cell tumor. Furthermore, the case of KS combined with retroperitoneal germ cell tumor is very rare.

Teratoma are one kind of germ cell tumors and can be divided into three categories: mature, immature, and monodermal. Most benign teratomas are better known in clinical parlance as dermoid cysts.¹⁵ After the gonads, the mediastinum is the second most frequent location for teratomas in adults. In children, the sacrococcygeal area is the most frequent site of teratomas, followed by the mediastinum. Unlike malignant germ cell tumors, benign teratomas occur with equal frequency in both sexes.¹⁶

The causes of the association of KS with germ cell tumors is yet unknown.¹² However, it is assumed that the source of extragonadal germ cell tumors are the primordial germ cells. These primitive cells can be identified from the fourth week of embryonic life between the endodermal cells and the yolk sac near the allantois. Part of these cells is incorporated into the embryo by migration along the posterior mesenterium of the hindgut to the gonadal ridge. In the sixth week, these cells continue to migrate in the

underlying mesenchyme and are incorporated within the primary sex cords. In certain cases, for reasons that are still unclear, part of the primordial germ cells during migration bypass their destination, migrating to other structures, particularly in the midline. Arens et al. suggested that in the KS there is an alteration in the gonadal ridge differentiation, leading to malinduction and desynchronization of migration of the primordial germ cells.¹⁷ Other possible explanations include abnormal embryonic hormonal influences resulting in germ cell mismigration or increased malignant potential of the dysgenetic germ cell in KS.⁸ Others have hypothesized that germ cell tumors originate from undifferentiated cells of the primitive streak.¹¹

Czauderna et al. and Hachimi-Idrissi et al. reported cases of KS with retroperitoneal teratoma.^{1,4} In Korea, three cases of KS with mediastinal germ cell tumors have been reported.¹⁸⁻²¹ But, to our knowledge, this is the first Korean case of KS associated with a germinal tumor in the retroperitoneal space. Clinical follow up would be needed to decide whether the tumor is primary or not, because testicular biopsy was not performed.

In summary, KS is usually suspected during adolescence and confirmed by cytogenetic analysis. This syndrome has an increased risk of having neoplasms, particularly of the breast and the germ cell in particular sites, mostly the mediastinum, which is quite different from the sites known for germ cell tumors in subjects without the syndrome.^{3,9,21} In contrast, KS with retroperitoneal germ cell tumor is very rare. Therefore, this syndrome might be difficult to be considered in patients with retroperitoneal teratoma.

This case suggests that patients with this syndrome might be at risk of having germ cell tumors in sites other than those usually reported. It also suggests that all cases with these tumors should be screened for the presence of karyotypic abnormalities to assess the exact correlation between the two disease entities and to treat them accordingly.

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