大韓病理學會誌 : 第17卷 第1號
K.J.P., Vol. 17, No. 1, 1983

Ovotestis

Yoon Seong Lee, M.D., **Chul Woo Kim**, M.D.
Sung Sik Shin, M.D. and **Je G Chi**, M.D.

Department of Pathology, College of Medicine, Seoul National University

=국문초록=

난 소 고 환

서울대학교 의과대학 병리학교실

이윤성 · 김철우 · 신성식 · 지제근

난소고환은 하나의 생식선에 고환의 조직과 난소 조직이 혼재하여 나타나는 비교적 드문 생식선의 발생 기형이다. 또한 난소고환의 존재로 바로 그 개체가 진성 반음양에 속하며, 다양한 외부 생식기 및 내생식기의 기형을 수반한다. 생식기의 기형으로 인한 반음양은 고대로부터 알려져 있으나 대부분의 예가 생식선은 단일의 성이나 다만 생식기의 발달이 모호한 가성 반음양의 경우이다.

따라서 진성 반음양은 더욱 드물며, 진성 반음양의 진단에는 반드시 조직학적 증거를 필요로 하게 되었다. 조직학적 증거와 생식선의 분포에 따라 진성 반음양은 ① 교환형 ② 양측형 및 ③ 단측형의 3가지 유형으로 구분하며 이미 수백 예의 진성 반음양이 보고되었다.

난소고환은 그 자체로 진성 반음양의 진단이 가능하며 대개 단측형에 속한다.

저자들은 서울대학교 의과대학 병리학 교실에서 3례의 난소고환을 경험하였기에 그들의 임상적, 병리학적 그리고 성염색체 검사 소견을 이미 국내의 문헌에 보고된 4례의 난소고환례와 비교하여 보고하는 바이다.

INTRODUCTION

The ovotestis is a gonad containing both testicular and ovarian tissues, and the presence of ovotestis means a person to be a true hermaphrodite.[1] Hermaphrodite, or intersexuality, has been recognized since antiquity. Grecian statues with the female escutcheon and external genitalia of the male demonstrate this cognizance. Hugh Hampton Young[2] recognized that pseudohermaphroditism by far exceeded true hermaphroditism in number[3,4] and stressed that some criteria should be established for the determination of true hermaphroditism. His criteria required histologic evidence of both gonadal tissues for the diagnosis of true hermaphroditism. Thereafter, more than several hundreds cases were reported. According to the gonadal tissues distributed, there are three main types of true hermaphroditism: 1) lateral variety; testis on one side and ovary on the opposite side, 2) bilateral variety; testis and ovary on each side either separate or united (ovotestis), and 3) unilateral variety; testis and ovary on one side either separate or united and testis or ovary on the opposite side.

We present three cases of the ovotestis that were studied at the Department of Pathology, College of Medicine, Seoul National University, because of its rarity and also for the interesting findings seen in the involved tissue.

접 수 : 1983년 2월 28일

CASE REPORTS

Case 1 (S77-323)

A child, aged 5 years, with ambiguous external genitalia was brought to an urologist. The ambiguity consisted of a short phallus, two labial folds and a mass at the enlarged labial fold. Those were noticed since birth, and the patient was named and raised as a boy.

Amputation of penile shaft and orchiectomy were performed. During the operation, surgeon noticed an ovary in pelvic cavity, but there was no structure indicative of uterus. Routine laboratory findings were not remarkable. Cytogenetic study showed 46,XX. Microscopically, the area of closely packed seminiferous tubules shared common stromal tissue with scattered primordial follicles (Fig. 1 & 2). The testicular tissue had little stromal cells but numerous undifferentiated cells in seminiferous tubules. Salpingeal tissue and epididymis were also observed.

Case 2 (S78-2740)

An adolescent boy, aged 14 years, came to the urology service. Six months ago, he noticed his breast enlarged. The gynecomastia progressed. He was encountered with intermittent, left flank pain for three months prior to the admission.

He had history of a urethroplasty and chordectomy made at 6 years of age. Otherwise, he had been healthy physically. He was quiet, at least at home, but he had few friends, both boys and girls. Often, he intended not to go to school because of fear of physical examination.

On admission, bilateral gynecomastia and urogenital abnormalities were noticed. The opening of urethra ended blindly. Instead, a reconstructed urethral opening was at the frenulum of penis. The small phallus showed ventral curvature. The right testis was palpable in the scrotum but vas deferens was not. The left testis was absent. The prostate was rudimentary.

Laboratory findings were within normal limits, including urinary 17-ketosteroid and 17-hydroxy corticosteroid. Study for bar bodies was made with 200 buccal cells, which revealed only 12 positive cells. Cytogenetical study showed that the patient was normal male with 46, XY chromosomes.

Subcutaneous mastectomy and intra-abdominal

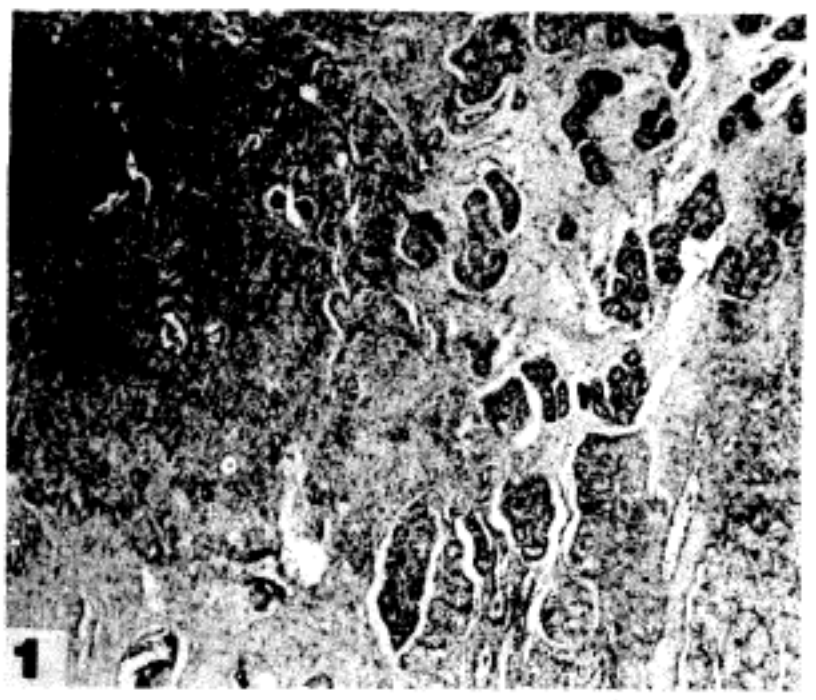

Fig. 1. Photomicrograph of ovotestis, case 1. Primordial follicles in cellular ovarian stroma, left, and lobules of seminiferous tubules at right. H&E, X40

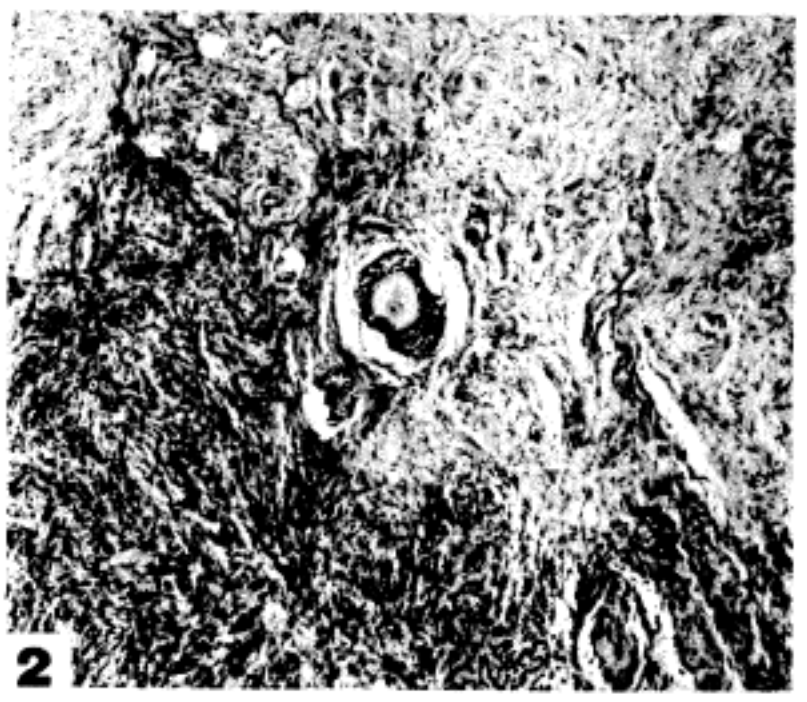

Fig. 2. Primordial follicles in rather hyalinized ovarian stroma. Case 1. H&E, X100

orchiectomy were carried out

A cystic, bean-shaped mass, 3×2×1.5 cm and attached tubular structure, 16 cm long, was submitted. Microscopically the mass contained several cystic follicles, primordial follicles within ovarian stroma and numerous seminiferous tubules and prominent Leydig cells (Fig. 3 & 4). Some cystic follicles had evidence of recent hemorrhage. But neither corpus albicans nor corpus luteum was present. The seminiferous tubules were filled with small undifferentiated cells. The tubular structure was made of salpingeal segment, vas deferens and tissue resembling epididymis.

Case 3 (S82-827)

A six years old child was brought to the Department of Pediatric Surgery for the correction of ambiguous external genitalia and the determination of sex. Ambiguity of external genitalia was noticed since birth but the child was raised as a boy, because of the presence of penis and absence of visible vaginal opening. The patient was of masculine appearance, healthy, alert but somewhat shy. As for the genitalia, a phallus was 5cm long with well formed glans and was straight without chordee. A narrow mucosal strip was bounded by two lateral lips which diverged slightly towards their termination in the perineum, where an urethral opening was situated 2 cm below the phallus. Additionally, two empty labial folds were observed. Vaginal opening was covered by perineal skin.

Ultrasonograph demonstrated a fine tubular structure, 3 cm long, posterior to the urinary bladder wall. Contrast study of vagina showed blind end and no communication with adjacent structure. Radiographs on urinary tract as well as other investigations remained within normal limits. The urinary 17-ketosteroid was 1.0 mg/24 hours. Karyotyping of blood cell was reported to be 46, XX without mosaicism.

Abdominal exploration showed a small fibrotic nodule, suggesting the rudimentary uterus, connected with a well formed, fimbriated fallopian tube and a gonad on the left side. Another gonad was located at internal ring of the right inguinal canal, which was connected to the lower segment of rudimentary uterus through a well formed spermatic cord. The left gonad was small and oval with smooth outer surface and shining peritoneal covering. The right gonad was reniform with a notch at the outer surface. (Fig. 5) The left gonad was considered to be an ovary. The right gonad was

Fig. 3. Seminiferous tubules with edematous stroma, where Leydig cells are prominent (arrows). Case 2. H&E, X200

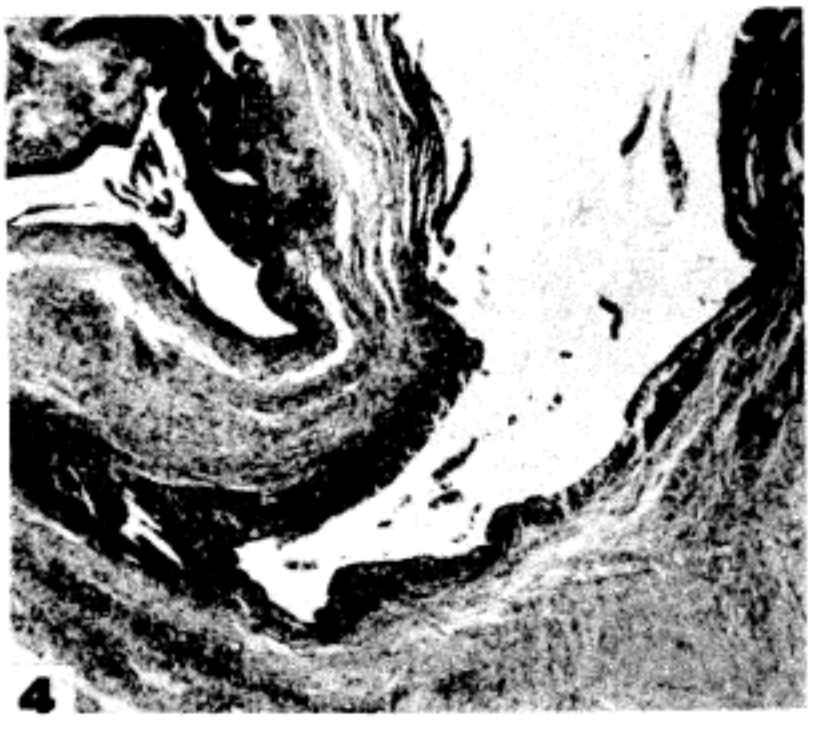

Fig. 4. Large cystic follicles lined by layers of granulosa cells. Case 2. H&E, X40

considered to be a testis, and was totally excised with spermatic cord. Additionally, reduction of phallus and vaginoplasty were done. The right gonad and spermatic cord were examined. It measured 2.2 ×1.2×1.0 cm and showed dark brown to tan color with grayish yellow, rather firm mass which was discriminated as two parts by a notch.

Microscopic examination proved the right gonad to be an ovotestis (Fig. 6). The testicular portion consisted of numerous seminiferous tubules and edematous stroma with tunica albuginea. The tubules were lined by undifferentiated cellls and a few spermatogonia. The Leydig cell was absent.

Ovarian tissue was well matured, being composed of numerous primordial follicles and graafian follicles embedded in ovarian stroma. A cystic follicle was associated. Rete testis, efferent ductules and connected pampiniform plexus were identified microscopically.

DISCUSSION

The description in medical literature of true hermaphroditism appeared much later than it did in historical documents.[5] True hermaphroditism is an infrequent condition which is defined as the development of a bisexual gonad whether it is separate or united, with consequent mixed bisexual somatic development.

The appearance of the external genitalia varies to distinguish five types.[6] Type 1 has completely female external genitalia. The other extreme of the spectrum are the true hermaphrodites with completely male external sex organs, although ovarian tissue is present in their organism (Type 5). But much more frequent are the intermediate forms, all of which have an uterus and an enlarged clitoris or penis with variable development of a urogenital sinus.

Young[2] recognized that many of bisexuality would be pseudohermaphroditism rather than true hermaphroditism. He insisted rigid criteria for the determination of true hermaphroditism, that is, a histological evidence of both ovarian and testicular tissues within an individual. Ovarian stroma tissue alone is not sufficient to identify an ovary. An exception to this rule may be made if there has been positive microscopic identification of ovarian tissue plus visible sperm in the semen ejaculated. On the basis of histologic determination, there are three main types of true hermaphroditism: 1) alternating or lateral variety; testis on one side and

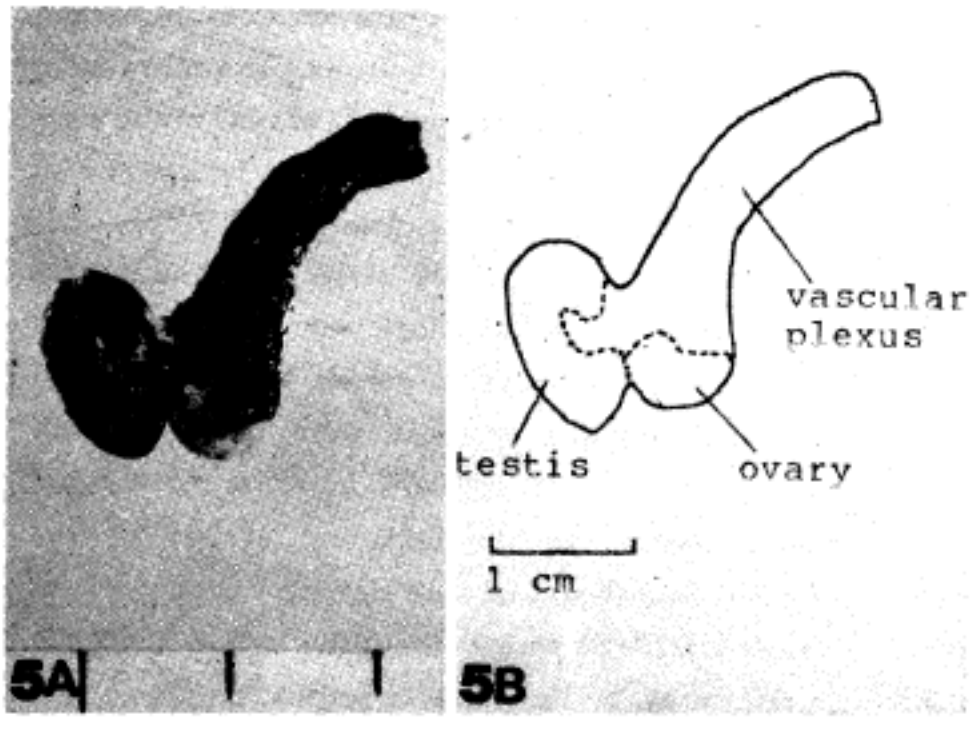

Fig. 5. Cut surface(A) and drawing(B) of ovotestis, case 3. Note the notching between testicular and ovarian tissues.

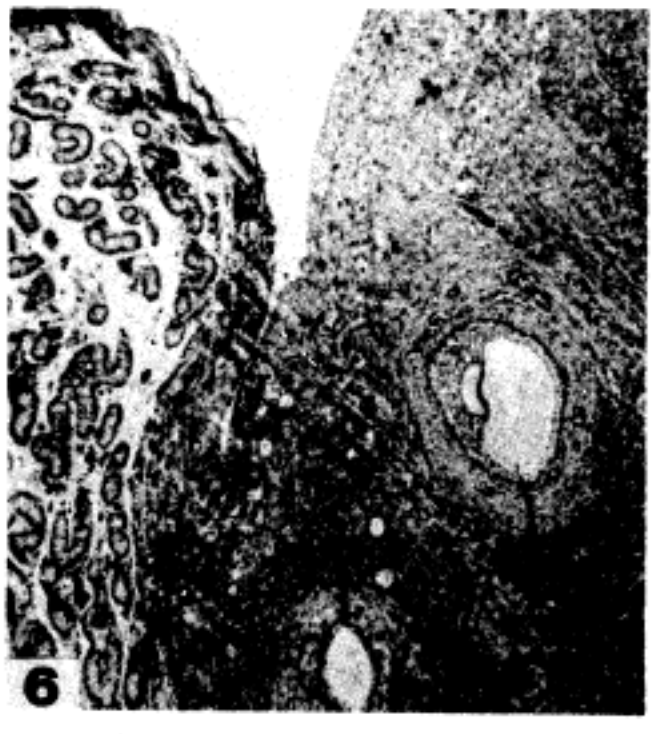

Fig. 6. Photomicrograph of the area of notching in Fig. 5. H&E, X40

Table 1. Classification of true hermaphroditism (Jones, 1971)

Group	Gonad on one side	on opposite side
Ⅰ. Alternating or lateral(O:T)	Ovary	Testis
Ⅱ. Bilateral(OT:OT)	Ovotestis	Ovotestis
	Ovary and testis	Ovary and testis
Ⅲ. Unilateral(OT:O)	Ovotestis	Ovary
	Ovary and testis	Ovary
	Two ovotestes	Ovary
Ⅳ. (OT:T)	Ovotestis	Testis
Ⅴ. (OT:—)	Ovary and Testis	No gonad
Ⅵ. (OT:?)	Ovotestis	not examined

ovary on the opposite side, 2) bilateral variety; ovary and testis on each side either separate or uni ted (ovotestis), and 3) unilateral variety; ovary and testis on one side either separate or united and ovary or testis on the opposite side. Two additional groups of unilateral variety are made. One is the case of absence of gonad opposite to ovotestis, and the other is the case of when the opposite side is not examined, histologically. Adopting these, Jones[1] introduced the classification of true hermaphroditism into six groups (Table 1).

Three quarters of true hermaphroditism have been reared as boys and men. This means that the greater number of such hermaphroditism have had rather masculine appearing external genitalia. Rearing as a male is particularly prominent in every groups except Group Ⅲ, as Jones indicated in his review[7]. Breast development is observed in most hermaphrodites who are old enough. Presence of menstration is determined in some extent by development of uterus. However, of those who are old enough and have uteri which are developed well, less than half have mensturation.

Chromosomal pattern of true hermaphroditism gathers more interests. The first reported chromosomal findings(46, XX) in true hermaphroditism were given by Hungerford et al.[8] Since then many authors have confirmed that more than half of true hermaphroditism have a chromosome complement of 46, XX, followed by 46, XY, mosaicism of 46, XX/46, XY, and other mosaicism in oder of frequency.[9]

The paradoxical development of testicular tissue in the absence of a Y chromosome, as in 46, XX, is quite unexplainable on the basis of current concepts of sexual development. Ferguson-Smith[10] postulated that the fertilization of an ovum by a sperm carrying an X unto which male determining genes from the Y chromosome were translocated. This hypothesis is partly evidenced by proving of presence of H-Y antigen in patients with a 46, XX karyotype.[11] And the antigen is believed to located at the short arm of Y chromosome.[12]

Surgical and hormonal treatments on true hermaphroditism depend on determination of sex of an individual. Sex chromatin, gonad, internal genitalia, external genitalia, hormonal levels, sex of rearing and gender role are identical in normal individual, while hermaphrodite exhibits one or more anomalies in morphologic criteria of sex. In the view point of psychiatry, the gender role is superior to any other criterion of sex determination.[13]

The three cases in this series are true hermaphrodites based on histologic confirmation of the ovotestis. But the opposite gonads were not biopsied in all, though the surgeons were confident with identification of the gonad. Therefore these cases should belong to the unilateral variety of true hermaphroditism and are classified Group VI of Jones classification because of the lack of histologic examination of the opposite gonads.

In domestic medical literatures, we could find at least 28 hermaphrodites.[14~19] Among them, eleven were true hermaphrodites proven histolo-

Table 2. Clinical, pathological and cytogenetic findings of the ovotestes

	Age	Sex of rear	External genitalia	Vagina	Uterus	Prostate	Breast	Hypospadia	Gonad Rt.	Gonad Lt.	Germ cell	Cytogenetics	Sources
1.	10	M	M	+	+	?	−	+	T	OT	+	?	Ref.[15]
2.	7	M	ambiguous	+	+	?	−	+	OT	O	?	M	Ref.[17]
3.	27	M	M	+	+	+	+	+	T	OT	+	F	Ref.[18]
4.	8	M	ambiguous	−	?	?	−	+	OT	O	?	46, XX	Ref.[19]
5.	5	M	ambiguous	−	−	?	−	+	OT	O	+	46, XX	present case
6.	14	M	M	−	?	±	+	+	T	OT	+	46, XY	present case
7.	6	M	ambiguous	+	±	−	−	+	OT	O	+	46, XX	present case

M: Male, F: Female, ±: rudimentary, ?: not checked, OT: ovotest, T: testis, O: ovary

gically, and four cases of ovotestis were included. Various findings of our cases compared with those of others in Table 2.

SUMMARY

Three cases of the ovotestis are presented. All of these cases were raised as boys, because of the presence of phallus and absence of vulva or visible vagina. Two of them were proved to be female by chromosomal study and the third one was the male. The clinical, pathological and cytogenetic findings are compared with four preceding cases of the ovotestis that were reported in Korea.

REFERENCES

1) Jones HW Jr, Scott WW: *Hermaphroditism, genital anomalies and related endocrine disorders. 2nd edition. Baltimore, The Williams & Wilkins Co, 1971*
2) Young HH: *Genital abnormalities, hermaphroditism and related adrenal diseases. Baltimore, The Williams & Wilkins Co, 1937*
3) Jones HW Jr, Wilkins L: *Gynecological operations in 94 patients with intersexuality. Am J Obstet Gynecol 82:1142, 1961*
4) Gross RE, Meeker IA Jr: *Abnormalities of sexual development, observations from 75 cases. Pediatrics 16:303, 1955*
5) Wilkins L, Grumbach MM, Van Wyk JJ, et al: *Hermaphroditism: classification, diagnosis, selection of sex and treatment. Pediatics 16: 287, 1955*
6) Warkany J: *Congenital Malformations. Chicago, Year Book Medical Publishers, Inc, 1971, p 1105*
7) Jones HW Jr, Ferguson-Smith MA, Heller RH: *Pathologic and cytogenetic findings in true hermaphroditism. Obstet & Gynecol 25:435, 1965*
8) Hungerford DA, Donelley AJ, Nowell PC, Beck S: *sited by Jones and Scott.*
9) Benirschke K, Nattolin F, Gitters R, et el: *True hermaphroditism and chimerism. Am J Obstet Gynecol 113:449, 1972*
10) Ferguson-Smith MA: *X-Y chromosomal interchange in the aetiology of true hermaphroditism and of XX Klinefelter's syndrome. Lancet 2:475, 1966*
11) Roy C, Roger M, Boccon-Gibod L, et al: *Clinical, cytogenetical, histological, immunological and hormonal studies in a case of true hermaph roditism. Clin Endocrinol 12:423, 1980*
12) Donahoe PK, Crawford JD, Hendren WH: *True hermaphroditism: a clinical description and a proposed function for the long arm of the Y chromosome. J Pediat Surg 13:293, 1978*
13) Wilkins L: *Abnormalities of sex differentiation, classification, diagnosis, selection of gender of rearing and treatment. Pediatrics 21:846, 1960*
14) 金東翰: *True hermaphroditism*의 1例. 大韓泌尿器科學會誌 *2:197, 1961*

15) 高聖健, 朱炳璇, 金世景, 高一香：眞性半陰陽의 一例. 現代醫學 *5:709, 1966*

16) 安雄俊：*Intesex*의 治驗例. 大韓泌尿器科學會誌, *8:109, 1967*

17) 이원석：*Intersex* 3예. 대한비뇨기과학회지 *12:127, 1970*

18) 김인선, 백승률, 이내일, 문국진：진성 반음양의 병리학적 고찰. 대한병리학회지 *10:149, 1976*

19) 신성수, 이희영：반음양 17예에 대한 임상적 고찰. 대한비뇨기과학회지 *18:511, 1977*