TRUE HERMAPHRODITISM: DIAGNOSIS AND SURGICAL TREATMENT

S. GUASCHINO (*) - E. STOLA (*) - A. SPINILLO (*)
M. MARCHETTI (**) - A. AGUZZI (***)
(*) Institute of Obstetrics and Gynecology, School of Medicine - University of Pavia (Italy)
(**) Inst. of Plastic and Reconstructive Surgery, School of Medicine - University of Pavia (Italy)
(***) Institute of Pathology, School of Medicine - University of Pavia (Italy)

Summary: We documented a new case of 46,XY true hermaphroditism in an 18-year-old patient, reared as a female at birth, with ambiguous genitalia and primary amenorrhea. At laparotomy, bilateral dysgenetic ovotestis containing gonadoblastoma were found. Karyotypes of peripheral lymphocytes and cells from tissue of both gonads were all 46,XY. Plastic surgery was conducted to transform ambiguous genitalia to the full female phenotype. Clitoreduction by glans resection and fastening of the corpora cavernosa in the labia major with enlargement of the vaginal orifice were performed. The result was a small eretcile organ with preserved sensitivity and a female capable of normal sexual activity.

INTRODUCTION

The contemporary presence of ovarian and testicular tissue in one or both the gonads of the same subject leads to the diagnosis of the most rare form of intersexuality: true hermafroditism.

Of the 400 cases reported in Literature, only half have been completely documented and still less have been subjected to a long term follow-up evaluating the results of both surgical and medical treatment ([1, 2, 3]).

Gonadectomy is always necessary due to the fact that intraabdominal Y-positive gonads are notorius for their high incidence of neoplastic transformation. Every case is considered to be individual with respect to both plastic surgery and substitutive hormonal therapy.

Recently, a new case has been observed at the Department of Obstetrics and Gynecology of the University of Pavia and is described below.

CASE REPORT

E. C., 18 years old, was referred to us because of external genitalia ambiguity, hirsutism and primary amenorrhea.

There were no reported cases of anatomical malformation of the uro-genital tract in her family. At birth her external genitalia were apparently normal and she was reared as a female.

The patient developed normally until puberty, at which time a progressive enlargement of the clitoris was noted. Muscular development and hair distribution became characteristic of a male phenotype.

The physical examination revealed a well-developed hirsuted female, 168 cm in height, and weighing 56 kg; Tanner stage II breasts; external genitalia with enlarged clitoris, with a shaft length of 4 cm and incomplete fusion of the labioscrotal folds (fig. 1). The urethra opened 2 mm above a quite small vaginal orifice (4 mm in diameter). With a vaginoscopy it was possible to examine the vagina (9 cm in length), lined with hypotrophic mucosa; the uterine cervix was infantile. A small uterus and gonads, in the normal position, were palpable at rectal examination. Ultrasound revealed hypoplasic uterus (6 cm in length) and gonads with hyperechoic areas.

Hormonal assays revealed FSH and LH elevated to 134 mUI/ml and 119 mUI/ml; ACTH 21.0 pg/ml (normal value 20-80); DHEA-S 3940 ng/ml (n. v. 1200-3020); androstenedione 1.1 ng/ml (n. v. 0.8-4.0); testosterone 3.8 ng/ml (n. v. 0.1-1.8); estradiol 31.0 pg/ml (n. v. 50-800); urinary 17-ketosteroids 9.3 mg/24 h (n. v. 7.0-20.0); 17-hydrocoticosteroids 6.6 mg/24 h (n. v. 3.0-15.0).

A 46,XY karyotype was revealed by chromosome analysis of peripheral blood lymphocytes.

At laparotomy there was a morphologically normal, infantile uterus and normal bilateral

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Fallopian tube (fig. 2). Macroscopically, both the gonads appeared to be composed of two distinct tissues, one firm, pearly and friable; the other yellowish, more compact. Wolffian structures were present on the inside of the left broad ligament (fig. 3). Bilateral salpingogonadectomy was performed.

Histologically, both the gonads revealed a testicular tissue with seminal atrophy and calcified gonadoblastoma; hyperplastic Leydig-type cells (fig. 9); ovarian stroma with very rare oocytes; elements derived from follicular atrophy and calcified gonadoblastoma; rete testis and epidydimis inside the left broad ligament (fig. 10). Chromosome culture of gonadal fibroblast (ovarian and testicular tissue) from both the gonads, showed a 46,XY karyotype. Clitoroplasty involved the following steps: removal of the skin of the penis (fig. 5), separation of the corpora cavernosa along the median septum (fig. 6), and their introduction (fig. 7) and fastening inside the labia major (fig. 8). Sectioning of the dorsal part of the glans was performed to form a small clitoris-like organ [4]. Enlargement of the vaginal orifice was conducted by multiple-Z plastic.

The only postoperative complication was a haematoma of the labia major that healed spontaneously.

Estroprogestinic therapy (Trigynon, Schering) per os and topical naturally conjugated estrogen were administered postoperatively. A follow-up two years later demonstrated that hair distribution and external genitalia were characteristically female, with preserved erection and sensitivity of the clitoris (fig. 4). The breasts were moderately enlarged and menstruation occurred with the cyclic interruption of estroprogestinic therapy. The patient's psychological status was much improved with respect to that prior to the interventions, facilitating normal social relations.

DISCUSSION

About 60% of true hermaphrodites have a 46,XX karyotype, 28% are mosaics or chimeras and only 12-16% have a 46, XY karyotype [5, 6].

All 46,XX true hermaphodites may result from the transfer of a testis-organizing gene(s) from the Y to either an X chromosome or an autosome during paternal meiosis [7]. Some Authors have suggested that all 46,XY true hermaphrodites are unrecognized chimeras or mosaics [8, 9]. In fact discordant karyotype in blood, skin (46,XX) and gonadal tissue (46,XY) [1, 10] and both studies on the genealogical tree and blood group transmission in 46,XY true hermaphrodites may confirm this hypothesis [11].

Above all, in patients with very small amounts of testicular tissue, its removal at an early age can increase the possibility of normal reproductive functions, since it would be less apt to interfere with development of the genital tract and gonadal function. Although simultaneous spermatogenesis and ovulation have been observed in a hermaphroditic individual [12], there is no suggestion of self-fertilization in humans. Uncomplicated pregnancies and vaginal deliveries have been described in the same patients [13]; this event is more frequent when only one of the gonads is disgenetic. In bilateral ovotestis, it is nearly impossible to preserve normal functioning ovarian parenchyma, given the extreme difficulty of the macroscopic separation of one tissue to the other, so that the entire gonad must be removed [1].

Although androgen production from testicular tissue may induce full masculinization in utero, more often clitoromegaly and incomplete differentiation of Wolffian and urogenital sinus structures occur [14]; in our case, the amount of androgens was not able to produce clitoromegaly in utero, so that the subject was reared as a female. The development of a normal Fallopian tube, even though testicular tissue was present can be explained by the absence of the Mullerian inhibiting factor or its nonfunctioning on the side of the ovotestis [15]. Masculinization may be delayed from any one of the following: the estrogenic production from the fetal gonads, a transitory insufficiency, or late activation of Leydig cells [16]. However, with time, androgen levels, increased by stimulation of gonadotropins, facilitate follicular atresy and develop a clearly virilizing action.

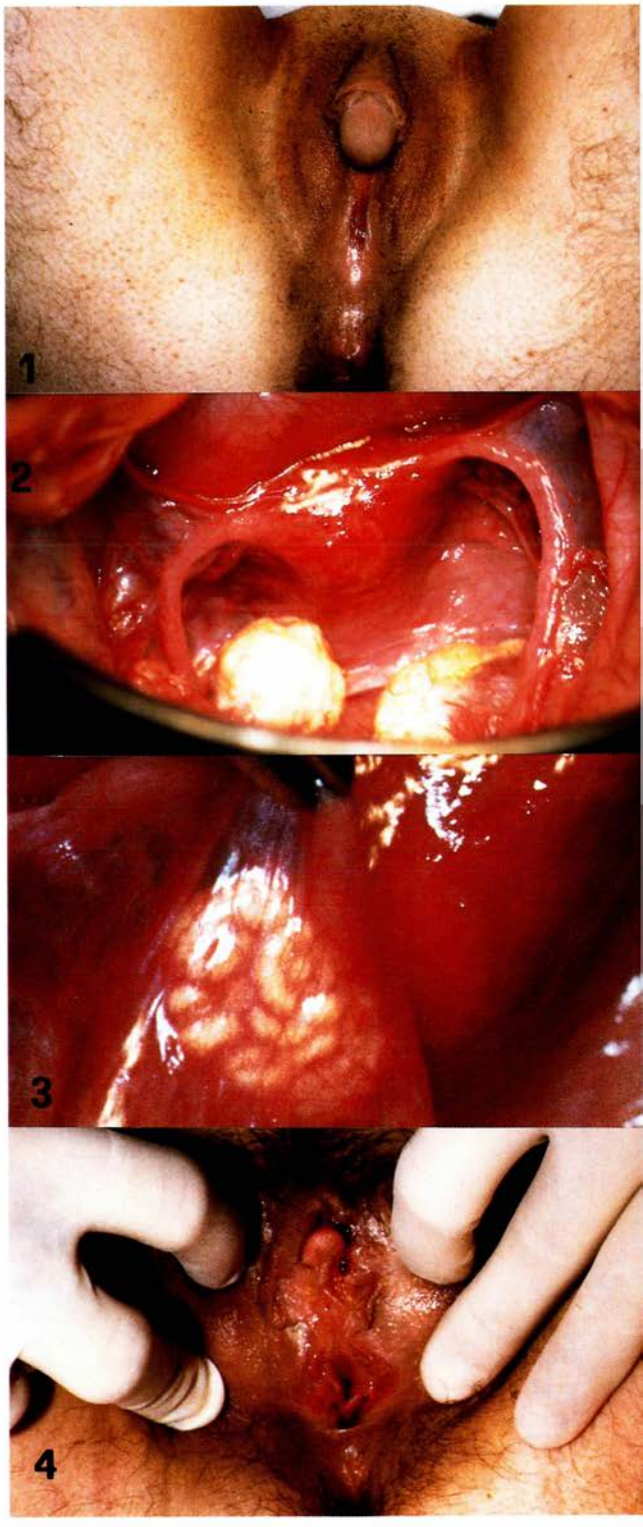


Fig. 1. — External genitalia before surgery.

Fig. 2. — Internal genitalia at laparotomy.

Fig. 3. — Macroscopical evidence of rete testis-like structure in the gonads.

Fig. 4. — External genitalia at two years follow-up.

Fig. 5. — Removal of the skin of the clitoris and sectioning of dorsal par of the gland to form a small clitoris - like organ.

Fig. 5*a*. — Schematic Drawing of this Surgical time.

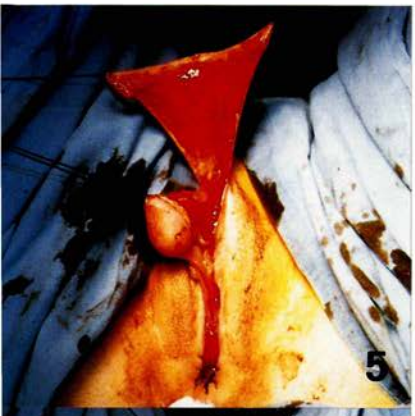
Fig. 6. — Separation of corpora cavernosa along the median septum.

Fig. 6*a*. — Schematic Drawing of this Surgical time.

Fig. 7. — Introduction of corpora cavernosa inside labia major.

Fig. 8. — Fastening of corpora cavernosa.

Fig. 8*a*. — Schematic Drawing of this Surgical time.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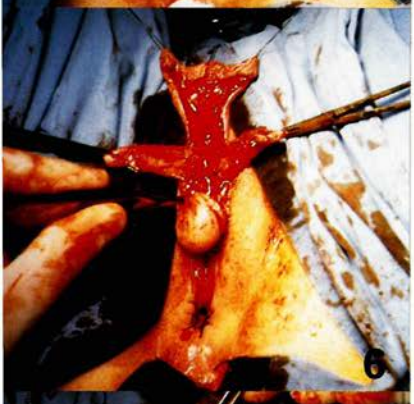
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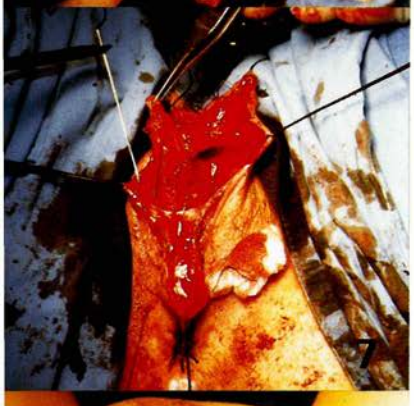
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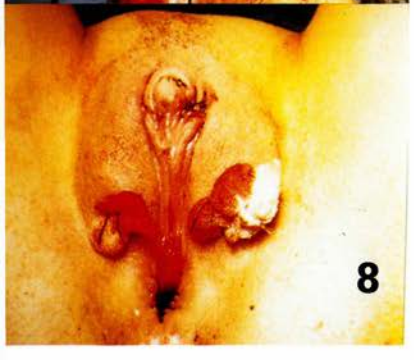
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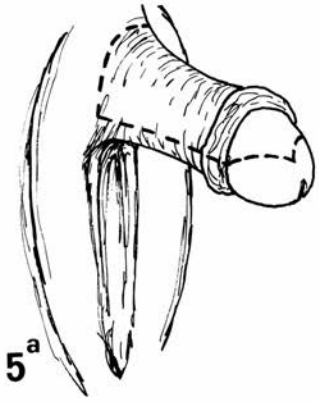
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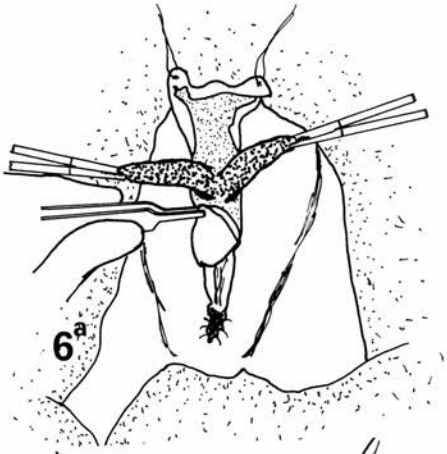
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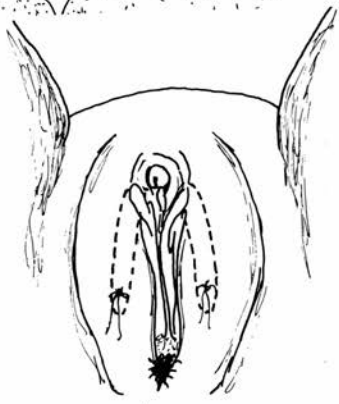

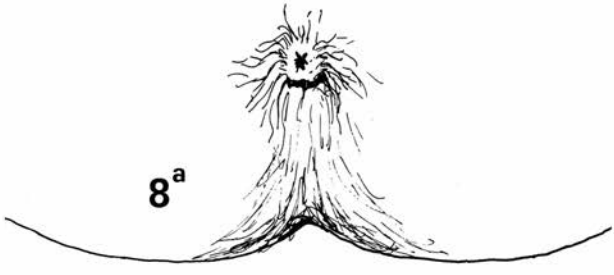
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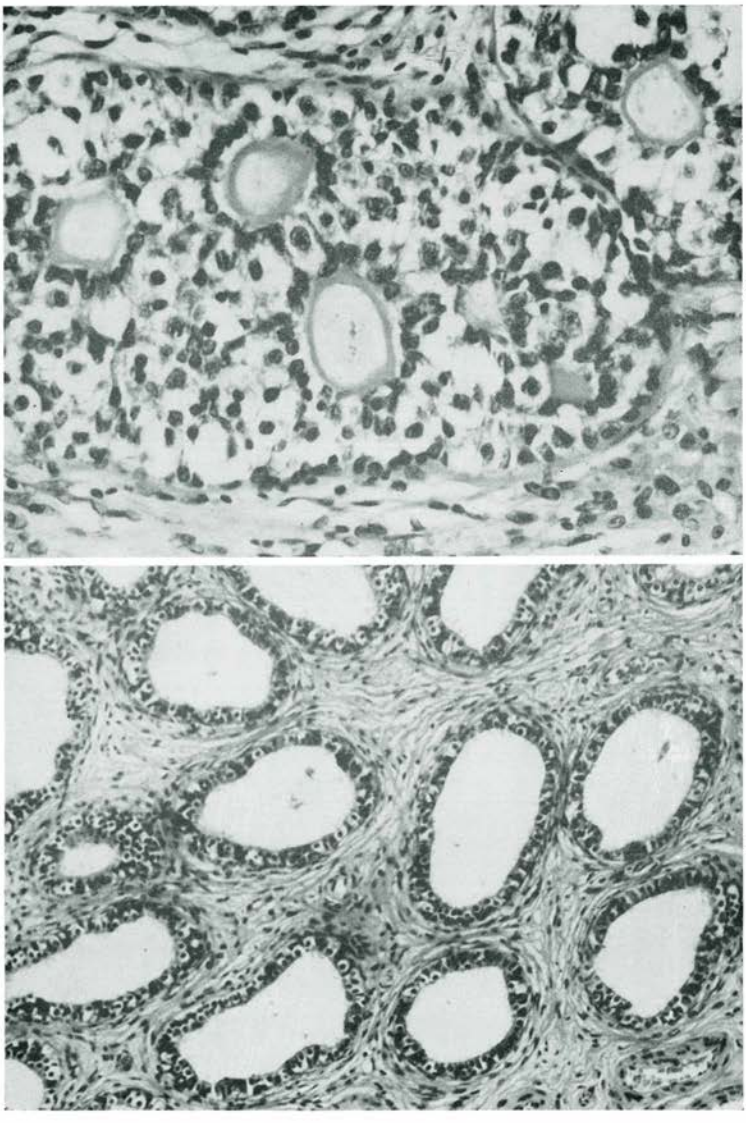

Fig. 9. — Gonadoblastoma. A cell nest containing germ cells, epithelial cells of granulosa or Sertoli type and numerous Call-Exner-like bodies. (EE × 300).
Fig. 10. — Rete testis (EE × 120).

Ovotestis produce in vitro more androgens than estrogens ([14]), due to a reduced aromatizing activity either in reference to a decreased follicular component or to the growth of a gonadoblastoma which replace ovarian parenchyma.

Gonadoblastoma develops in 20-30% of 46,XY gonadal dysgenesis ([8]) and is rarely seen in the normal ovary or testis ([17]). Some hormonal abnormalities, especially increased gonadotropins, appear to be the main promoting factor ([17]).

The case described above contains many of the rare observations contained in Literature; especially the presence of a bilateral ovotestis with a developing gonadoblastoma. While gonadectomy is the best way to treat these patients, a surgical approach to ambiguous genitalia is controversial. Surely clitorectomy should be avoided, if at all possible, because of the role of the clitoris as an erotic organ. Clitoroplasty, by excision of the shaft and corpora cavernosa with retention of the glans ([19, 20]), and clitoral recession ([21]) have been proposed.

Our experience showed that the reduction of glans preserves the erectile function of this organ; while the corpora cavernosa fastened inside the labia major undergoes atrophy. Substitutive estroprogestinic therapy prevents hypogonadism due to gonadectomy, restoring trophism of genital mucosas and permits normal sexual activity.

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