True hermaphroditism associated with microphthalmia

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Abstract

A 4-year-old boy with an undescending left testis, penoscrotal hypospadia and bilateral microphthalmia was admitted to our hospital. Chromosome analysis revealed a karyotype of 46, XX del(x)(p22.31) and the sex-determining region of the Y chromosome (SR Y) was negative. The right testis was located in the scrotum and a left cystic ovary-like gonad, a salpinx and a unicorn uterus were found in the left inguinal canal. Histologically the gonad was an ovotestis in which primordial follicles covered infantile seminiferous tubules. Microphthalmia is observed in some congenital syndromes caused by interstitial deletion of the X chromosome. This case suggested that the short arm of the X chromosome was involved in the differentiation of the gonad. Very closely located follicles and infantile seminiferous tubules indicated that induction of meiosis in the fetus was controlled by the local microenvironment in follicles and seminiferous tubules, and not by the systemic hormonal condition.

Introduction

True hermaphroditism is an entity of abnormal sexual development (1, 2), which includes the presence of both follicles and seminiferous tubules in an individual. The phenotype varies from females to males. The karyotype also includes a variety of types and 46, XX is found in approximately half (50–60%) of true hermaphrodites (2).

A major difference in the differentiation and development of ovaries and testes is the behavior of coelomic epithelial, mesonephric and germ cells incorporated into the primordial gonad. In the ovary, oogonia begin meiosis during fetal life, and they become arrested after producing primary oocytes and resume the second step of meiosis at the time of ovulation, whereas germ cells in the testis have a prolonged period of premeiotic arrest which lasts until the initiation of spermatogenesis at puberty (3, 4).

The current report presents a true hermaphrodite with microphthalmia with a karyotype of 46,XX del(x)(p22.31), in whom follicles and seminiferous tubules were located very close together.

Case report

A 4-year-old boy was admitted to our hospital for urethroplasty and correction of an undescending left testis. His initial gender assignment was male and no mental retardation was found. He had penoscrotal hypospadia (Fig. 1) and bilateral microphthalmia with a cataract on the left eye. The right testis was in its normal position in the right scrotum and what was believed to be the left testis was found in the left inguinal canal.

Chromosome analysis revealed a karyotype of 46, XX del(x)(p22.31) (Fig. 2). The sex-determining region of the Y chromosome (SR Y) was not detected by polymerase chain reaction of DNA prepared from peripheral blood lymphocytes. A cystic ovary-like gonad, a salpinx and a unicorn uterus were found in the left inguinal canal at operation (Fig. 3). These tissues were extirpated and one-stage urethroplasty was performed. Histological examination demonstrated that primordial follicles covered infantile seminiferous tubules and both were located close together and mingled with each other in the boundary zone (Fig. 4).

Discussion

True hermaphroditism is a variant of abnormal sexual development and is defined as the presence of both follicles and seminiferous tubules in an individual (1, 2). Its etiology still remains unexplored (1, 5). The ovotestis is the most common type of gonad in true hermaphroditism (2), constituting 44% of gonads in a survey of 409 cases reported up to 1981 (6). On the other hand, microphthalmia is an abnormality usually caused by interstitial deletion of chromosome 13, 18 or X, and rarely by an X-linked abnormality because X-linked disorders in males are not uncommonly a lethal disorder.
Furthermore, the relationship between the deletion of the short arm of the X chromosome, abnormal sexual development, and the possible role of the short arm of the X chromosome locus involved in human sex determination has already been suggested (10). The present case had two rare conditions: true hermaphroditism and bilateral microphthalmia possibly related to 46,XX del(x)(p22,31) and also suggests that the short arm of the X chromosome is involved in the differentiation of the gonad.

The majority of ovotestes are made up of testicular and ovarian tissues combined side by side. As observed in the current case, testicular tissue is occasionally enveloped by ovarian tissue completely, indicating that the ovary and testis develop from the cortex and medulla of the primordial gonad respectively. In the male, the medulla develops into a testis and the cortex regresses, whereas in the female the medulla regresses and the cortex develops into an ovary (11).

The ovotestis in the current study demonstrated that meiosis of germ cells is induced in ovarian follicles and not in testicular seminiferous tubules while both tissues are located close together. Meiosis of oogonia in the human fetus usually begins around 66 days and reaches a peak at about 18 weeks of fetal life but meiosis of spermatogonia is never induced before puberty. In the female fetus, it has been considered that a significant number of germ cells enter meiotic prophase to characterize the transition of oogonia into oocytes under the increasing secretion of follicle-stimulating hormone (FSH) and luteinizing hormone. Since the peak level of gonadotropin secretion correlates with the peak level of oogonial multiplication in the fetus (4, 12–15) and FSH levels are much lower in the male fetus than in the female, it has been considered that the initiation of meiosis in the fetal ovary is dependent on FSH (11).
Infantile seminiferous tubules and follicles are mingled with each other in the boundary zone of the current ovotestis. Meiosis has been induced in the latter but not in the former. Ectopic mouse germ cells of both sexes located in the adrenal begin meiosis at the time when female germ cells in the ovary enter meiosis (16), substantiating the concept that a meiotic clock operates autonomously. Further, female and male germ cells simultaneously enter meiosis when these cells are placed in the adrenal or vicinity of the mesonephric tissues outside the gonads (3). Therefore, it appears most likely that a meiosis-preventing substance(s) is present in fetal and infantile seminiferous tubules. On the other hand, c-mos proto oncogene, maturation-promoting factor and mitogen-activated protein kinase have been recently reported as possible localized factors for the initiation and progression of meiosis, because they are expressed during the meiosis of germ cells (12–14).

Figure 3 The unicorn uterus (U), left ovotestis (LOV) and salpinx (S) found at operation. C: connective tissue attached to the pubis; arrow: resected end of the uterus.

Figure 4 (A) Ovarian tissue with primordial follicles in the cortex covers seminiferous tubules in the medulla (hematoxylin and eosin stain; × 20). (B) Infantile seminiferous tubules and primordial follicles are located close together and mingled with each other in the boundary zone (hematoxylin and eosin stain; × 68). (C) Primordial follicles with oogonia in the cortex (hematoxylin and eosin stain; × 160). (D) Infantile seminiferous tubules in the medulla (hematoxylin and eosin stain; × 160).
References


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