表1　血液・尿検査項目

血液検査	尿検査
電解質，血清コレステロール 性腺系：テストステロン，(LH, FSH) 副腎系：17OHP，コルチゾール，ACTH，PRA，PAC， その他のステロイドホルモン (遺伝子検査用の検体採取) AR，5αR，SF-1，WT1等	検尿（尿蛋白） 尿中ステロイド分析

注）ステロイドの測定はアッセイにより検査値が異なること，目的のステロイド以外の代謝物をはかり込む可能性があることから，検査結果が絶対ではないことを認識し，診断は総合的に行うこと．

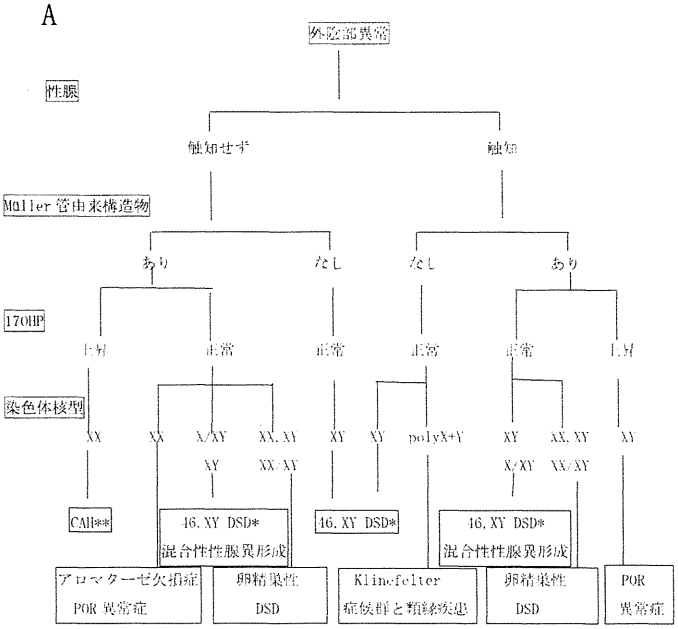
表2　泌尿器科・内科治療の実際（原疾患の治療は除く）

時期		泌尿器科的治療	内科的治療
～6～12ヶ月		外陰形成術（I期） 性腺生検・性腺摘出術（必要に応じて）	男児：テストステロン療法（エナルモンデポー®，T/DHT軟膏）
～1歳半		外陰形成術（尿道形成II期・膣形成） 性腺生検・性腺摘出術（必要に応じて）	
小児期	男児	外陰形成術（尿道形成III期）	
思春期年齢	男児 ～15歳	外陰形成術	性腺補充療法：テストステロン（エナルモンデポー®），HCG・FSH(ゴナトロピン®，ゴナールエフ®)，塩酸メテノロン（プリモボラン®），T/DHT軟膏
	女児 ～14歳	膣鏡・尿道鏡・膣形成術（全麻下で行うこと）	性腺補充療法：エストロジェン(プレマリン®，ジュリナ®，エストラーナ®など)，カウフマン療法
成人期*1		(必要に応じ）外陰形成術，泌尿器科的治療（漏尿等）	HRT継続 挙児希望の場合のLHRH療法（ヒポクライン®），HCG-FSH療法は産婦人科・泌尿器科にて行う*2．

*1 思春期以降は成人内科，成人泌尿器科，産婦人科への移行を考慮する．

*2 女性のFSH療法は多胎妊娠等の問題がある．

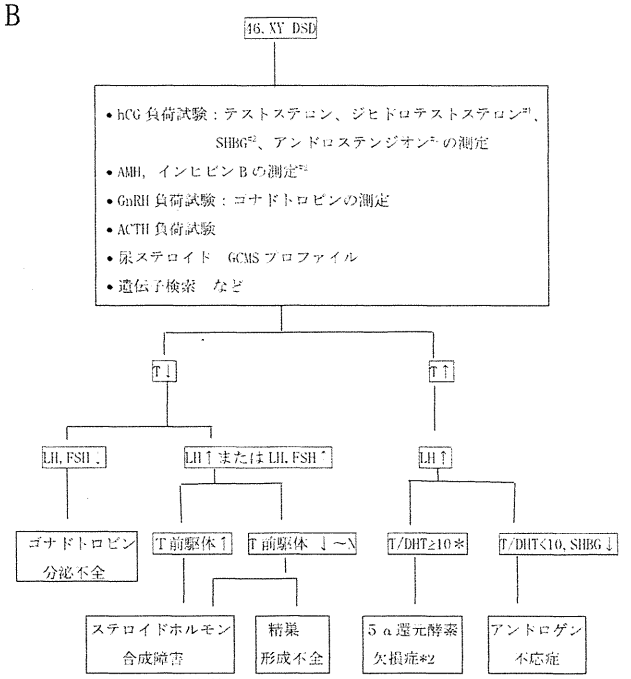
A



*46, XY DSD: 図1-Bに続く

**CAH: 21 水酸化酵素欠損症、3β水酸化ステロイド脱水素酵素欠損症、11β水酸化酵素欠損症、POR 異常症

B



＊ 基準値はないので参考値。年齢によって測定系の問題（胎児副腎産物との交差）があるので注意を要する。

＊2 生化学的には早期診断が困難であるので、確定診断には遺伝子診断が必要である.

#1 保険未収載だが鑑別のために測定が望ましい。

#2 保険適応となっておらず、測定可能施設も限られるため、必須の検査ではない

図1

附：戸籍の届出・戸籍法について

(1) 届出

戸籍法第四章第二節　出生

第四十九条　出生の届出は，十四日以内(国外で出生があったときは，三箇月以内)にこれをしなければならない．

○2　届書には，次の事項を記載しなければならない．

一　子の男女の別および嫡出子又は嫡出でない子の別

二　出生の年月日時分および場所

三　父母の氏名および本籍，父又は母が外国人であるときは，その氏名および国籍

四　その他法務省令で定める事項

説明：上記の出生届が原則であるが，以下が可能である．

1) 戸籍の未載について

●男女性別は未載可，医師の証明書を添付し「追完」できる．

●名前も未載可,「追完」できる．

●ただし，いずれの場合も「追完」の記録は残る．

2) 届出そのものを遅らせることについて

●14日以内が原則であるが，遅れても受理はする．

●ただしその場合，以下の過料が課せられる可能性がある．

戸籍法第九章　罰則

第百三十五条　正当な理由がなくて期間内にすべき届出又は申請をしない者は，五万円以下の過料に処する．

(2) 戸籍における性の変更について

●医学的事由があり，妥当と認められる診断書が提出され家庭裁判所で認められれば性の変更は可能．

●変更の記録が残るが，転籍・結婚で性変更の記録は消える．

注) 性同一性障害と性分化疾患における性同一性障害を伴わない性の変更の異同について

性同一性障害者の性別変更については，厚生労働省令で定める事項が記載された医師の診断書の提出などが定められている．基本的に性同一性障害を伴わない性分化疾患における性の変更(診断の変更など医学的事由による)とは区別して扱うべきである．ただし，完全に別個に扱うことが不可能な事例もあることを認識して対処する．

戸籍法第三章　戸籍の記載

第二十条の四　性同一性障害者の性別の取り扱いの特例に関する法律（平成十五年法律第百十一号）第三条第一項の規定による性別の取り扱いの変更の審判があった場合において，当該性別の取り扱いの変更の審判を受けた者の戸籍に記載されている者（その戸籍から除かれた者を含む．）が他にあるときは，当該性別の取り扱いの変更の審判を受けた者について新戸籍を編製する．

外陰部奇形の診断と対応

大山建司*

はじめに

2006年に性分化の専門家による国際会議が開催され，Disorders of Sex Differentiation は Disorders of Sex Development（DSD）と改称され，同時に侮蔑的意味合いや倫理的問題を含む疾患名の変更が行われた。この会議の詳細の和訳は『日本小児科学会雑誌』に掲載されている[1]。わが国でも，日本小児内分泌学会を中心に日本語名の変更が行われた。従来，性分化異常症として総称されていた疾患群を性分化疾患とし，インターセックス（間性），半陰陽，仮性半陰陽，雌雄同体，類宦官症，睾丸性女性化症，副腎性器症候群などの疾患名を使用しないこととした。主な変更点を表に示す。今後，疾患名の変更は小児科医のみならず産婦人科，泌尿器科医などにも周知していく必要がある。

小児領域で把握されている性分化疾患は，現在約10,000人程度と推測されているが，そのほかに医療機関に受診していない症例もかなり存在する可能性がある[2]。外性器奇形は隠蔽されやすい傾向が今でも強く残っており，患者は gender identity（性自認）などの問題も含めて，一人で苦悩を背負っていかなければならない状態が長く続くことになる。早期診断と患者，保護者・家族への適切な対応と支援が重要である。

表　性分化疾患診断名の主な変更点

今後使用しない名称	新たな名称
性分化異常症	性分化疾患（DSD）
真性半陰陽	卵精巣性性分化疾患
インターセックス（間性）	削除
雌雄同体	削除
類宦官症	削除
高（低）ゴナドトロピン性類宦官症	削除
男性仮性半陰陽	46,XY 性分化疾患
女性仮性半陰陽	46,XX 性分化疾患
副腎性器症候群	削除
睾丸性女性化症	削除
睾丸	卵巣に対応する場合は精巣とする
停留睾丸	停留精巣
睾丸機能低下症	精巣機能低下症
睾丸形成不全	精巣形成不全

I 診断の手順

性分化疾患は，「染色体，性腺または解剖学的性が非定型である先天的状態」と定義されている。

出生に立ち会うのは産科医と助産師である。医療者が外性器奇形を疑わなければ，小児科医はよばれることなく，異常は看過されることになる。結果的に望ましくない性の判定が行われると，将来，性の変更，名前の変更が問題となる場合がある。

1．現症の把握

出生時，外性器が典型的な男性型・女性型と若干異なる印象を受けたとき，外性器の形状を正確に視触診することが大切である。外性器の異常を疑った場合には，一人で判断せずに，小児内分

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泌，小児泌尿器の経験豊かな医師に相談すべきである。外性器の写真，検査結果などをメールで送ることにより，遠隔地であっても相談は可能である。小児内分泌学会では学会員を対象とした性分化疾患の相談窓口を設けている。

1）陰茎か陰核肥大か

陰茎か陰核肥大かの判断では，亀頭が露出しているように見えるときは陰核肥大を疑う。先天性副腎過形成症（21 水酸化酵素欠損）女児では陰核肥大のため亀頭部が露出したように見えることが多い。軽症または高度の男性化では亀頭が露出していないこともある。女児の陰核肥大の大部分は 21 水酸化酵素欠損である。本症では色素沈着を伴うので，皮膚色とくに粘膜の色素沈着に注意する。

2）色素沈着はないか

前述した色素沈着の有無も重要な所見である。外陰部の色素沈着は個人差があり，判定が困難な場合もあるが，全身の皮膚色と口唇，腋窩などの色素沈着を確認する。

3）尿道口の開口部位はどこか

尿道口が亀頭頂部に開口しているか，尿道下裂となっていないか，外性器が女性型の場合は膣と尿道口の確認（泌尿生殖洞の有無）が重要である。

4）大陰唇か陰嚢形成不全か

大陰唇は男性化すると皺が寄って，色素沈着してくる。大陰唇の触診で腫瘤を触知したときは精巣の可能性が高い。一方，男性ホルモン作用が減弱すると陰嚢は低形成となる。アンドロゲン受容体異常症ではアンドロゲン効果を推測するうえで重要である。

5）精巣は触知するか

触診による陰嚢内の精巣の確認は大切である。精巣の下降が完了するのは 4 か月ごろと考えられており，新生児期には下降していないこともある。鼠頸部にも触知しないときは画像による確認が必要である。また生後 1～2 か月ごろの血清テストステロン濃度は精巣機能の判定に重要である。4 か月健診で陰嚢内に触知しなければ停留精巣である。

6）膣はあるか，盲端ではないか

卵管・子宮欠損では膣は盲端となる。膣の形状は，膣形成の可否に重要であり，性判定に際して考慮すべき重要な情報である。

2．問　診

妊娠中の罹病，内服薬，ホルモン作用を含有する食品・入浴剤・塗布剤・整髪剤などの使用を詳しく聴取する必要がある。外性器の分化は妊娠 8 週ごろから始まり 12 週でほぼ完成するため，形態異常に関する問診はこの時期が重要である。

3．診　断

性分化疾患に適切に対応するには，集約化が重要である。診断・治療方針の作成，親への対応は，経験豊富な医師を含む集団が整った施設で行うべきと考えている。生活している地域からの隔離の意味もあり，可能であれば遠隔地であっても搬送を考慮すべきである。しかし搬送前に，早急に鑑別すべき疾患がある。女児（46,XX）の先天性副腎過形成症である。出生時，外性器異常を呈する疾患のなかで最も頻度が高い疾患である。90%以上を 21 水酸化酵素欠損が占め，次いで *StAR* 異常症，*POR* 欠損，11β 水酸化酵素欠損が占めている。急性副腎不全（低ナトリウム，高カリウム血症）の発症に注意を要する。46,XX-21 水酸化酵素欠損は，基本的に女児として成育する疾患である。

性分化のプログラムの基本型は女性であり，出生時に外性器異常を伴う 46,XX 性分化疾患は，先天性副腎過形成症を除けばまれである。卵巣，子宮，膣の形成異常は一般的に女性型外性器として出生するため，出生時には性分化疾患を疑われない場合が多い。

性腺の発生・分化の段階の異常で発生頻度が高い疾患は，卵精巣性性分化疾患，*WT1* 異常症，*DAX1* 異常症である。ほかに *SRY* の異常，XY 性腺形成異常症，*SF1* 異常症などがある。これらの疾患の外性器の形状は多様である。

46,XY 性分化疾患ではアンドロゲン受容体異常症の頻度が高く，次いで胎児期精巣退縮症候群（多くは外性器男性型）が多い。受容体機能が完全に喪失したアンドロゲン受容体異常症では，外性器は完全女性型で，大陰唇部に精巣を触知する。

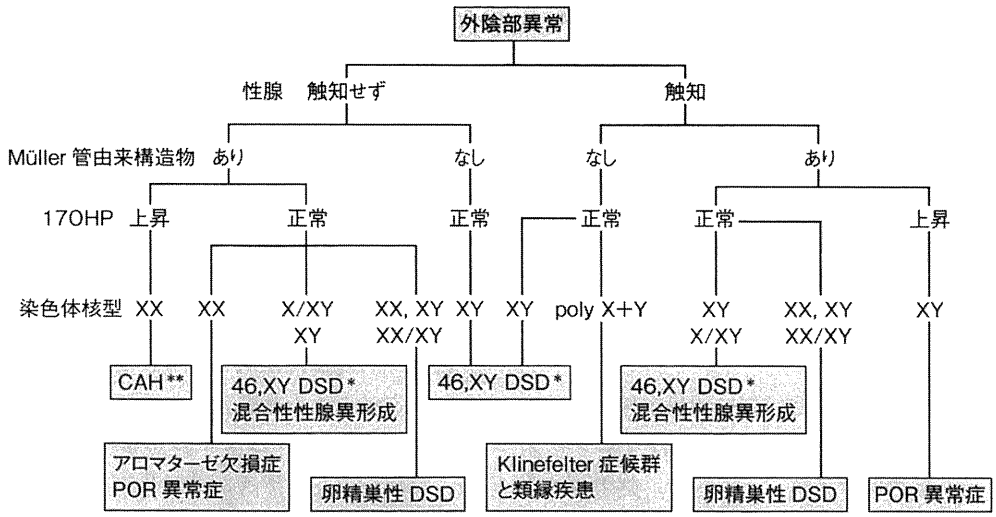

図 1　性分化疾患診断のアルゴリズム（日本小児内分泌学会性分化委員会作成）

* 46,XY DSD：図 2 に続く。** CAH：21 水酸化酵素欠損症，3β水酸化ステロイド脱水素酵素欠損症，11β水酸化酵素欠損症，POR 異常症

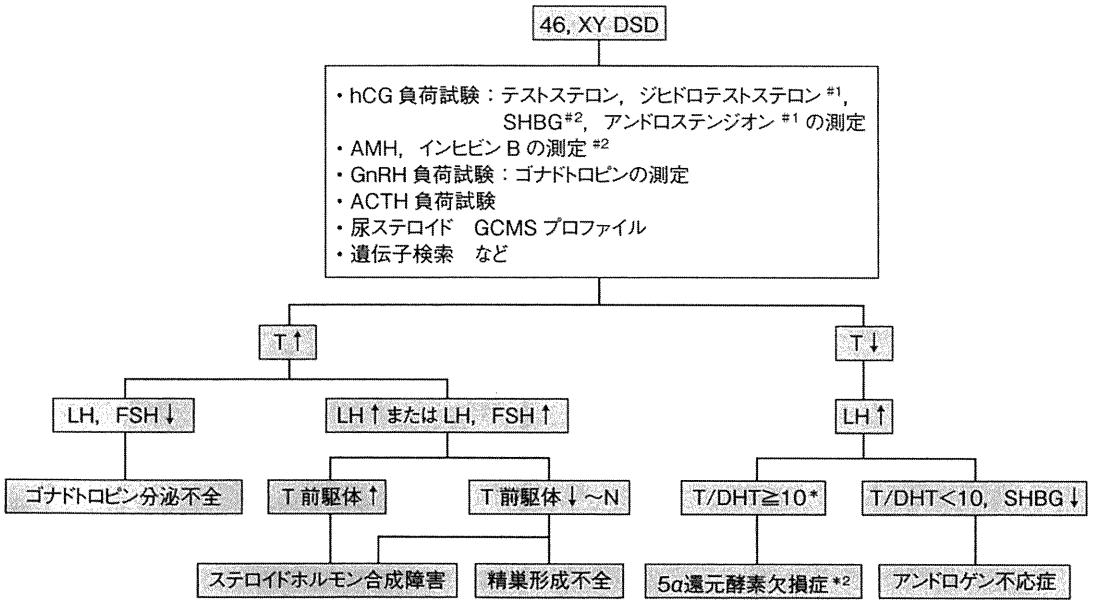

図 2　46,XY 性分化疾患の診断のアルゴリズム

* 基準値はないので参考値。年齢によって測定系の問題（胎児副腎産物との交差）があるので注意を要する。

*2 生化学的には早期診断が困難であるので，確定診断には遺伝子診断が必要である。

#1 保険未収載だが鑑別のために測定が望ましい。

#2 保険適用となっておらず，測定可能施設も限られるため，必須の検査ではない。

46,XY-5α還元酵素欠損はまれな疾患で，外性器の男性化が不完全で，女性型に近い場合が多い。胎児期に高濃度のテストステロンに曝露されており，脳の性分化は男性に傾いている。最近，女性として成育した本症の多くが男性に性転換しているとの報告が散見されており，外性器の形状だけでは性判定が困難な疾患である。

日本小児内分泌学会性分化委員会（委員長：大

山建司）が作成した性分化疾患診断の手順を図1，2に示す。新生児期においては，戸籍上の性の決定が最も緊急な課題であり，そのための検査を優先する必要がある。性分化疾患を疑い，先天性副腎過形成症が否定された場合は，経験豊富な施設と緊密に連携して，検査，診断，治療方針の決定，性判定を行うべきである。

II 保護者への初期対応

出生直後の説明は，親に強い印象を残すため言葉を選んで，ていねいにくり返し行う必要がある。また，説明内容を統一するため，説明者を決めておいたほうがよい。出生時，親や家族の関心は，5体満足か，男か女か，にほぼ限定されている。本来祝い事であるはずの出生の瞬間に，「男の子か女の子かわからない」，「外陰部に異常がある」などと言われると，親はそれだけで動転してしまう。「わからない」，「異常」，「不完全」という言葉は使うべきではないと考えている。性別がわからないと言うと，子ども自体が男でも女でもない，ととられる可能性がある。説明は母親だけにするのは避け，両親に，または祖父母を加えた場で行う。以下は初期対応の説明の1例である。

「外性器の成熟が遅れていて，性分化疾患が疑われます。性分化疾患とは，卵巣・精巣や性器の発育が非典型的となる疾患です。外性器からは性別を正確に判断できないので検査をしましょう」。

最初の段階で担当医は，印象を受けた性を安易に告げることは避けねばならない。最終的に，性を変更するようなことになると，親を混乱させるだけでなく，周囲への影響もあり，問題を複雑化してしまう。

児の問題点が性分化に関わることだけであれば，ほかの機能は健常であることを積極的に伝え，祖父母にも児の状態を説明して理解を求め，両親を支援するように促す。家族内で責任論が起きないように注意し，とくに精神的に不安定な状態にある母親への配慮，支援が大切である。そのためには，医師以外に病態をよく理解している心理療法士，助産師などの協力も必要となる。

今後の見通しについても説明する必要がある。検査には1週間以上かかること，2週間以内に結果が出せるように努力すること，出生届は急いで出す必要がないこと，2週間では結論が出なくても性・名前は保留できること，医療保険も性・名前保留で提出可能なこと，を説明する。

説明は出生時だけではなくくり返し行い，性分化疾患への理解を深めるように努め，心理カウンセリングの介入も早期から始める。

以上が出生7日目までの初期対応の概略である。経験の少ない医師が性分化疾患に遭遇したとき，すべて一人で対応しようと考えるのではなく，必ず経験豊富な小児内分泌または小児泌尿器の医師に相談すべきである。性分化疾患は同一の疾患であっても症状，検査所見はさまざまであり，診断名から性別を判断することはできない疾患である。長期にわたるフォローが必要であり，安易な対応は厳に慎まなければならない。

Key Points

❶出生時，外性器の形状を詳しく観察する習慣をつける。
❷外性器異常を疑ったときは，必ず経験豊富な医師に相談する。
❸親への初期対応，とくに言葉使いは慎重を要する。
❹先天性副腎過形成症以外の性分化疾患では，経験豊富な施設への転送をためらわない。

文　献

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Acquired Undescended Testes in Boys With Hypospadias

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Abbreviations and Acronyms

CGRP = calcitonin gene-related peptide

GFN = genitofemoral nerve

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Purpose: We determined the incidence of acquired undescended testes in boys with hypospadias.

Materials and Methods: We retrospectively reviewed the records of 566 boys with hypospadias who were referred to our outpatient clinic between January 2000 and September 2009. Acquired undescended testes were defined as testes that were documented at the bottom of the scrotum at least once after birth by the pediatric urologist at our institution but were subsequently documented to have moved from a satisfactory scrotal position by the same pediatric urologist or an equally experienced pediatric urologist. However, this definition did not include undescended testes after inguinoscrotal surgery. We excluded boys with gender development disorders with testicular dysgenesis, those who underwent bilateral inguinoscrotal surgery and those without congenital cryptorchidism who were followed less than 3 months.

Results: Of the 566 boys with hypospadias 100 met study exclusion criteria. Of the 466 boys included in analysis 29 (6.2%) had congenital cryptorchidism and 15 (3.2%) had acquired undescended testes. Urethroplasty was performed in 413 boys, including 91 with distal, 132 with mid and 181 with proximal hypospadias. The incidence of congenital cryptorchidism and acquired undescended testes in boys with proximal hypospadias was significantly higher than that in boys with other types of hypospadias ($p = 0.03$ and 0.001, respectively).

Conclusions: Boys with proximal hypospadias are at a higher risk for acquired undescended testes than those with other mild types of hypospadias. Thus, testicular location should be monitored regularly until after puberty.

Key Words: testis, cryptorchidism, hypospadias, abnormalities

In clinical practice acquired undescended testis is occasionally observed in boys with hypospadias. The pathological factors of hypospadias may include disruption of androgen and the androgen regulated inguinoscrotal phase of testicular descent.[1–3] Theories on the mechanism of testicular ascent remain controversial. Tasian et al reported that proximal hypospadias is associated with acquired undescended testes.[4] However, it is unclear whether distal and middle hypospadias carry a similar risk. We present what is to our knowledge the first study to determine the incidence of acquired undescended testes according to hypospadias severity.

MATERIALS AND METHODS

We retrospectively reviewed the medical records of 566 boys with hypospadias who were referred to our outpatient clinic between January 2000 and September 2009. We excluded 100 boys from study, including 18 with gender development disorders

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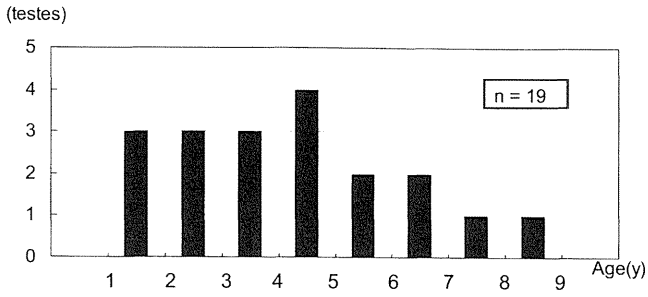
with testicular dysgenesis, eg mixed gonadal dysgenesis and true hermaphroditism, 24 who underwent bilateral inguinoscrotal surgery and 58 without congenital cryptorchidism who were followed less than 3 months. A total of 466 boys were included in the analysis.

We defined the distal type as glanular, coronal and subcoronal hypospadias, the mid type as distal penile, mid shaft and proximal penile hypospadias, and the proximal type as penoscrotal and more proximal hypospadias. We ascertained testicular position, age at the diagnosis of acquired undescended testes and orchiopexy findings. An acquired undescended testis was defined as a testis that was documented to be at the bottom of the scrotum at least once after birth by the pediatric urologist at our institution but was subsequently documented to have moved from a satisfactory scrotal position by the same pediatric urologist or an equally experienced pediatric urologist. However, this definition did not include undescended testes after inguinoscrotal surgery. Followup was considered complete if bilateral orchiopexy or inguinoscrotal surgery was performed. Statistical analysis was performed using the chi-square test with $p < 0.05$ considered significant.

RESULTS

A total of 466 boys were included in this study. Mean age at the initial visit was 1.1 year (range 0 to 12.8) and mean followup was 42.4 months (range 3 to 123). Of the 466 boys 29 (6.2%) had congenital cryptorchidism and 15 (3.2%) had acquired undescended testes. Primary urethroplasty was done at our institution in 413 boys, including 181 with proximal, 132 with mid and 91 with distal hypospadias. Another 26 boys underwent primary urethroplasty elsewhere and 27 did not undergo urethroplasty. Of the 181 boys with proximal hypospadias 15 (8.3%) had congenital cryptorchidism and 12 (6.6%) had acquired undescended testes. Six of the 132 boys (4.5%) with mid hypospadias had congenital cryptorchidism and 2 (1.5%) had acquired undescended testes. Two of the 91 boys (2.2%) with distal hypospadias had congenital cryptorchidism and none had acquired undescended testes. The incidence of congenital cryptorchidism and acquired undescended testes in boys with proximal hypospadias was significantly higher than in boys with other types of hypospadias ($p = 0.03$ and 0.001, respectively). In 15 boys (19 acquired undescended testes) mean age at diagnosis was 4.3 years (range 1.3 to 8.5 years) (see figure). We performed a total of 17 orchiopexies in 13 boys with acquired undescended testes. Of the testes 12 (70.6%) were at an extracanalicular site, 3 (17.6%) were in the superficial inguinal pouch, 2 (11.8%) were intracanalicular and none was intra-abdominal.



Patient age at diagnosis of acquired undescended testes

DISCUSSION

In 1966 Vellumsen and Zachau-Christiansen reported that 69 of 4,300 boys (2%) showed unilateral or bilateral ascent of the testes from the normal scrotal position at birth by age 3 years.[5] Since then, many reports have described acquired undescended testes. Retrospective analysis of the scrotal position of testes reported by other physicians is common but the accuracy of previous examinations cannot be confirmed. Some reports may have included patients in whom a retractile testis was misdiagnosed as an acquired undescended testis. Discrepancies in the incidence of acquired undescended testes have been noted in different reports and, thus, its true incidence remains controversial. In reports of patients who were followed for a long period and in whom the previous testicular position was substantially documented boys with apparent testicular ascent represented 2% to 20% of all who underwent orchiopexy.[6–8] Conversely the orchiopexy rate is as high as 2% to 3% in all males up to ages 14 to 17 years despite an expected childhood prevalence of congenital cryptorchidism of approximately 1%.[9–14] Thus, the generalized incidence of acquired undescended testes is estimated to be 0.04% to 0.6%.

Our results show that the incidence of congenital cryptorchidism and acquired undescended testes in boys with hypospadias was 6.2% and 3.2%, and the incidence of these types of testicular maldescent in patients with proximal defects was 8.3% and 6.6%, respectively. These conditions were predominantly observed in boys with proximal defects ($p = 0.03$ and 0.001, respectively) while the incidence of congenital cryptorchidism was 2.2%. To our knowledge acquired undescended testes have not been reported in boys with distal defects.

It was previously reported that congenital cryptorchidism is predominant in boys with proximal hypospadias.[15] We observed that acquired undescended testes was also predominant in such boys. Tasian et al reported that proximal hypospadias is associated with acquired undescended testes[4] but it is unclear whether distal and mid hypospadias carry a similar risk. To our knowledge we report

the first study showing that the risk of acquired undescended testes increases directly with hypospadias severity.

Ethnic characteristics may be a reason why the incidence of acquired undescended testes was higher in the study by Tasian et al[4] than in our series. Of their study patients 48.7% were white and 15% were Asian. However, all patients in our study were Japanese, ie Asian. The overall incidence of distal, mid and proximal hypospadias in white boys is approximately 50%, 30% and 20%, respectively.[16] On the other hand, proximal hypospadias is predominant in Japanese boys. In our study the overall incidence of distal, mid and proximal hypospadias was 22%, 32% and 44%, respectively. Thus, similar to the difference in the incidence of proximal hypospadias in the 2 races, there is a difference in the incidence of acquired undescended testes.

Barthold and Gonzalez reported data[17] from reviews of patients with substantial documentation of acquired undescended testes.[6,8,18–23] Mean age at diagnosis was 6.6 to 8.1 years and the most common testicular site identified at orchiopexy was distal to the inguinal ring. In our series mean age at diagnosis in boys with hypospadias was 4.3 years, which is lower than that in the unselected acquired undescended testes series reviewed by Barthold and Gonzalez.[17] We observed the same testicular site, identified at orchiopexy, as that reported by Barthold and Gonzalez. Since details on the processus vaginalis and gubernaculum, and testicular pathology were unavailable, we could not analyze these parameters.

Theories on the mechanism of testicular ascent remain controversial but some mechanisms have been proposed to explain this phenomenon. A theory is that a fibrous remnant of the processus vaginalis remains tethered to the testis and peritoneum, and can pull the testis up into the inguinal canal during growth.[20,22] Cremaster muscle spasticity is a possible cause of acquired undescended testes, eg in patients with cerebral palsy, but the proposed etiology of this spasticity in otherwise normal boys is unclear.[24] In this study neither cerebral palsy nor myopathy was observed in the 15 boys with acquired undescended testes. The GFN may have a role in testicular ascent. Hutson and Hasthorpe proposed that the GFN acts as a second messenger for androgen by releasing CGRP to control descent.[3] Shono et al reported that the proximal division of the GFN in neonatal rats causes inguinoscrotal testicular maldescent and may also induce testicular ascent in adulthood.[25] They proposed that testicular ascent may be caused by some intrauterine disorders of the GFN.

To our knowledge a relationship between acquired undescended testes and hypospadias has not yet been reported. It is not clear why boys with hypospadias are at high risk for acquired undescended testes. Nazir et al reported that compared with the normal prepuce the hypospadiac prepuce is hypo-innervated for CGRP positive nerves.[26] Androgen disruption caused by hypo-innervation of CGRP positive nerves may be responsible for the high incidence of acquired undescended testes in boys with hypospadias.

Previous studies of acquired undescended testes indicate that these testes show germ cell maldevelopment, similar to that in age matched patients with congenital cryptorchidism.[8,21,24] Orchiopexy is commonly recommended for acquired undescended testes.[27] At our institution orchiopexy is done soon after the diagnosis of acquired undescended testes. Conversely Sijstermans et al reported that acquired undescended testes have a high tendency of spontaneous descent during early and mid puberty, and orchiopexy may be recommended during mid or late puberty in cases of nondescent.[28] Thus, more comprehensive data on the natural course of acquired undescended testes and on testicular growth after orchiopexy are urgently required.

The limitations of this study are similar to those of other retrospective reviews. Followup was short. Longer followup may allow the detection of acquired undescended testes at an older age. Also, approximately 70% of acquired undescended testes cases were diagnosed within the first 5 years in this study. However, Guven and Kogan reported the diagnosis of acquired undescended testes in 14-year-old boys.[29] This pattern indicates that the testicular site in boys with proximal hypospadias should be monitored regularly until after puberty.

CONCLUSIONS

To our knowledge we report the first study to determine the incidence of acquired undescended testes according to hypospadias severity. Since a high incidence (6.6%) of acquired undescended testes was observed in boys with proximal hypospadias only, there may be a strong association between acquired undescended testes and proximal hypospadias. Thus, testicular location should be monitored regularly until after puberty in boys with proximal hypospadias.

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Original Article: Clinical Investigation

Long-term outcome of ovotesticular disorder of sex development: A single center experience

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Objectives: To describe the clinical features of children with ovotesticular disorder of sex development (DSD) and to review cases of ovotesticular DSD in Japan.

Methods: Medical records of eight children diagnosed with ovotesticular DSD at our institute during the past 17 years were retrospectively evaluated. A review of 165 reported cases of ovotesticular DSD from Japanese institutions was carried out.

Results: Mean follow up was 8.2 years for six children, with two children lost to follow up. Mean age at first presentation was 2.4 months. All children were Japanese. The most common initial manifestation was ambiguous genitalia. The female-: male ratio as the sex of rearing was 1:1. Gender reassignment, from male to female, was carried out in one child at 4-months-old. Genital surgery was always carried out in early childhood as per family desire. Appropriate gonadal tissue was preserved except for one child. No gonadal tumors were detected during follow up. Spontaneous pubertal development occurred in one boy. In reviewing Japanese data, the frequency of testes was higher than in other ethnicities and this was related to the higher incidence of 46,XY.

Conclusions: According to our experience, most families in Japan desire early genital surgery in the case of ovotesticular DSD. Chromosomal and gonadal distributions in patients with ovotesticular DSD differ between Japanese and other ethnic groups. Treatment for these patients needs to be provided after considering the cultural and social backgrounds of DSD in Japan.

Key words: follow-up studies, gonads, sex differentiation disorders, treatment outcome, true hermaphroditism.

Introduction

A consensus statement on the management of intersex disorders was published in 2006.[1] The term "true hermaphrodite" has been replaced by ovotesticular disorder of sex development (DSD), defined as the presence in the same individual of ovarian tissue containing ovarian follicles and testicular tissue containing seminiferous tubules.[2] The incidence and constituting karyotype in patients with ovotesticular DSD reportedly show geographic variations.[3] Cultural and social differences in dealing with DSD influence gender assignment and consecutive management.[4] However, there is a paucity of data regarding clinical features, gender assignment and treatment outcomes in children with ovotesticular DSD in Japan.[5] We present herein the clinical, anatomical, histological, cytogenetic and hormonal findings of ovotesticular DSD and assessed gender assignment and treatments for children with ovotesticular DSD treated at our single center. We also reviewed the 165 cases of ovotesticular DSD reported in Japan to date.

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Methods

Eight children at our hospital were diagnosed with ovotesticular DSD between 1991 and 2008. Ovotesticular DSD was defined by histological findings of the gonads. We retrospectively assessed clinical, anatomical, histological, cytogenetic and hormonal data, gender assignment and treatment in these eight children.

Clinical examination included the degree of virilization of the external genitalia according to Prader's classification,[6] and palpation of the gonads in inguinal and labioscrotal areas. Associated malformations were recorded.

Anatomical examination included the position of the gonads, the presence of Müllerian and Wolffian derivatives, and the presence of a urogenital sinus. These findings were ascertained by endoscopy and laparotomy or laparoscopy in all children.

Gonadal tissue was assessed by careful examination and on biopsy sections or resected gonads that were discordant

with the sex of rearing. Tissue specimens were fixed in formalin and embedded in paraffin wax. Paraffin blocks were sectioned and stained using hematoxylin and eosin. Histological evaluation was carried out by one pathologist (MN).

Cytogenetic analysis of karyotype was carried out using peripheral blood in all children. The sex-determining region of the Y chromosome (SRY) gene was studied by fluorescence *in situ* hybridization in all children.

Before surgery, Leydig cell function was evaluated by measuring plasma testosterone (T) concentration before and on days 4 and 5 after stimulation with human chorionic gonadotropin (hCG) at 3000 units/m^2/day given on three consecutive days in all children. Mean age at hCG stimulation was 9.4 months (range 2–27 months). A maximum T concentration after stimulation of >200 ng/dL was defined as a normal response to hCG. Maximum T concentration after stimulation of 100–200 ng/dL was defined as a borderline response to hCG. A maximum T concentration after stimulation of <100 ng/dL was defined as a poor response to hCG with the modification previously reported.[7] After resection of the testicular portion of the ovotestis in children raised as females, the hCG stimulation test was carried out to ensure that no testicular remnant was left.[8]

When we treated children with DSD, we promptly held a meeting of the in-hospital gender assignment committee, which comprises pediatric urologists, endocrinologists, neonatologists and a clinical geneticist. We considered many factors that influence gender assignment, including diagnosis, genital appearance, surgical options, need for lifelong replacement therapy, potential for fertility and social factors. After the meeting, we talked with the patient's family several times and then proposed the gender considered most appropriate for the child with DSD.

Gonadal tissue and duct structures inappropriate to the sex of rearing were removed after histological confirmation and gender assignment. When the gonad was an ovotestis, the appropriate portion was preserved wherever possible (Fig. 1). For children raised as females, clitoroplasty and vaginoplasty were carried out as needed. Clitoroplasty was carried out using Schmid's technique based on the preservation of the neurovascular bundle.[9] For children raised as males, urethroplasty, scrotoplasty and uterocolpectomy were carried out when needed. Penile reconstruction was carried out in a 1-stage operation using a preputial pedicled flap or free skin graft or 2-stage operation. Resection of the vagina was carried out with the preservation of at least one vas deferens for the possibility of spontaneous male fertility. Gonadal surveillance ultrasonography for tumor development was carried out annually.

Pubertal development was evaluated by pediatric endocrinologists. At puberty, hormonal replacement was instituted in cases of androgen or estrogen deficiency.

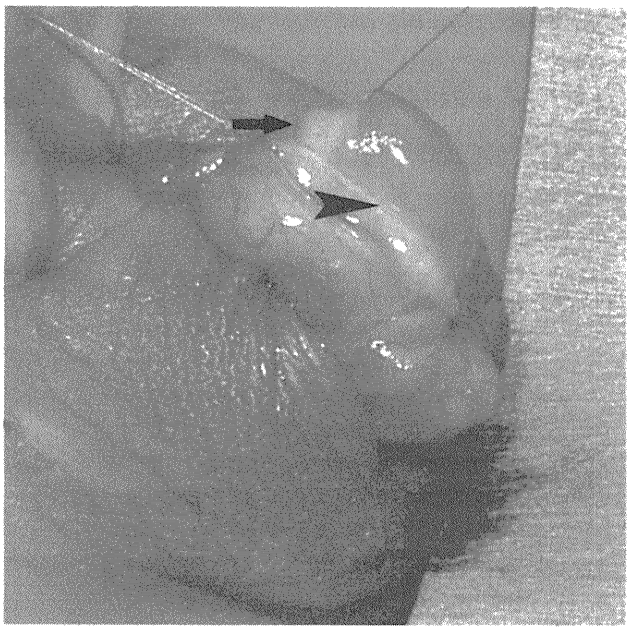

Fig. 1 Macroscopic findings of ovotestis. Ovarian portion (arrow) is firm and yellow in an upper pole, whereas testicular portion (arrowhead) is soft and pink in a lower pole. There is a distinct line of demarcation between the two portions.

We reviewed 165 cases of ovotesticular DSD reported in Japan. Relevant published studies were identified in a database search of PubMed (1966 to January 2010) for articles written in English, and of J Dream II (1981 to January 2010) for articles written in Japanese and references from selected citations.

Data were analyzed using Statistical Package for the Social Sciences statistical software version 14.0 (SPSS, Chicago, IL, USA). Associations between variables were examined using χ^2-test and Mann–Whitney *U*-test. Values of $P < 0.05$ were considered statistically significant.

Results

Clinical, anatomical, histological and cytogenic data

Clinical, anatomical and cytogenic data are shown in Table 1. The mean age at first presentation was 2.4 months (range birth–13 months). Six of the eight children (75%) presented within 1 month. All children were Japanese. All cases were sporadic, with no family history of sexual ambiguity. Initial manifestations were as follows: ambiguous genitalia in four cases (patients 1, 4, 5, 6); isolated clitoromegaly in two cases (patients 3, 8); perineal hypospadias in one case (patient 2); and identification during surgery for cryptorchidism in one case (patient 7). The diagnosis of ovotesticular DSD was made within a month after referral in all except patient 2. Initial manifestation in patient 2 was perineal hypospadias, and bilateral gonads were located in

Table 1 Clinical, anatomical, histological and cytogenetic data for eight children with ovotesticular disorder of sex development

Patient	Age at first evaluation	Karyotype	External genitalia		Urogenital sinus	Prader grade	Vagina	Uterus	Right gonad	Right duct	Left gonad	Left duct	Postoperative gonadal status R/L	Sex of rearing	Age in years
			Right gonad	Left gonad											
1	Newborn	46,XX	NP	Inguinal	–	II	+	+	Streak	Tube	Ovot	Vas	–/–	Female	16
2	Newborn	46,XX	Labioscrotal	Labioscrotal	+	IV	+	Hypo	Ovot	Vas	Ovot	Vas	Testis/testis	Male	13
3	3 weeks	46,XX	NP	Inguinal	–	II	+	+	Ovary	Tube	Ovot	Tube	Ovary/ovary	Female	Lost
4	Newborn	46,XX	Labioscrotal	NP	+	IV	+	+	Ovot	Tube	Ovary	Tube	Ovary/ovary	Male→female	11
5	1 month	46,XX	Labioscrotal	Labioscrotal	+	IV	+	–	Ovot	Vas	Ovot	Vas	Testis/testis	Male	Lost
6	Newborn	46,XY	Labioscrotal	Labioscrotal	+	IV	+	+	Testis	Vas	Ovot	Vas	Testis/testis	Male	3
7	13 months	46,XX/46,XY	Labioscrotal	Inguinal	+	V	+	+	Testis	Vas	Ovot	Vas + tube	Testis/–	Male	3
8	4 months	46,XX	NP	NP	–	II	+	+	Ovot	Tube	Ovot	Tube	Ovary/ovary	Female	3

Hypo, hypoplastic; NP, non-palpable; Ovot, ovotestis; Tube, fallopian tube; Vas, vas deferens.

the scrotum, with a testis-like consistency. The diagnosis of ovotesticular DSD was made 7 years later, after referral when he underwent orchiopexy for ascending testes to an inguinal lesion and the gonads revealed ovotestis. According to Prader's classification, four children were classed as stage IV, three as stage II, and one as stage V. Palpation of labioscrotal and inguinal areas revealed the presence of at least one gonad in seven children. No gonad was palpable in the remaining child. No child showed associated somatic malformations.

A vagina was detected in all children and seven children had a uterus. Gonadal distribution was as follows: bilateral ovotestis in three children (37.5%); ovary plus ovotestis in two children (25%); testis plus ovotestis in two children (25%) and ovotestis plus streak gonad in one child (12.5%). The most frequently seen gonads were ovotestis (68.8%). Ovotestes were generally located on the left side (right, $n = 4$; left, $n = 7$). The adjacent duct was a vas deferens in six gonads, a fallopian tube in four gonads and both vas deferens and fallopian tube in one gonad. Ovaries were located on both sides equally and all adjacent ducts were fallopian tubes. All testes were located on the right side and the adjacent duct was vas deferens. Of the 11 gonads palpated, nine gonads were ovotestis and two were testis. The five gonads not palpated comprised two ovotestis, two ovaries and one streak gonad. All testes were located in the labioscrotal area, while all ovaries were located intra-abdominally.

Histological examination showed all ovarian tissues were normal with primordial follicles and ovarian stroma. Seminiferous tubules were found in all and spermatogonia were found in 11 of the 13 testicular tissues (84.6%). However, only a very small number of spermatogonia was seen in a seminiferous tubule. In some tissues, the density of seminiferous tubules was decreased and interstitial tissue was increased. Increased interstitial tissue was found in descended testicular tissue as well as in undescended testicular tissue. Sertoli cells were found in all cases and Leydig cells were present in three cases (23.1%). No gonadal tumors were found in all gonads.

The most common karyotype was 46,XX (75%). The other karyotypes were 46,XY (12.5%) and 46,XX/XY (12.5%). All six children with 46,XX showed negative results for the SRY gene. A 46,XY child and a 46,XX/XY child had the SRY gene.

Hormonal data

Hormonal data are shown in Table 2. In the three children younger than 6 months, mean basal T concentration was 118.6 ng/dL (range 85–186 ng/dL). For five children aged 6 months and older, mean basal T concentration was 4.8 ng/dL (range 3–8 ng/dL). After hCG stimulation, mean T concentration was 284.2 ng/dL (range 36.5–590 ng/dL).

Table 2 Preoperative testosterone response after human chorionic gonadotropin stimulation for eight children with ovotesticular disorder of sex development

Patient	Plasma testosterone (ng/dL)		
	Basal	After hCG	Response
1	5.0	36.5	Poor
2	8.0	235.0	Normal
3	5.0	188.6	Borderline
4	69.8	508.1	Normal
5	270.0	590.0	Normal
6	98.3	311.1	Normal
7	3.0	283.1	Normal
8	3.0	120.9	Borderline

hCG, human chorionic gonadotrophin.

Five children showed normal response to hCG, two showed borderline response and one showed poor response. No differences were seen in response with or without a Y chromosome (with, 311.6 ng/dL; without, 238.4 ng/dL, not significantly different). Three children raised as females who underwent resection of the testicular portion of ovotestis showed no postoperative testosterone response, with the exception of one female child who underwent a bilateral gonadectomy.

Gender assignment and treatment

Four children (50%) were being raised as girls and four (50%) as boys. Gender reassignment, from male to female, was carried out in one child (patient 4) at 4-months-old, because the child had a capacious vagina, a normal appearing uterus and a unilateral ovary. Six children were followed from 3 to 16 years (mean 8.2 years). Two children were lost to follow up.

Among the four children being raised as girls, three children had a preserved ovary or ovarian portion of the ovotestis. One child (patient 1) underwent a bilateral gonadectomy, as one gonad was a streak gonad and the other ovotestis had no distinct demarcation between ovarian and testicular tissue. All children underwent clitroplasty. One child who had a urogenital sinus underwent vaginoplasty using a perineal skin flap. Mean age at feminizing genitoplasty in combination with partial or total gonadectomy was 15.5 months (range 5–36 months). Among the four children being raised as boys, all children had a preserved testis or testicular portion of the ovotestis. Three children underwent urethroplasty and scrotoplasty. Three children underwent uterocolpectomy. The mean age at partial gonadectomy was 39.3 months (range 12–90 months). Mean ages at urethroplasty and uterocolpectomy were 24 months (range 11–37 months) and 18 months (range 5–31 months), respectively. No gonadal tumors were detected on follow up in all children.

Table 3 Gonadal combination of 165 patients with ovotesticular disorder of sex development published in the literature in Japan

Gonadal distribution	*n*	%
Ovot – Ovary	56	33.9%
Ovary – testis	40	24.2%
Ovot – ovot	34	20.6%
Ovot – testis	27	16.4%
Ovot – streak	2	1.2%
Others	6	3.6%
Total	165	100.0%

Ovot, ovotestis.

Pubertal development could be assessed in two patients who reached pubertal age. Hormonal replacement was initiated in one girl at 13 years-of-age, as she had undergone a bilateral gonadectomy. She showed breast development at 13 years-of-age and menses at 14 years-of-age. One boy began spontaneous pubertal development at 13 years-of-age, with basal T concentration rising to 202.9 ng/dL. No cases of pregnancy or paternity were encountered.

Chromosomal and gonadal distribution, and gender assignment of ovotesticular DSD published in the literature in Japan

Chromosomal analysis was carried out using peripheral blood, gonad or skin fibroblast in 125 cases. A karyotype of 46,XX was the most frequent finding (61.6%), followed by chromosomal mosaicism containing a Y chromosome (24.8%), whereas 46,XY occurred in 12.8% of cases (Fig. 2). The 324 described gonads of 165 cases were distributed as shown in Figure 3. The most common gonad was ovotestis (49.1%), followed by ovary (29.6%) and testis (20.7%). The gonadal combination of ovotestis plus ovary was most common, followed by ovary plus testis, and bilateral ovotestis (Table 3). Patients with a Y chromosome more often had a testis than patients without a Y chromosome (58.3% *vs* 24.7%; $P = 0.0002$). In 142 patients, the sex of rearing was presented. A total of 86 patients (60.6%) were reared as male and 56 (39.4%) as female.

Discussion

Most children with ovotesticular DSD have presented with ambiguous genitalia as neonates or infants. Rarely, ovotesticular DSD is detected later in individuals with normal

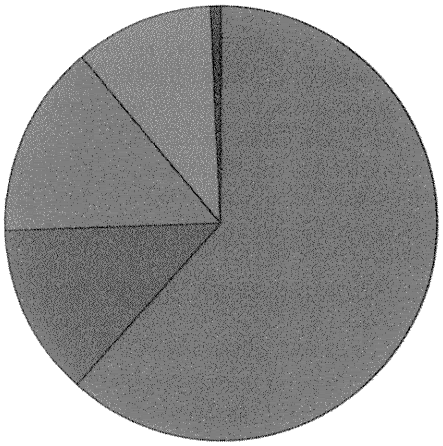

Fig. 2 Chromosomal distribution of 125 patients with ovotesticular DSD published in the literature in Japan. ■, 46,XX (77 patients, 61.6%); ■, 46,XY (16 patients, 12.8%); ■, 46,XX/XY (18 patients, 14.4%); ■, other mosaicism (13 patients, 10.4%); ■, other (1 patient, 0.8%).

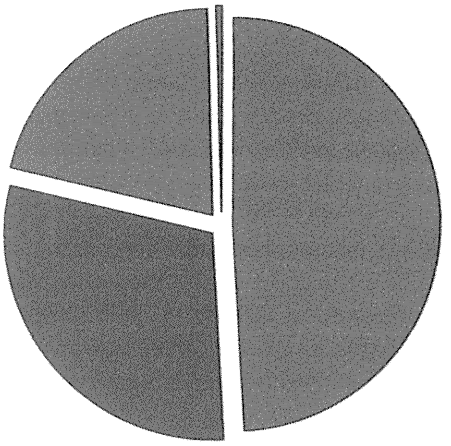

Fig. 3 Gonadal distribution of 324 gonads of a total of 165 patients with ovotesticular DSD published in the literature in Japan. ■, ovotestis (159 gonads, 49.1%); ■, ovary (96 gonads, 29.6%); ■, testis (67 gonads, 20.7%); ■, streak (2 gonads, 0.6%).

female or male phenotype.[10] Actually, in the present study, external genitalia ranged from phenotypically nearly female to normal male.

The most common karyotype was 46,XX, constituting 61.6% of patients in the present study and reviewed cases from Japan. This finding was consistent with the published literature from other countries.[2,3,11] A large review of ovotesticular DSD has shown geographic variations.[3] In the largest review, the 46,XX karyotype was reported as being particularly frequent in South and Western Africa, whereas chromosomal mosaicism containing the Y chromosome is relatively common in Europe and North America, and 46,XY is equally distributed over Asia, Europe and North America.[3] In contrast, the present review showed that the incidence of 46,XY was higher in Japanese than in other ethnicities reported in the literature (12.8% *vs* 7.0%, respectively). The incidence of chromosomal mosaicism in Japan (24.8%) was less than in Europe (40.5%), but was equal to that in North America (21.1%).[3]

Frequency of the SRY gene in children with 46,XX ovotesticular DSD varies in the literature from 0 to 100%.[12,13] The present study showed that no children with 46,XX ovotesticular DSD had the SRY gene in peripheral lymphocytes. Only a few reports from Japan showed the SRY gene in ovotestis in children with 46,XX ovotesticular DSD.[14] In contrast, a study by Ortenberg *et al.* showed the SRY gene in all ovotestes, suggesting that somatic mosaicism might be a cause of 46,XX ovotesticular DSD. However, the exact mechanisms leading to testicular development in SRY-negative ovotesticular DSD remain unclear.

In our review of data from Japan, the most common gonad was ovotestis, followed by ovary and testis as has already been described in other ethnicities.[3,11] However, the frequency of testis was higher in Japan than in other ethnicities (20.7% *vs* 12.5%, respectively).[3] This difference might be explained by the high incidence of the Y chromosome in Japan.

Spermatogonia were found in the present study (84.6%) more than in previous reports (0–67%).[2,3,15,16] This is possibly because most of the children in the present study underwent biopsy before 3 years-of-age. According to previous reports, testicular tissue becomes dysgenetic and germ cells disappear with age.[15,17] The density of seminiferous tubules and interstitial tissue varied quite widely in the present study. This finding was unrelated to the position of testicular tissue or the timing of the operation. Ovarian tissues were normal, with the presence of numerous follicles, as previously reported.[2,3]

Few published data are available for Leydig cell function in children with ovotesticular DSD.[16,17] More than 60% of children showed a normal T response to hCG stimulation in infancy. Response to hCG stimulation did not correlate with the presence of a Y chromosome. However, this finding must be considered in light of the fact that the present study investigated a small series of children with ovotesticular DSD.

The female : male ratio as the sex of rearing was 1:1 in the present study, similar to findings from a previous review.[3,11] Surgery is generally necessary after gender assignment. This includes removal of gonads and internal ducts inappropriate to the sex of rearing, and genitoplasty to construct the appropriate external appearance. However, the timing of surgery remains contentious.[1] Some advocate early surgery to reduce psychological trauma and facilitate acceptance in children and parents.[18,19] Conversely, some patient groups, such as the Intersex Society of North America, advocate deferring the irreversible genital surgery until children are mature enough to make the decision for themselves. According to our 20-year experience in Japan, despite informing

families of all treatment options available, they have often desired early gonadal surgery and genitoplasty. We believe early operations improve the attachment between a child and parents, and benefit the development of gender identity in childhood. Kuhnle and Krahl[4] identified cultural differences as an important factor in dealing with DSD patients. As a result, we carried out gonadal surgery and genitoplasty in early childhood, preserving gonads appropriate to the sex of rearing in 87.5% of children to allow normal pubertal development. On 8.2-year mean follow up, none of these children had gender identity disorder or gender dysphoria.

The frequency of gonadal tumors in patients with ovotesticular DSD has been reported as 2.6–4.6%.[2,3] In the present study, no patients showed gonadal tumors on follow up. Patients with 46,XY and 46,XX/XY ovotesticular DSD tend to develop gonadal tumors more frequently than those with 46,XX ovotesticular DSD.[20] Tumors have been described in both ovarian and testicular portions. The incidence of gonadal tumors increases with age in DSD patients with the Y chromosome.[21] Whether descent of the testis into the scrotum, removal of inappropriate gonads or early surgery influence the occurrence of tumors is unclear.

Some limitations of the present study must be acknowledged. The study involved a small series of patients with ovotesticular DSD and most patients were too young for assessment of sexual and gonadal function. Also, there are no outcome data about gender identity and quality of life in the form of standardized questionnaires. Further studies on long-term follow up are needed to evaluate gender identity, quality of life and sexual function in children with ovotesticular DSD.

We evaluated clinical features, gender assignment and treatment outcomes in children with ovotesticular DSD treated at our institute. According to our experience, most families have desired early gonadal surgery and genitoplasty in Japan. Reviewing data from Japan, chromosomal and gonadal distributions differed between Japanese and other ethnic backgrounds. Consideration of the cultural and social backgrounds of DSD in Japan is needed when providing treatment for children with ovotesticular DSD.

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胎生期性ホルモンの空間認知能への影響を粘土の造形表現からみた検討

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1. 目的

これまで，胎生期の性ホルモン環境が脳機能や行動の性差に影響することは，ヒトにおいても確認されている。先天性副腎過形成症（ＣＡＨ）の女児は活発で，乗り物やブロック遊びなど男児が好むとされている物や遊びに興味関心がある[1,2),3)]。Iijimaらは，ＣＡＨ女児の自由画の表現にも男児特有の特徴がみられると報告している[4)]。その特徴とは，描くモチーフが自動車などであること，スピード感のある描写表現がみられること，色使いも寒色系が中心であること，が挙げられている[3)]。ＣＡＨ女児の描画表現では，一般的な男児の特徴と重なったが，空間認知脳を反映すると考えられる立体的な造形表現では，どのような傾向がみられるのか把握したいと考えた。

そこで，立体的造形作品の素材として，可塑性があり完成した作品を保存することが可能である紙粘土の造形表現について，一般幼児を対象に調査を行った。その結果，モチーフは描画表現の性ごとの特徴に類似しており，男児はダイナミックで，少ない作品数をつくり，女児は細かく小さな作品を複数作る，粘土ベラを用いて細かな表現技法をするなどの表現が認められたことをすでに報告した[5,6)]。

今回，いくつかの性分化疾患（ＤＳＤ）の粘土表現の特徴について，作品のモチーフ，作品個数，表現技法について検討した。

２．対象および方法

（１）　対象

ＣＡＨ（２１水酸化酵素欠損）の女児３例（４歳２例，３歳１例），Ｐ４５０オキシドレダクターゼ（ＰＯＲ）欠損症の女児１例（７歳），卵精巣性ＤＳＤの女児１例（６歳）の計５例を対象とした。いずれの患児も生後より女児として養育されている。

（２）　手続き

紙粘土と粘土板，粘土ベラ，マッチを渡し，好きなものを作るよう指示した。道具などの使用の有無は自由とし，制作に関して助言や援助などは一切行わない。制作後，何を作ったか質問し，記録した。

（３）　材料

紙粘土，粘土板，粘土ベラ，赤い軸のマッチを材料として，それぞれに渡した。

（4）　調査時間

特に時間を設けず，本人が完成，または終了を認めるまでとした。

3．結果

①CAH，女児（4歳）

各作品は，左上から時計まわりに，「ハンバーガー」，「葉っぱ」，「ゴルフクラブとボール」，「顔（2個）」，「バットとボール」，「パトカー」，「わからない」であり，男児が好むモチーフが含まれており（図1），8作品と数が多い。
表現技法では，丸める，くっつける，つなぐ，のばす等，に加え，女児の特徴的な粘土を薄く，細く，模様をつける等が認められた。

②CAH，女児（4歳）

5本のマッチをろうそくに見立てた「私のバースディケーキ」である（図2）。この作品には「女児の丁寧な表現」，「男児の本物への再現性」があると考えられる。一般的な女児は，自分のイメージする小さなケーキを並べ装飾的な表現をするが，これほど細かな表現を持つ作品はない。ケーキを作る男児も多いが表現技法が大きく異なる。しかし，昆虫を作る男児の再現性と，このケーキの再現性には共通性もある。大きくとらえながらも昆虫の特徴をこだわるように，ケーキの人形を作ることで，バースディケーキであることを表している。

③CAH，女児（3歳）

昨品は，左上から時計回りに「トンカチ」，「デッドバロン（ウルトラマン）」，「お皿にお肉」，「わからない」，「お誕生日ケーキ」，の5作品である（図3）。作りたいものの特徴をよく捉えて表現している。「お皿にお肉」では，粘土板の凹凸のある模様を写し取った粘土をお皿にし，その上にお肉の塊を乗せている。「お誕生日ケーキ」では，一般女児と同じように粘土の制作技法がみられ，粘土をまるめて軽くせんべい状にし，マッチ棒をロウソクに見立てている。「ウルトラマン」を作る女児は一般的にほとんどいない。「トンカチ」の道具類も男児が好む傾向がある。

④POR欠損症，女児（7歳）

「スーパーマリオの弟」を制作した（図4）。調査例のなかではもっとも大きく，ダイナミックな印象である。人形（人間）のような作品だが，一般女児の作る「女の子」，「お姫さま」の可愛らしい表現とは異なる。作る際に，粘土の芯材にマッチ棒を使った組み立てをしている。芯材の用い方や体の粘土の付け方，加え方は，粘土あそびの経験が豊富であることや，考えて組み立てながら，粘土やマッチ棒をつないでいることがわかる。粘土のつけ方は男児のように荒々しく，女児は仕上げる際に表面の凹凸を滑らかに整えようとする傾向が多いが，この作品にはそうした形跡はない。

⑤卵精巣性DSD，女児（6歳）

作品は「かごの中にうさぎ」で，完成したものは，図5の左のようにかごの中にうさぎが入った状態である。

女児らしい作品である。「うさぎ」，「かご」は女児が好むモチーフである。「う

さぎ」の耳や手足は，細長く繊細な印象を与えている。胴から手足を作るために粘土を細くひねり出し，ちぎれないよう注意深く形を整えた様子がみられる。別の粘土を細くのばして耳に，目や鼻も別の粘土を丸めてつぶし，あとからつけている。「かご」は平らにのばした粘土をいくつも貼り合せながら，凹みのある器状の形態にし，取っ手はひも状に作ってから側面につけている。モチーフはもちろん，小さな作品の細かい部分まで丁寧につくっていることからも女児的な特徴を持つ作品である。

4．考察

これまでの著者らの一般幼児（369 名）における粘土造形表現の技法の検討においては，一般女児の場合，一人の子どもが制作する作品の数が多く，さらに「丸める」，「つまむ」，「包む」，「輪にする」，および「おせんべいにする」などの，指先を使って細かく表現しようとする技法が多くみられた。一方，男児の場合，作品数が少なく，また，「巻く」，「つなぐ」，「包む」などの細かい技法を用いることなく，シンプルな形態で表現する特徴がみられた。このことは，女児では目の前の物の詳細を表現しようとする傾向があること，男児では俯瞰して物の全体を見てとらえ表現する傾向があると考えられた[5, 6]。

今回の検討でＣＡＨ女児は，男女両方の造形表現を持ち合わせていることが認められた。モチーフの一部に男児の好みとされるものがあったこと，また，表現技法では女児的な指先の巧緻性が高い表現がある一方，大きく形をとらえて表現する，実物と同じ構成にする，といった男児的な表現もあった。

ＰＯＲ欠損症では，女児では出生時に外性器の男性化を認める症例もあるが，ＣＡＨとは異なり出生後は進展しない。今回検討した症例では，粘土の付け方がダイナミックで表面は粗いなど，男性的な表現が認められた。胎児期の脳へのアンドロゲンの作用があったと考えられた。

卵精巣性ＤＳＤでは，粘土表現は，繊細さと大胆さが融合し，男女それぞれの特徴が認められた。本疾患における胎生期の性ホルモン環境は複雑であり，脳の性分化の程度は，脳へのアンドロゲンが作用する量や時期によって多様であると考えられる。

5．結語

空間認知脳を反映すると考えられる粘土の造形表現を介して，性分化疾患にける立体的な造形表現の特徴を把握することを試みた。胎生期に脳へのアンドロゲンの暴露を受けた女児は，一般女児には少ない表現技法である，積む，重ねる等を用いて，形の全体をとらえ立体的に作っていた。

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