Cytogenetic Profile of Patients with Isolated Hypospadias in Semarang

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Abstract

Back ground: Hypospadias is one of the most common anomalies among newborn boys. Most cases of hypospadias occur as an isolated defect. Cytogenetic study in patients with isolated hypospadias has not been conducted in Indonesia.

Purpose: The aim of this study is to ascertain the cytogenetic profile of patients with isolated hypospadias.

Methods: We retrieved a total of 44 medical records of patients with isolated hypospadias who underwent chromosome analysis in Molecular and Cytogenetics Unit of Biotechnology Laboratory, Medical Faculty of Diponegoro University during the period of January 2003 to May 2007.

Results: The age at presentation of a total 44 patients ranging from 47 weeks to 15 years old with a mean 7.10 years. Meatal position was classified as anterior in15.9% of the cases, midpenile in 45.5% and posterior in 38.6%. Karyotype results of all patients were 46, XY. There was no chromosomal abnormality neither structure nor number.

Conclusion: The etiology of isolated hypospadias is still obscure until now. All patients with isolated hypospadias had normal karyotype. Number of patients with isolated hypospadias tends to increase each year. Broad study including molecular genetic, endocrine and environmental is needed to find definite etiology of isolated hypospadias. Education to medical personnel about isolated hypospadias especially in primary care is very important to avoid misdiagnosis and late management.

Keywords: Isolated hypospadias, Cytogenetic profile.

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Profil Sitogenetika Pasien *Hypospadia Isolated* di Semarang

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Abstrak

Latar belakang: *Hypospadia* adalah salah satu kelainan yang paling sering ditemukan pada bayi laki-laki. Sebagian besar kasus *hypospadia* terjadi dalam kondisi *isolated*. Penelitian sitogenetika pada pasien *hypospadia isolated* belum dilakukan di Indonesia.

Metode: Kami memeriksa 44 rekam medik dari pasien *hypospadia isolated* yang menjalani pemeriksaan kromosom di unit molekular dan sitogenetika laboratorium bioteknologi Fakultas Kedokteran Universitas Diponegoro selama periode Januari 2003 hingga Mei 2007.

Hasil: Usia 44 pasien berada dalam rentang 47 minggu hingga 15 tahun dengan usia rata-rata 7,10 tahun. Lokasi meatus urethra diklasifikasikan dalam anterior (15,9%), midpenil (45,5%), dan posterior (38,6%). Hasil kariotip semua pasien adalah 46, XY. Kelainan struktur dan jumlah kromosom tidak ditemukan.

Kesimpulan: Penyebab dari *hypospadia isolated* masih belum jelas hingga kini. Semua pasien *hypospadia isolated* memiliki kariotip yang normal. Jumlah pasien *hypospadia isolated* cenderung meningkat setiap tahunnya. Dibutuhkan penelitian yang lebih luas meliputi genetika molekular, endokrinologi, dan lingkungan untuk menemukan penyebab pasti hypospadia isolated. Edukasi kepada tenaga medis terutama yang berada pada pelayanan tingkat pertama sangat penting untuk menghindari kesalahan diagnosa dan penanganan yang terlambat.

Kata kunci: *Hypospadia isolated*, profil sitogenetika.

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INTRODUCTION

Hypospadias defined as a congenital defect of the penis resulting the incomplete development of the anterior urethra.[1] According its meatal position hypospadias can be classified as anterior or distal, middle, posterior or proximal.[2,3] Hypospadias is one of the most common anomalies among newborn boys ranging from 0.4 to 8.2 per 1,000 live male births.[3] Most cases of hypospadias occur as an isolated defect [2], that is not associated with intersex, other genitourinary anomalies, systemic endocrine abnormalities, or congenital malformations of other system.[4,5] The etiology of hypospadias is assumed to be multifactorial, including genetic, endocrine, and environmental factor.[2,6]

Previous study in Spain reported that chromosomal abnormalities was absent in patients with isolated hypospadias.[7] Cytogenetic study in patients with isolated hypospadias has not been conducted in Indonesia. In the current study, we involved larger series of patients presenting with isolated hypospadias to ascertain the cytogenetic profile of patients with isolated hypospadias.

METHODS

We retrieved a total of 44 medical records of patients with isolated hypospadias who underwent chromosome analysis in Molecular and Cytogenetics Unit of Biotechnology Laboratory, Medical Faculty of Diponegoro University during the period of January 2003 to May 2007. Cytogenetics result was supervised by laboratory supervisor and monitored by quality assurance program human genetic society of Australasia (Australia). Patients were excluded from study when there were intersex, other genitourinary anomalies, systemic endocrine abnormalities, congenital malformations of other system, or the patient had incomplete medical record. The majority of patients were referred by sexual adjustment team in Dr. Kariadi university hospital and working group on ambiguous genitalia in Medical Faculty Diponegoro University.

RESULTS

The age at presentation of a total 44 patients ranging from 47 weeks to 15 years old with a mean 7.10 years. We distributed patients into six groups based on age at presentation (Fig 1). Meatal position was classified as anterior in15.9% of the cases, middle in 45.5% and posterior in 38.6% (Fig 2). Karyotyping profile of all patients were 46, XY. We also found neither abnormality of the number nor structure of chromosome in patients with isolated hypospadias. Patients were grouped according year at presentation (fig 3).

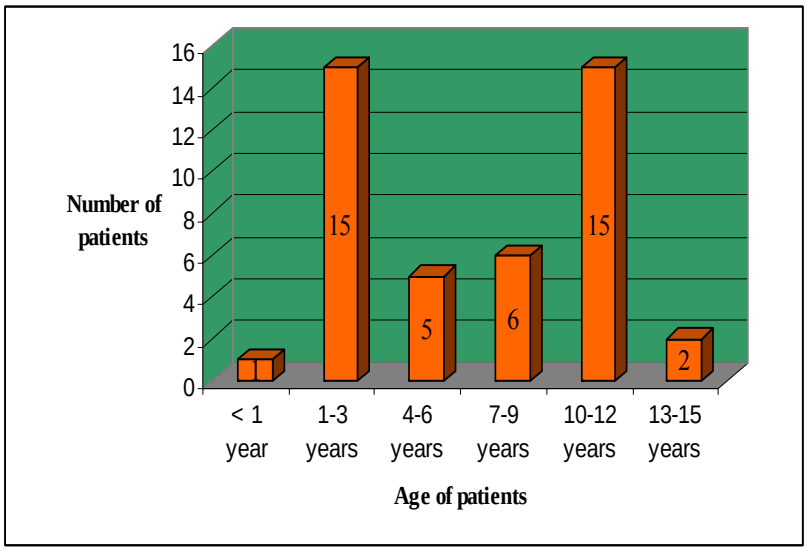

Fig.1. Age at presentation of patients with isolated hypospadias

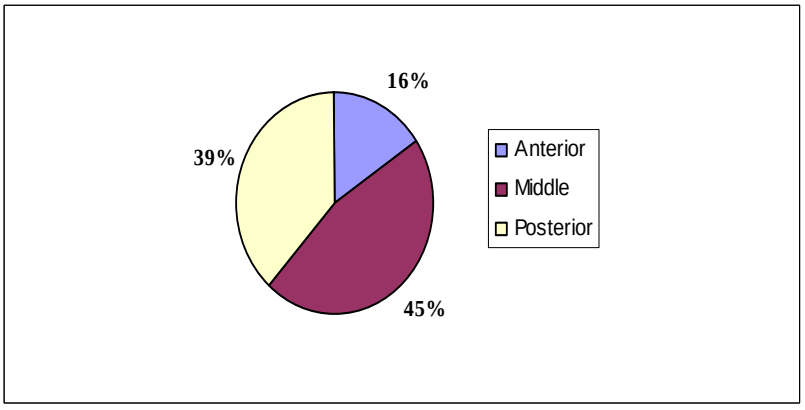

Fig. 2. Distribution of urethral meatus in patients with isolated hypospadias

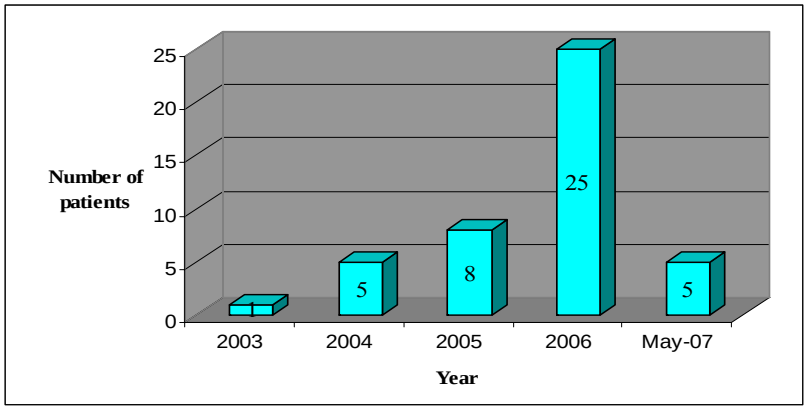

Fig. 3. Number of patients with isolated hypospadias annually

DISCUSSION

Most patients with isolated hypospadias came late to seek medical managent. The mean age presented to us is 7.10 years old and only one patient came in one year of age (see fig.1). There are several explanations possible to account this result. The first reason is the lack of awareness and knowledge from both primary medical care and the parent of patients particularly when urethral meatus in distal or anterior. The second reason is limited access to hospital because most patients were from low socio economic level. All reasons above also explain disparity between distributions of urethral meatus in our patients compare with literature. The distribution of urethral meatus in our study was in anterior (15.9%), middle (45.5%), and posterior (38.6%) (see fig.2). Literature demonstrates that approximately 65% to 70% cases are in anterior, 10% to 15% midpenile and 20% posterior.[1,2]

The number of patients with isolated hypospadias annualy in our study had a tendency to increase (see fig.3). Hypospadias rates was reported increased in United States [8,9] and Netherlands.[11] However in other countries hypospadias rate demonstrated constant [11,12] or decreased.[13]

Chromosomal abnormality was not found in in patients with isolated hypospadias. This fact confirm previous studies.[7,14] Molecular studies in patients with isolated hypospadias did not find sufficient evidence that isolated hypospadias was caused by mutations of 5a-reductase type 2 mutations gene (SRD5A2), androgen receptor gene (AR), homeobox gene A13 (HOXA13) and Wilms' tumor 1 associated protein gene

(WTAP).[4,5,15] Patients with isolated hypospadias was reported had normal endocrine testicular and androgen end organ function.[16] According these findings, transient exposure to environmental factors acting as morphogenetic disruptors in a critical stage of development may be probable mechanism for isolated hypospadias.[16] Some antiandrogenic compounds such as, fungicide vinclozolin, pesticide DDT, and plasticizer diethylhexyl phthalate (DEHP) caused hypospadias in experimental animals. These antiandrogens inhibit androgen binding, androgen synthesis, and androgen-induced gene expression during critical periods of embryonics.[6] Exposure to these substances may occur particularly in the occupational setting but also through more general environtmental exposure in the home, food packaging, and diet.[17]

CONCLUSION

The etiology of isolated hypospadias is still obscure until now. All patients with isolated hypospadias had normal karyotype. Number of patients with isolated hypospadias tends to increase each year. Broad study including molecular genetic, endocrine and environmental is needed to find definite etiology of isolated hypospadias. Education to medical personnel about isolated hypospadias especially in primary care is very important to avoid misdiagnosis and late management.

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