Pediatric Surgery International (2019) 35:985–987
https://doi.org/10.1007/s00383-019-04511-3

ORIGINAL ARTICLE

A cloacal anomaly is not a disorder of sex development

Andrea Bischoff[1] · Andrew Trecartin[1] · Veronica Alaniz[2] · Sarah Hecht[3] · Duncan T. Wilcox[3] · Alberto Peña[1]

Accepted: 20 June 2019 / Published online: 29 June 2019

Abstract

Aim of the study Misdiagnosing a cloaca as a disorder of sex development may lead to inappropriate testing, treatment, and negative emotional consequences to families. We were impressed by the fact that a significant number of patients suffering from a cloaca were referred to us with the diagnosis of a "disorder of sex development" previously referred as "ambiguous genitalia" or "intersex". On re-evaluation, none of them truly had a disorder of sex differentiation. This prompted us to conduct the following retrospective review to try to find the cause of the misdiagnosis and the way to prevent it.

Methods A retrospective review of our colorectal database was performed to identify the total number of patients with cloacas and the number initially diagnosed as "ambiguous genitalia, intersex"/disorder of sex development. The external appearance of their genitalia and unnecessary testing or treatment received were recorded.

Main results A total of 605 patients with cloacas were identified. Of these, 77 (12.7%) were referred to us with the diagnosis of "ambiguous genitalia" and 13 of them (17%) went on to receive an intervention that was not indicated: karyotyping (10), steroids (3), and ovarian biopsy (1). The karyotype result in all patients was XX. The misdiagnosis was triggered by the external appearance of the perineum, simulating a case of virilization with a hypertrophic clitoris, but was simply prominent labial skin. Careful examination of the perineal structure allowed us to determine that it consisted of folded skin with no evidence of corpora.

Conclusion Patients born with a cloaca are at risk for mismanagement from being erroneously labeled as disorders of sex development. The diagnosis of a cloacal anomaly is a clinical one. The practitioner must distinguish between phallus-like clitoral hypertrophy and a normal clitoris with prominent labial skin.

Keywords Cloaca · Disorders of sex development · Intersex · Ambiguous genitalia · Anorectal malformation

Introduction

Families experience stress when their baby is born with a cloacal malformation. Some families are unnecessarily subjected to added anxiety by misdiagnosis of a disorder of sex development. In addition to the family's uncertainty regarding their child's gender, the infant may suffer testing and treatment related to a proposed disorder of sex development. We met patients with cloacas and their families who experienced a misdiagnosis of ambiguous genitalia or disorder of sex development. Their babies were subjected to a series of otherwise unnecessary diagnostic tests including empiric glucocorticoid therapy and karyotype analysis. Even more importantly, they experienced the emotional turmoil of not knowing if their baby was a boy or a girl. We determined to evaluate the frequency and predisposing factors for this misdiagnosis among all of our patients.

✉ Andrea Bischoff
andrea.bischoff@childrenscolorado.org

[1] Department of Pediatric Surgery, International Center for Colorectal and Urogenital Care, Children's Hospital Colorado, University of Colorado, Anschutz Medical Campus, 13123 East 16th Avenue, Box 323, Aurora, CO 80045, USA

[2] Division of Pediatric and Adolescent Gynecology, International Center for Colorectal and Urogenital Care, Children's Hospital Colorado, Aurora, CO, USA

[3] Department of Urology, International Center for Colorectal and Urogenital Care, Children's Hospital Colorado, Aurora, CO, USA

Methods

All cloaca patients in our database from 1980 to 2019 were evaluated. A retrospective chart review was performed to identify which patients had been diagnosed with ambiguous genitalia, also known as a disorder of sex development. Any testing or treatment of a disorder of sex development was recorded. The common channel length, when recorded, was analyzed with the standard error of the mean and a two-tailed *t* test. The number of patients with posterior cloacas was recorded. Most importantly, the physical exam characteristics in a cloaca that predispose to misdiagnosis were described. IRB approval was obtained for this study (COMIRB #19-0387).

Results

Six-hundred and five patients had cloacas and 77 (12.7%) had been diagnosed as ambiguous genitalia or having a disorder of sex development. Thirteen patients (17%) of those misdiagnosed as a disorder of sex development underwent therapy or diagnostic tests related to that diagnosis. Karyotyping was performed in ten patients. The genotype result was XX in all patients karyotyped. Glucocorticoids were administered empirically for congenital adrenal hyperplasia in three patients. A 17-OH-progesterone level was tested on one patient. One patient received an ovarian biopsy.

The recorded average common channel length for cloacas with a misdiagnosis of ambiguous genitalia was 4.6 ± 0.2 cm ($n = 60$) vs. 3.2 ± 0.1 cm without misdiagnosis ($n = 440$) ($p < 0.001$). Of the 528 cloaca patients without a misdiagnosis, 20 (4%) were born with a posterior cloaca. Out of the 77 patients with cloacas misdiagnosed as a disorder of sex development, 16 patients (21%) had posterior cloacas.

Physical exam characteristics were notable for folds of labial skin that, without palpation by the examiner, could be mistaken for clitoromegaly or phallic tissue (Fig. 1). With careful palpation, the genitalia were unequivocally folded skin, without any firmness to suggest clitoral or penile corpora cavernosa. In the entire series of cloacas, no patient truly had a disorder of sex development.

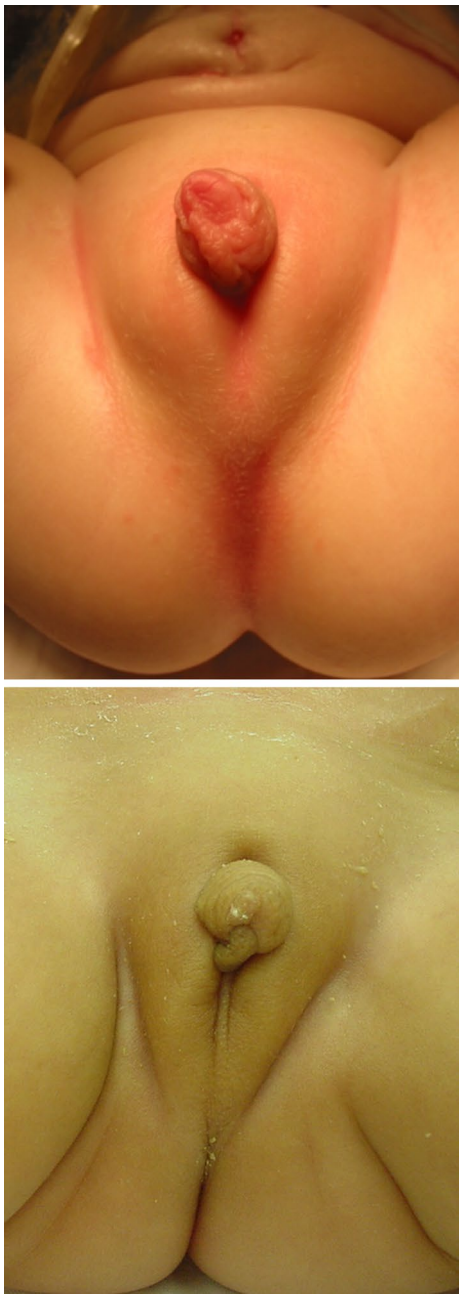

Fig. 1 Images representing the external appearance of cloacas that could be mistaken for clitoral hypertrophy. Meticulous palpation in each case reveals simply prominent labial skin without any corpora of a true hypertrophic clitoris

Discussion

The misdiagnosis of a disorder of sex development in patients with cloacas can be avoided by simple, meticulous examination of the genitalia. Many of our patients have suffered from this misdiagnosis that could have been prevented by careful evaluation. Management of a cloaca must start promptly after birth and not be confused with a disorder of sex development. The newborn with a cloaca will undergo evaluation for additional anatomic malformations, receive a colostomy, and may require hydrocolpos drainage [1].

An infant born with a disorder of sex development is treated much differently than one with a cloaca. Management of a suspected disorder of sex development includes obtaining a 17-hydroxyprogesterone level, empirically treating

with hydrocortisone, and genotyping [2, 3]. Glucocorticoid therapy is common, but may have undesired effects [4]. The price estimate for a karyotype at our facility is $1047. One of the most concerning repercussions from the diagnosis of a disorder of sex development is the emotional trauma parents' experience [5]. Consequently, a detailed physical examination is required to confirm or rule out the diagnosis of a disorder of sex development prior to involving patients and their parents in its management. Failure to make the correct diagnosis leads to considerable additional expense and emotional stress.

Out of our 605 cloacas, there were zero patients with a disorder of sex development. Cloacas make up approximately 10% of anorectal malformations representing 1 in 50,000 newborns [6]. The completely unrelated diagnosis of a virilized 46 XX female is most commonly caused by congenital adrenal hyperplasia and occurs in 1 in 15,000 births [2]. It would be extremely unlikely for a cloaca to occur together with a disorder of sex development. More importantly, the two diagnoses are distinguishable by examination of the genitalia. A clitoris that is hypertrophied from excess adrenal androgens will demonstrate enlarged, palpable corporal or erectile tissue [2, 7]. Visual inspection alone is insufficient to make a diagnosis of a disorder of sex differentiation.

Patients with a cloacal common channel length longer than 3 cm have more complex anatomy, associated defects and decreased chances for bowel control [8]. Our study shows that the external genitalia may also be more abnormal and misleading in patients with a longer common channel length. However, careful examination will still prevent the observer from making an error in diagnosis.

Cloacal anomalies with a diagnosis of "ambiguous genitalia" from an enlarged "phallic structure" are reported in the literature; however, the photos are consistent with simply notable labial skin folds and no mention is made of palpable corpora [9]. A case of a posterior cloaca "pseudohermaphrodite" with a "hypertrophied clitoris" was recently published [10]. However, again, no palpation of the labial tissue was reported and it appears to be simply prominent labial skin. The first reported series of posterior cloacas employed the term "pseudophallus [11]". However, this term referred to skin folds appearing like a phallus, but there was no true corporal tissue. Posterior cloacas were more commonly associated with a misdiagnosis of ambiguous genitalia in our study, but remained clearly distinguishable from the latter by meticulous physical examination.

Conclusion

The visual appearance of the external genitalia in some patients with a cloaca resembles that of congenital adrenal hyperplasia. However, a meticulous palpation of the "phallic-appearing" structure allows the clinician to confirm that there is only redundant skin and no palpable corpora. This careful examination will prevent unnecessary treatment, expensive testing, and emotional trauma associated with a misdiagnosis of a disorder of sex development in a patient with an absent anus.

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