Uncommon vulvar findings in children and adolescents referred to a tertiary center over 14 years: a retrospective study and review of the literature

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ABSTRACT

Background and Purpose: Vulvar complaints are particularly common among children and adolescents; the etiologies largely depend on patient age. Most clinicians are not familiar with the normal variations of the female external genitalia, and this results in many unnecessary referrals. The aim of this study was to describe the frequencies of uncommon vulvar findings (other than ambiguous genitalia or vulvovaginitis) in children and adolescents examined in a tertiary referral center over a 14-year period.

Methods: Records of girls (ranging from newborns up to the age of 18 years) who attended a tertiary Pediatric-Adolescent Gynecology and Reconstructive Surgery Center with vulvovag-inal complaints during the period 2004-2017 were studied retrospectively. Patient age, rea-son for referral, presenting complaints, key aspects of clinical examination, diagnosis and management were recorded for each patient. Patients with ambiguous genitalia or vulvo-vaginitis were excluded from the analysis.

Results: A total of 67 females (37 adolescents and 30 children) were included in the study. Labial minora hypertrophy and labial adhesions were the most common findings in 18 (26.9%) and 17 (25.4%) of the cases, respectively. Less common diagnoses were genital warts in 7 (10.4%) patients, genital trauma in 5 (7.5%) patients, labia minora masses in 5 (7.5%) adolescents, and unilateral labial majora inflammation in 2 (3%) patients. Among the adolescents with labia minora masses, three were diagnosed with vascular malfor-mations, one patient underwent cyst removal, and one suffered labial minora inflammation. Other rare diagnoses included stenosis of the vaginal opening secondary to lichen sclerosus in 1 (1.5%) adolescent and extensive unilateral hemangioma of the vulva in 1 (1.5%) 15-month-old child. Finally, in 11 (16.4%) girls, no pathology was identified.

Conclusions: Comprehensive external genitalia examination is an important part of periodic health checks in girls (children and adolescents), given that there are some, albeit relatively few, genital findings that require immediate referral to a child and adolescent gynecologist in order to ensure timely intervention and the best possible long-term outcome for the young girl.

KEYWORDS

Vulva, labial adhesions, labial hypertrophy, genital warts, straddle injury, vascular malfor-mation, lichen sclerosus.

Introduction

Examination of the external genitalia is an important part of periodic health checks in female patients, starting from the neonatal period until adulthood. There are significant morphological differences in the external genitalia of prepubertal girls compared with adolescents. It is important for the clinician to be familiar with these differences, as well as with their physiological variations, in order to avoid unnecessary referrals to specialized centers, which place a significant burden on health systems and also cause anxiety, both to the young girl and her parents. However, it is also important that any suspicious finding is not missed and promptly referred to a specialized center.

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In childhood, vulvovaginitis is the most common reason for referral to pediatric gynecology clinics, with rates as high as 80% [1]. Other conditions which might present with similar symptoms include labial adhesions, lichen sclerosus, urethral

meatus prolapse, ulcers and straddle injuries [2]. In adolescence, external genitalia symptoms are usually expressed in the context of vulvovaginal infections, including sexually transmitted infections. Adolescents may also seek medical advice if they are concerned about the appearance of their external genitalia [3]. The aim of this study was to describe the frequencies of uncommon clinical findings of the external genitalia in prepubertal and adolescent girls presenting with vulvovaginal complaints (excluding ambiguous genitalia or vulvovaginitis) at a tertiary pediatric–adolescent gynecology and reconstructive surgery department over a period of 14 years.

Methods

This is a retrospective study of patients who presented with vulvovaginal complaints at the Pediatric–Adolescent Gynecology and Reconstructive Surgery Clinic of the 2nd Department of Obstetrics and Gynecology of the National and Kapodistrian University of Athens, based at the Aretaieion Hospital in Athens, Greece. Records of the period from 2004 to 2017 were retrieved and data were extracted for analysis. Study participants included females from birth up to the age of 18 years. Patient age, reason for referral, presenting complaints, key aspects of the clinical examination, diagnosis and management were recorded for each patient. Patients with a diagnosis of ambiguous genitalia or vulvovaginitis were excluded from the analysis. Images of external genitalia were also retrieved, and parental permission for their publication was obtained.

Results

The records of a total of 3250 patients were reviewed. Among them, 67 patients (age range 13 months – 18 years) were identified as having vulvovaginal symptoms. Patients were divided into 30 children (aged 13 months to 9.5 years) and 37 adolescents (aged 8.5 to 18 years) depending on their pubertal development (Table 1). Labial minora hypertrophy and labial adhesions were the most common findings.

Labial adhesions of varying degree (35% to 95% of labial length) were identified in 17 (25.4%) cases (Figure 1). In the vast majority (94.1%) this condition was observed in prepubertal girls (mean age ± SD, 4 ± 2.3 years); indeed, it was observed in only one adolescent, aged 13 years. Symptoms of vulvovaginitis were reported by 4 (23.5%) of these patients, with cultures from a high vaginal swab revealing mostly gut flora. In symptomatic patients, labial adhesions were bluntly separated in the clinic, with the aid of the "pull-down maneuver", after local application of lidocaine/prilocaine cream. In order to avoid recurrences, parents were instructed to ensure daily application of a water-based lube and proper local hygiene. Re-evaluation at 6 months post-treatment revealed recurrence of labial adhesions in 3 patients (17.6%), but to a lesser extent (10% to 30% of labial length).

Reported "deformities of external genitalia" was the reason for referral in 18 (26.9%) adolescents with a mean (± SD)

Figure 1 Extensive labial adhesions in a toddler.

Table 1 Vulvar findings in children and adolescents.

	CHILDREN - N = 30 AGE (RANGE) 13 MONTHS – 9.5 YRS	ADOLESCENTS - N = 37 AGE (RANGE) 8.5 – 18 YRS	TOTAL SAMPLE - N = 67 AGE (RANGE) 13 MONTHS – 18 YRS
Labial adhesions	16	1	17
Minor labial hypertrophy	-	18	18
Labial hematoma (injury)	3	2	5
Genital warts	5	2	7
Vascular malformations	-	3	3
Cyst of the minor labia	-	1	1
Labial minora inflammation	-	1	1
Labial majora inflammation	-	2	2
Lichen sclerosus	-	1	1
Hemangioma	1	-	1
No pathology identified	5	6	11

age of 14.6 ± 2.8 years. All these referrals were cases of labial minora hypertrophy i.e. a labial minora stretched length of more than 4 cm, either unilateral or bilateral (Figure 2a). Although the adolescents and their parents were informed about the benign nature of this condition, four adolescents requested to undergo labiaplasty, which was performed after the age of 18 years (Figure 2b).

Vulvar and perianal genital warts were identified in 7 (10.4%) patients, 5 of whom were toddlers and prepubertal girls without any evidence of sexual abuse (age range 22 months to 4.2 years); the other two were sexually active adolescents (Figure 3). Two of the children were treated with cryotherapy and three with cauterisation, while the adolescents received imiquimod cream. Accidental injuries were the reason for urgent referral in 5 (7.5%) females (age range 3 to 13 years). Careful history taking revealed straddle injuries, while clinical evaluation revealed, in all cases, unilateral vulvar hematomas with localised edema without hymenal lacerations. All patients were managed conservatively.

Five (7.5%) adolescents complained of labia minora masses. One of these patients was found to have a simple cyst, one had a labial mass related to local inflammation, while three adolescents had vascular malformations of the vulva. In the latter, further ultrasound investigation revealed venous (Figure 4) and lymphatic vessel malformations (Figure 5) in two cases and one case respectively. Conservative management with regular

Figure 2a Labial minora hypertrophy in a 18-year-old adolescent girl.

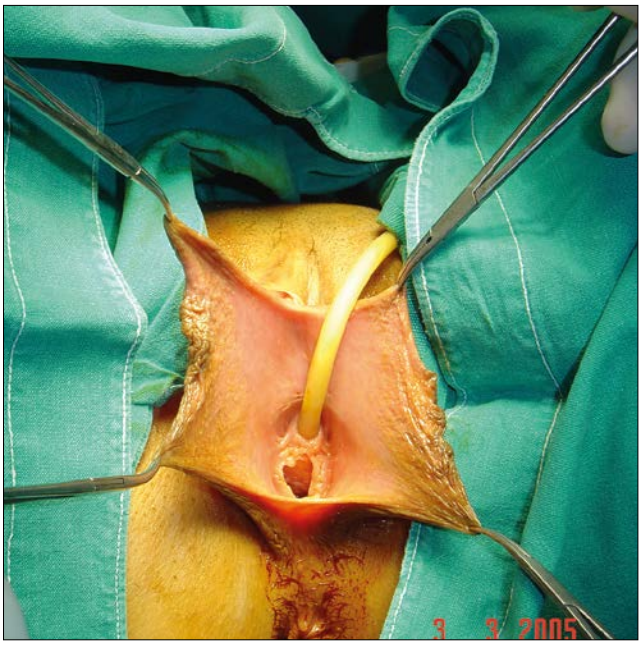


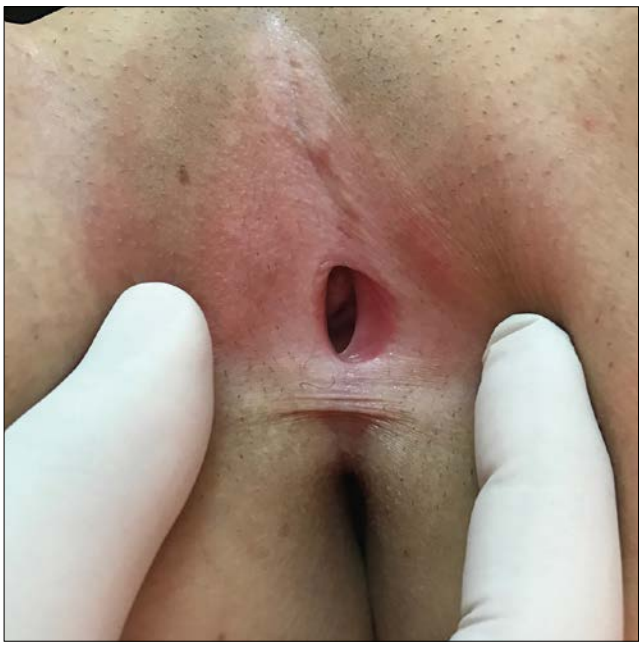
Figure 2b External genitalia of the same patient after labiaplasty.

Figure 3 Genital warts in the vulva of a prepubertal girl.

Figure 4 Venous vascular malformation in external genitalia of an obese 12-year-old adolescent girl.

Figure 5 Lymphatic vascular malformation of the vulva (labia minora) in an 18-year-old adolescent girl.

Figure 6 Lichen sclerosus-related vaginal introitus stenosis.



follow-up was suggested.

Other rare cases included localized unilateral inflammation of the labia majora without evidence of Bartholin's gland abscess in 2 (3%) patients, one (1.5%) case of lichen sclerosusrelated vaginal introitus stenosis (Figure 6), and one (1.5%) case of extensive unilateral hemangioma of the vulva in a 15-month-old toddler.

Physical examination was normal in the remaining 11 (16.4%) cases; these patients, 5 pre-pubertal girls (aged 13 months to 5.8 years) and 6 adolescents (aged 10.5 to 18 years), had been referred with non-specific vulvovaginal complaints. In this group, minor labial size discordance was found in 3 patients, but it was nevertheless within the spectrum of normal variation.

Discussion

According to the findings of this 14-year retrospective study, "vulvovaginal complaints" were the presenting symptoms of a heterogeneous group of disorders (Tables 2 & 3). The most common finding in the prepubertal girls (average age 4 years) was the presence of labial adhesions. In the current literature, labial adhesions have been reported at ages ranging from 3 months to 6 years, with the peak incidence found to occur at the age of 2 years [4]. Rarely, labial adhesions present for the first time after the age of 6 years or persist in puberty. Girls with labial adhesions may be asymptomatic and adhesions can be detected incidentally by parents or pediatricians during a physical examination. Very occasionally, the vaginal orifice is completely covered, causing postvoid dripping of urine or vaginal secretions or non-specific vulvar complaints. In cases of recurrent urinary tract infections or vulvovaginitis treatment is required [5]. In the present study vulvovaginitis complicated about 1 in 4 cases of labial adhesions.

The exact causes of labial agglutination have not yet been clarified. The condition has been associated with low estrogen levels prepubertally, while in newborns the effect of maternal estrogens seems to exert a protective action [4]. Contributing factors include topical irritating agents, vulvovaginitis and minor local injuries. It has been suggested that sexual abuse might predispose to labial agglutination, but this theory has been challenged as the presence of other signs has been more robustly associated with abuse [6,7].

Table 2 Common symptoms of vulvar pathology.

	LABIAL ADHESIONS	LABIAL MINORA HYPERTROPHY	GENITAL TRAUMA	GENITAL WARTS	VASCULAR MALFORMATION	LICHEN SCLEROSUS	LABIAL INFLAMMATION
Asymptomatic	+	+		+	+		
Vaginal secretions	+					+	
Vulvar pain		+	+		+	+	+
Vulvar hematoma/ bleeding			+	+	+	+	
Pruritus				+		+	
Edema			+		+		+
Non-specific vulvar complaints	+	+			+		

Table 3 Key features of clinical examination.

VULVAR DISEASE	CLINICAL FINDINGS
Labial adhesions	Erythema, a thin, pale membrane between labia minora partly covering the vaginal introitus, urine retention, vaginal secretions, normal labia majora
Labial minora hypertrophy	Enlargement of one or both labia minora
Genital trauma	Ecchymoses, abrasions, lacerations, hematoma ± trauma of hymen, vagina, anus, rectum
Genital warts	Single or multiple, small, flesh-colored or hyperpigmented papules or plaques in the perianal or genital region, bleeding
Venous vascular malformation	Asymmetric labia majora, soft, non-pulsating, painless mass, enlargement with Valsava maneuver
Lichen sclerosis	White, atrophic, parchment-like skin, chronic ulceration, inflammation, subepithelial hemorrhages, scarring of the clitoral hood, thickening of the posterior fourchette, bleeding, hourglass configuration
Labial inflammation	Erythema, edema ± vaginal discharge

Diagnosis of labial adhesions can be based on the observation, on visual inspection, of a thin, pale membrane between the labia minora partially or even entirely covering the vaginal introitus. Differential diagnosis includes hymenal atresia, complete transverse septum of the lower vagina, Mayer-Rokitansky-Küster-Hauser syndrome and complete androgen insensitivity syndrome.

Spontaneous separation of labial adhesions has been reported in up to 80% of cases, especially in the case of small adhesions at the posterior fourchette and following estrogenization in puberty [5,8]. Adhesiolysis is recommended when labial fusion is symptomatic. This can be easily performed in the physician's office with gentle traction or with the use of a thin cotton swab, usually after application of local anesthetic gel. In rare cases of dense adhesions, lysis can be performed in hospital under regional or general anesthesia. Irrespective of the method used for treatment, it is essential to instruct parents to ensure adequate local hygiene, and to prevent adhesion recurrence by frequently separating the labia minora and by regularly applying a water-based lubricant gel for 6 to 12 months. Parents can be instructed on labial separation technique i.e. the use of two index fingers (one on each side) to gently pull down and push outwards the labia majora.

Local application of estrogen cream is another method for treating labial agglutination with success rates ranging from 50% to 88% [9-13]. Side effects of estrogen creams include breast budding, local discoloration and irritation of the skin and, more rarely, vaginal spotting or bleeding [9]. All the aforementioned symptoms subside after treatment discontinuation. Success rates of up to 70% have been reported after local treatment with betamethasone ointment, with commonest side effects being localized erythema, atrophic dermatitis and folliculitis [14, 15].

Recurrence rates of labial adhesions are estimated to be between 11.6 % and 14%, or even as high as 17.6% in studies with longer follow-up [16]. Local application of estrogen cream after adhesiolysis is considered to be protective [9, 11, 16].

Labia minora hypertrophy is defined as labial tissue protrusion beyond the labia majora. It can be either unilateral or bilateral. In this study labial hypertrophy was found in almost half of the adolescent patients referred to our center.

There is no agreement on a cut-off value of "normal" labia minora size. Friedrich *et al*. [17] suggested a cut-off value of 5 cm for the maximal length from midline to the lateral edge of the labia minora. More recent studies have proposed smaller sizes of 3 to 4 cm [18-20]. However, in many cases, simple measurement of labia minora length is not sufficient to diagnose hypertrophy and other factors should be taken into account. Since there is no international consensus on normal size values, in the present study the criteria for a diagnosis of labial hypertrophy were a labial length >4cm in an adolescent with subjective symptomatology. Symptoms may include psychological distress, irritation (especially with activity), painful intercourse, and discomfort from tight fitting clothes [21]. In this study four adolescents underwent labiaplasty due to increased stress associated with their genital appearance. In a UK-based study of 33 women, this was the commonest reason for requesting surgical management [22]; while only two of these women had labia longer than 4 cm, five had labia measuring 4 cm and 26 women had a labial length of between 1 and 3 cm.

The cause of labial hypertrophy remains unknown, but it has been associated with genetic factors and elevated levels of estrogen and inflammatory factors, as well as with chronic mechanical irritation [23]. Masturbation had also been proposed as a potential contributing factor, but this theory has been disputed for several decades [24].

The initial approach to asymptomatic patients should be conservative, and counseling should include reassurance that hypertrophic or asymmetrical labia constitute normal variations of external genitalia anatomy, growth and development. Surgical treatment should be considered after the age of 18 years in adolescents with severe functional symptoms and psychosocial distress. According to the Committee on Adolescent Health Care of the American College of Obstetricians and Gynecologists [25], surgical correction in girls younger than 18 years should be considered only in those with significant congenital malformation or persistent symptoms that the physician believes are caused directly by labial anatomy, or both. Labiaplasty involves careful excision of excessive labial tissue, with great care being taken to maintain symmetry. Early complications include hematoma, edema and infection. Longterm complications include scarring, local hypoesthesia or chronic vulvar pain and. Dissatisfaction with the esthetic outcome has also been commonly reported.

Genital warts or condylomata acuminata are skin lesions caused by human papillomavirus (HPV) infection that typically appear as fleshcolored or hyperpigmented papules or plaques in

the perianal or genital region. In adults they are associated with the HPV types 6 and 11 in 90% of cases. Other HPV types have also been implicated, including types 16, 18, 31, 33 and 35, usually in combination with types 6 and 11 [26]. The HPV types detected in lesions from children are more variable and, as well as the aforementioned types, they may include types 1, 2, 4, 7, 27, 57, 60 and 63. In infants and toddlers up to the age of 2 years, the perianal region is the commonest lesion site, while in older children warts can be found in the vulva, vagina and periurethral region. The transmission route in this age group is uncertain, and although genital warts were considered to be a sign of sexual abuse, it is now believed that HPV contamination can happen through non-sexual routes i.e. during labour, self-inoculation, [27-33] etc. In these studies, [27, 29, 32] prepubertal girls with HPV infection had no evidence of sexual abuse and the exact route of HPV transmission could not be identified. Two of these girls (aged 2.5 and 4 years) had perianal warts, while the rest had warts on the perineum and the vulva.

Epidemiological data on childhood warts are scarce. The mean age of wart appearance ranges from 2.8 to 5.6 years [34]. According to a CDC report, 18.3% of sexually active adolescents aged 14 to 19 years have acquired at least one of the 23 HPV types associated with genital warts [35].

In most cases, warts are incidental findings during pediatric examination. Symptoms are rare and vary from an itching or burning sensation to accidental bleeding. Spontaneous remission rates can be as high as 35% within 4 months, rising to 50% in 12 months and 90% after 24 months, thus making treatment during diagnosis unnecessary [36]. Available treatment regimens aim to obtain localized lesion destruction (through cauterization, cryotherapy, surgical excision or topical application of antimitotic agents). There are studies reporting satisfactory results with local application of imiquimod cream, but this treatment is not officially approved for use in children and adolescents [37]. All the aforementioned methods are associated with localized side effects, including erythema, edema, skin abrasion or symptoms such as pain, pruritus and burning sensation that may reduce compliance in this age group [37]. Considering all the above, it is recommended that treatment should be individualized and reserved only for persisting lesions or severe symptoms [26, 38-40]. The risk of HPV transmission is considered to be minimized after treatment, but since it cannot be eliminated, counseling should also include sexual and non-sexual protection education as well as promotion of anti-HPV vaccination especially in populations with low vaccination uptake [26].

Vascular anomalies, according to the updated classification of the International Society for the Study of Vascular Anomalies, have been classified in two groups, vascular tumors and vascular malformations [41]. Hemangiomas are the commonest benign vascular tumors in infancy caused by the rapid proliferation of vascular endothelial cells [42]. Risk factors include white ethnic origin, female sex, prematurity and prenatal testing with chorionic villus sampling. Hemangiomas of the vulva tend to be superficial and of limited size and can be associated with congenital anomalies of the urogenital tract or of the perianal region. Lesions of the vaginal wall and the perineum are prone to abrasion and infection due to mechanical irritation [43]. In most cases, diagnosis is made by clinical evaluation. In cases with multiple skin hemangiomas it is essential to offer ultrasound examination of abdominal organs. Treatment should be reserved for symptomatic cases when functional problems or bleeding occur. Ulcers should be treated with local application of antibiotics combined with corticosteroids, hydrating creams and adequate analgesia [1]. Systematic administration of corticosteroids can inhibit the growth or even contribute to the involution of hemangiomas. The use of the betablocker propranolol has also been shown to be beneficial, but there are no standardized treatment protocols yet [44]. Other treatment methods that have been proposed include interferon, vincristine, embolization and laser treatment.

Vascular malformations are considered to result from developmental errors during embryogenesis which lead to the persistence of vascular plexus cells with a certain degree of differentiation. They are divided into 4 groups i.e. simple malformations, combined malformations, malformations of major named vessels, and malformations associated with other anomalies. Simple malformations are further categorized, according to the prevailing vessel type, into capillary, lymphatic, venous or arteriovenous malformations and arteriovenous fistulas [41]. On the basis of their flow characteristics they are further grouped into low flow (capillary, lymphatic and venous) and high flow (arterial/arteriovenous malformations and arteriovenous fistulas) velocity [45]. The exact prevalence of vascular malformations remains unknown, due to the fact that classification systems have changed over time. Venous malformations seem to be the commonest lesions and comprise about 2/3 of total cases.

Venous malformations can be visible after birth and tend to increase in size as the infant grows or can become apparent for the first time during adult life. The increased prevalence in females as well as their rapid growth during puberty and pregnancy suggest that the hormonal milieu plays a significant role in their pathophysiology [46-48]. They are more frequently located in the perineum and the labia majora and tend to become more apparent after periods of prolonged standing, walking or intense exercise, with concomitant intensification of symptoms like edema, pain and localized pressure [49]. Clinical examination is sufficient to establish the diagnosis. There is usually a visible soft, non-pulsating, painless mass that lends the labia majora an asymmetric appearance. Venous malformations tend to increase in size with the Valsava maneuver. Differential diagnosis includes haematomas, varices, neoplasms and other vascular malformations.

Lymphatic malformations consist of dilated lymphatic channels or cysts, lined with lymphatic endothelial cells. They are classified as microcystic, macrocystic and mixed subtypes. The most common sites are the head and the upper limbs, and rarely the female genital tract. They can be associated with venous or capillary malformations. Symptoms include intermittent pain and edema, infections and hemorrhage; they can also cause appearance dissatisfaction.

Investigations for the diagnosis of vascular malformations include Doppler sonography and magnetic resonance imaging [50]. Treatment is typespecific, but also depends on lesion location and flow characteristics. Most of the vulvar dysplasias can be managed with the use of sclerotherapy or surgical excision.

In the abovecited study, [50] all patients were successfully managed conservatively.

Lichen sclerosus is a complex chronic inflammatory skin condition which mainly manifests itself in the vulvar area of preadolescent and adolescent females [51]. The pathophysiology of lichen sclerosus is not clearly understood; it is considered an autoimmune disease with genetic component as suggested by studies in monozygotic twins [52]. The most common symptoms are pruritus, dryness, dysuria and hemorrhage, while bowel-related symptoms and abnormal vaginal discharge have also been reported. Clinical examination reveals a whitish fragile atrophic lesion with a cigarette paperlike appearance. Signs of chronic ulceration, inflammation and subcutaneous hemorrhage can also exist. Progression to more severe disease stages causes disruption of the normal vulvar anatomy with formation of scar tissue over the clitoris and the labia minora as well as thickening of the labial posterior fourchette. Involvement of the perineum and the perianal area along with the labia may give the affected area an hourglass configuration. Diagnosis is based on the typical appearance and biopsies are rarely required.

Mild cases can be managed conservatively through application of hydrating creams, improvement of hygiene and avoidance of irritating factors. Should these prove to be inadequate, local corticosteroids can be applied until complete remission of symptoms. Recurrences are common and are also treated with topical corticosteroids. Surgical intervention may be needed later if loss of vulvar architecture and adhesions around the clitoris develop. After the onset of pubertal development, the effect of estrogens may aid disease remission [53, 54].

Trauma in the genital area in childhood and adolescence can result from an isolated injury (e.g. straddle injury) or from multiple injuries (e.g. after a car accident). When there is a marked discrepancy between findings and the possible mechanism of injury, sexual abuse should always be part of the differential diagnosis [55]. A study [56] of 358 cases demonstrated an increased prevalence of genital trauma in those aged under 10 years. In particular, trauma, as a result of sexual abuse, occurred more frequently in infants and toddlers up to the age of 4 years, falls or bicycle accidents were more prevalent in the ages between 5 and 9 years, whereas car accidents were more frequent in adolescents older than 15 years. It has been hypothesized that perineal and genital area tissues are more fragile in the preadolescent years. Perineal trauma accounts for almost 0.2% of all traumas in girls younger than 15 years [57]. Clinical findings include bruises, lacerations, tears and hematomas.

About 15-20% of reported cases required surgical treatment, while in the absence of sharp object injury, this risk drops to 9% [56, 58, 59]. Conservative management includes reduced activity, sitz baths and adequate analgesia, especially within the first 24 to 48 hours [58].

In children under the age of 14 years, straddle injuries are the most common cause of genital trauma that occurs as a result of tissue compression between a hard object (bicycle saddle, seesaw, home furniture) and the bony pelvis. In the present study all cases of genital traumas were caused by straddle injuries, with labial hematomas being the most common finding. One case presented with introital hematoma and another one with marked edema of the hymen without evidence of rupture. Generally, the genital areas that are more commonly affected by non-penetrating injuries are the labia majora, the pubic area and the clitoris, while the vagina and the hymen usually remain intact.

Other genital injuries reported in the literature include accidental penetrating injuries, vaginal trauma caused by extreme water pressure (e.g. jet-ski accidents), trauma caused by fractured pelvic bones, bites, burns and penetrating trauma during intercourse (consensual or non-consensual). A special mention should also be made of female genital mutilation, which is still performed in various regions around the world [60].

Conclusions

External genitalia problems can be a source of distress for both the young girl and her parents. In most cases, though, they are associated with benign conditions which require either no or only minimal intervention. In every case, evaluation by child and adolescent gynecologists or other specialized clinicians, familiar with the rare conditions and the physiological variations of the female genital area, is warranted in order to ensure the best possible longterm outcome.

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