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CLINICAL AND PSYCHOLOGICAL FEATURES OF CHILDREN WITH ANOGENITAL LICHEN SCLEROSUS. APPROACHES TO THE CHOICE OF THERAPY

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Abstract

Lichen sclerosus (scleroatrophic lichen) is a chronic inflammatory dermatosis of the dermal papilla, manifested by ivory white or rose-colored papules and plaques, with atrophy in the center. Lichen sclerosus morphological changes are characterized by a thin flat epidermis, a subepidermal zone of oedematous and hyalinized collagen. It is still not established, but more and more clinicians state lichen sclerosus is associated to localized scleroderma. Lichen sclerosus can affect any parts of the body, but genital involvement is the most common. Extragenital lichen sclerosus occurs in 6-20% of the population.

We carried out a retrospective analysis of clinical presentations and treatment response of 12 patients with anogenital lichen sclerosus in children aged 3-14 years. We presented the clinical features and identified a combination of lichen sclerosus with localized scleroderma in 41% of the examined patients, revealed psychoemotional disorders in the patients. The treatment of the disease varied greatly in the group of these patients. The anogenital lischen sclerosus therapy was stepwise. It started with local treatment using topical corticosteroids and calcineurin inhibitors. If such treatment was ineffective, it was enhanced by using of oral immunosuppressants, which significantly improved the prognosis and outcome of the disease. The assessment of the effectiveness of the treatment was implemented using the visual scales of activity, skin fibrosis and the scale of local pain. The psycho-emotional status of children was assessed using the Luscher test and the Childrens Manifest Anxiety Scale. Dynamic follow-up of our patients verified significant problems of emotional-volitional and motivational spheres, as well as severe anxiety, which correlated with the activity of the skin processes. Also we report uneven reverse reduction of clinical and psychological manifestations, such as normalization of psychoemotional disorders previously to somatic improvement. Deep psychoemotional impairment status revealed that children with anogenital lischen sclerosus require psychological adjustment and, if necessary, medical treatment provided by a neuropsychiatrist.

Keywords: *anogenital lichen sclerosus , children, adolescents, clinical picture, psychological characteristics of the disease, treatment.*

Introduction

Lichen sclerosus or scleroatrophic lichen (LS) is a chronic inflammatory dermatosis of the dermal papilla. It manifestes by ivory white or rose-colored papules and plaques, with atrophy in the center. Clinical presentations of LS were first described in 1889 by the French dermatologist François Henri Hallopeau, and its histology pattern was defined by the French dermatologist and pathologist Jean Darier in 1892. LS is also defined as chronic inflammatory, idiopathic fibrotic skin disease with genital and extragenital localization [*Becker K, 2011*].

Lichen sclerosus morphological changes are characterized by a thin flat epidermis, a sub-epidermal zone of edematous and hyalinized collagen. To date, it is still not established whether LS and localized scleroderma (ScL) belong to associated conditions of scleroderma spectrum diseases. Some investigators [*Sawamura D et al., 1998*] have re-

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ported, via sequential biopsies, a transition from LS to morphea or vice versa, while others [*Patterson J et al., 1984; Cabral1 M et al., 2016*] insist on significant clinical and histological differences between LS and ScL. In a study with 472 patients with LS, Kreuter A. [*Kreuter A et al., 2018*] found that the incidence of LS in patients with ScL was higher than in the general population, thus indicating the correlation between the two diseases. In another report [*Fujimura T, 2015*], in a woman with LS plaques accompanied by simultaneous morphea manifestations, immunohistochemical similarities were found out in biopsy specimens. Nikitina M.N. and co-authors (1983) pointed out the similar nature of the extragenital lesions in both ScL and genital LS children. The authors consider all the observed cases of genital lesions in children as a superficial circumscribed morphea. According to the classification formulated by Peterson S. and co-authors, LS is one of the clinical types of circumscribed morphea [*Peterson L et al., 1995*].

The etiology of LS is unknown. In the literature, there is evidence of association of LS with human papillomavirus infection and spirochete Borrelia burgdorferi, hormonal phenomena and skin injuries [*Dinh H et al., 2016*]. Along with this, genetic factors [*Sherman V et al., 2010*] and autoimmunity mechanisms are also implicated. Immunological changes on the level of T and B cells have been detected in LS patients. About 20% [*Kreuter A et al. 2013*] - 28% [*Marren P et al.,1995*] – up to 54 % [*Cooper S et al., 2008*] of women with LS are reported to have autoimmune diseases, such as autoimmune thyroid disease, vitiligo, inflammatory bowel diseases, rheumatoid arthritis, psoriasis. In girls with LS, according to various authors, autoimmune conditions occur from 6.6% [*Powell J et al., 2000*] to 14% of cases [*Lagerstedt M et al., 2013*].

Men and boys have a combination of LS with autoimmune diseases in only 3% of cases [*Azurdia R et al., 1999*], which suggests the role of estrogen in the pathogenesis of the disease.

Lichen sclerosus may affect all areas of the body, but classically it occurs in the genital area. Extragenital LS incidence data vary between 6 to 20% of general population [*Kreuter A et al., 2013*], which is far less common than anogenital lichen sclerosus (AnLS) [*Chi C et al., 2011*]. AnLS is more prevalent in postmenopausal females, though the disease also occurs in women of reproductive age, significantly affecting the quality of life. In recent decades, there has been an increase of AnLS in postmenopausal women. Thus, according to the Danish registry, the incidence of AnLS in women increased from 7.4 per 100,000 women in 1991 to 14.6 per 100,000 women in 2011 [*Bleeker M et al., 2016*]. Anogenital LS (AnLS) may result in severe complications, such as labial adhesion, vaginal stenosis, cicatricial phimosis that should demand surgery in adults [*Rangatchew F et al., 2017*]. Squamous cell carcinoma of the vulva is a well-recognized risk of AnLS in adults, with an estimated lifetime risk of up to 5% [*Crum C, 1992; Bleeker M et al., 2016*]. There are some reports of carcinoma in young adults, suffering from untreated AnLS since childhood [*Crum C, 1992*]. Approximately 7-15% of all AnLS cases occur in prepubertal females [*Sahn E et al., 1994*].

AnLS is more prevalent in females than males, with a ratio of 10: 1,4 . It has bimodal age distribution in females, with a peak incidence in prepubertal girls and postmenopausal women. The true prevalence of AnLS in children is difficult to determine, since in many patients the disease is asymptomatic. According to data, AnLS in childhood has an estimated prevalence of 1 in 900-1000 children. [*Powell J et al., 2000; Lagerstedt M et al., 2013*]. The disease affects girls more frequently than boys. According to various data, the appearance of the first symptoms of AnLS in children usually occurs at the ages between 2 and 5-7 [*Lagerstedt M et al., 2013; Singh N, Ghatage P, 2020*]. The incidence of spontaneous remission in girls reaches 25% of all cases. Disease activity is likely to be reduced in puberty, but it rarely goes into complete remission [*Ridley C, 1993*].

The certain contradictions in the epidemiological data on AnLS are apparently due to the fact that the classification and case statistics of the disease are not unified, since the diagnosis and treatment of AnLS is carried out by specialists of different fields - pediatricians, dermatologists, gynecologists, urologists, rheumatologists.

In children AnLS manifests initially with slight redness of the skin and mucosa, later areas of ivory white or rose-colored plaques appear, followed by depigmentation of the skin. Young females present with swollen labia and clitoris of a cyanotic shade .The border of the

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

affected lesion is usually distinct. The process can often spread to the perianal region causing a classic "figure of eight" shape. The plaques can be atrophic with a shiny or crinkled "cigarette paper" appearance, followed by cracks or ulcerations, or can be thinned due to hyperkeratosis as a result of repeated excoriations. The repeated excoriations can lead to ecchymoses, hemorrhage, and superficial erosions. The superficial erosions can be painful, cause burning sensation during urination and defecation, and are at risk for secondary superimposed infection. Sometimes the disease is asymptomatic, not accompanied by pain or itching in the anogenital region [*Burova E, 1989; Ukolova I, 2006*].

Children with AnLS usually present with complaints in case of secondary genital infection, dysuria or constipation [*Poindexter G, Morrell D, 2007*]. In boys AnLS is highly associated with phimosis and meatal stenosis of urethra, so according to some authors, it is reasonable to perform circumcision as a potential treatment approach [*Alyami F et al., 2018; Green P et al., 2019*].

Adult patients with AnLS are reported to have various psychological and depressive disorders, caused by sexual dysfunction due to the disease [*Edmonds E et al., 2012; Wehbe-Alamah H et al., 2012; Jin Chong-Rui et al., 2016; Sokolova A, 2017*]. There is far less research on psycho-emotional disorders in children with AnLS. So, according to the Lagerstedt M. and co-authors (2013) and the survey of teenage girls with AnLS, 67% of patients had a decrease in quality of life due to the disease. Also patients point out a low awareness of doctors and medical personnel about their disease, which makes it difficult to obtain recommendations on AnLS, including suggestions about physical activity.

Teenagers are deeply uncomfortable due to the need to expose their genitals during a physical examination, restrictions on playing sports, wearing fashionable teenage clothes due to hygiene requirements. The literature reports some cases when it is necessary to differentiate AnLS with the consequences of sexual violence of children and adolescents [*Isaac R et al., 2007*].

Based on evidence-based guideline on AnLS [*Kirtschig G et al., 2015; Kirtschig G, et al., 2017*] , biopsies of the affected skin area should be performed if the clinical diagnosis is uncertain, malignancy is suspected or therapy failed.

Currently there is no single strategy for the treatment of AnLS [*Bercaw-Pratt J et al., 2014; Batyrova Z et al., 2016; Kirtschig G et al., 2017*]. The recommended initial treatment for AnLS is a three-month application of potent (class III) to ultra-potent (class IV) topical corticosteroids [*Kirtschig G et al., 2015; Kirtschig G et al., 2017*].

Randomized studies show that application of topical corticosteroids significantly improves AnLS in 75% - 90% of the patients, as compared with roughly 10% in placebo groups [*Bercaw-Pratt J et al., 2014; Casey G et al., 2015*]. There are reports [*Nerantzoulis I et al., 2017*] of clobetasol ointment, which was used 2 times a day for 2 weeks, followed by topical corticosteroids (triamcinolol and hydrocortisonone) with a less strong effect. This led to an improvement of symptoms in 93% of girls with AnLS.

In male patients with AnLS a complete circumcision is recommended if the treatment with topical steroids does not lead to remission. This procedure is reported to lead to permanent, lifelong remission in 90%-100% of the cases [*Bercaw-Pratt J et al., 2014; Green P et al., 2019*].

Topical calcineurin inhibitors (tacrolimus and pimecrolimus) are second choice of treatment options. Topical calcineurin inhibitors for external application have an immunosuppressive and anti-inflammatory effect due to a specific association with the T lymphocyte receptor (macrophyllin-12), which binds calcineurin, a molecule necessary to initiate gene transcription determining the synthesis of cytokines. The ointment containing tacrolimus does not affect the synthesis of collagen and, thus, does not cause skin atrophy. The topical calcineurin inhibitors effects are inferior to those of topical corticosteroid, according to some authors [*Sotiriou E et al., 2009; Chi C et al., 2011; Bercaw-Pratt J et al., 2014; Kirtschig G et al., 2017*]. However, there are some other authors who state that topical corticosteroids may cause skin atrophy which makes their use in children more short-term, or topical calcineurin inhibitor is immediately preferred [*Bercaw-Pratt J et al., 2014; Dinh H et al., 2016*]. Topical calcineurin inhibitor is not recommended for children under two years of age.

Systemic treatment with glucocorticosteroids and cytostatics is indicated in refractory cases. The retrospective study of Kreuter A. and co-authors (2009) demonstrated the effectiveness of the combined use of pulsed steroid and methotrexate. Patients received an oral dose of methotrexate 15 *mg/wk* with high-dose intravenous methylprednisolone (1000 *mg*), given for three consecutive days monthly. They showed an improvement after a three-month treatment and re-

mission was achieved in 6 months. In another study [*Nayeemuddin F, Yates V, 2008*], a patient with generalized morphea and AnLS was successfully treated with systemic methotrexate 10*mg/week* remission was achieved in 8 months. Improvement was noticed in 3 weeks and an excellent response was obvious after 5 months. At the 6-month follow-up the patient was still in remission after complete cessation of treatment.

MATERIALS AND METHODS

We used retrospective analysis of 12 case histories of AnLS patients, who received treatment at the rheumatology department of Sechenov First Moscow State Medical University children's clinical hospital. The diagnosis of AnLS was established clinically, based on the characteristic manifestations of the disease. There was no need for a morphological study for diagnostic purposes, a biopsy was not performed so as not to cause additional psychological trauma to patients. The examined group of patients consisted of 12 children, The age of the patients at the time of the disease onset varied from 3 to 13 years, the average age was 5 years (M = 5.2 ± 08). Among 12 patients, there was only one boy in our series (female/male ratio 11:1). The disease onset was at pubertal age of the boy, while the average onset age in the girls was 2 years and 3 months. The clinical characteristics of the patients are presented in table 1. In addition to AnLS, scleroderma lesions involving the trunk were detected in 5 out of 12 patients (41%). Extragenital scleroderma plaques were located mostly in lower abdomen and inguinal region, but in one patient the plaque was on the neck. In 3 cases parents contacted the hospital with complaints of plaques on the trunk, and AnLS was diagnosed for the first time at the doctor's examination, while the parents had not previously seen the lesions. None systemic manifestations of scleroderma were detected, according to the results of the study.

The clinical changes of anogenital area were manifested by induration or intensive skin fibrosis. In 11 out of 12 patients lichen lesions involved vulva (penile) and the area around anus at a time causing a classic "figure of eight" shape (Fig. 1). None of the patients suffered from urinary tract infection or chronic constipation. The main complaint was itching (in 50% of cases). In one girl urination and defecation were painful, due to indurated lesions of perineum; another 4-year-old fe-

TABLE 1.

Clinical characteristics and treatment outcomes of patients with anogenital lichen sclerosus (AnLS).

Patient No	Age (Sex) (*years*)	Age of disease onset (*years*)	Extragenital skin manifestations	Antibodies	**Treatment of medications**							Efficacy after12 and 24 months	
					Medication name (complex)	index of activity		fibrosis index		discomfort index			
						Bef	Aft	Bef	Aft	Bef	Aft		
1.	7 (F)	3	CDM	ANF 1:160	Pr+Pre	3	0	2	0	1	0	G	G
2.	11 (F*)	3	-	-	Pr+Pre	3	0	2	1	2	0	S	S
3.	12 (F*)	4	-	-	Pr+Pre	4	0	2	1	3	0	S	S
4.	6 (F)	5	CDM	ANF 1 :320 RF +	Pr+Mtx	4	0	2	0	1	0	G	G
5.	9 (F)	8	GM	ANF 1 :640 RF +	Pr+MTX	3	0	2	0	1	0	G	G
6.	8 (F)	7	GM	ANF 1 :640	MTX	3	0	1	0	0	0	G	G
7.	8 (F)	6	GM	-	MTX	4	0	2	0	1	0	G	G
8.	9 (F)	6	-	-	MTX	3	0	2	0	2	0	G	G
9.	4 (F)	4	-	-	MTX	4	0	1	0	0	0	G	G
10.	3 (F)	3	-	-	Tac	3	0	1	0	0	0	G	G
11.	4 (F)	4	-	-	Tac	2	0	1	0	0	0	G	G
12.	14 (M)	13	-	-	Tac	3	1	1	0	0	0	G	-

Notes: **-siblings , Abberviations used in the table: Pr – Prednisone, Pre - Penicillamine, Tac – Tacrolimus ointment, Mtx – methotrexate, Pr+Pre - Prednisone with Penicillamine, Pr+Mtx – Prednisone with methotrexate, CDM - Circumscribed deep morphea, GM – Generalized morphea, RF- rheumatoid factor , G –good, S – satisfactory, Bef – Before , Aft – after, F – Female , M - Male*

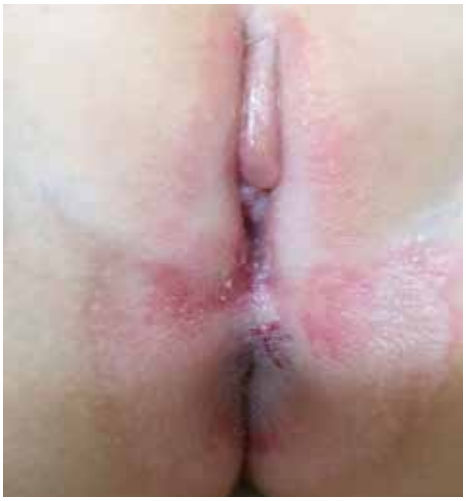

Figure 1. *Anogenital lichen sclerosus, involved vulva and area around anus –"figure of eight".*

male patient presented with masturbation before the debut of AnLS. Among our patients there were two siblings, girls, with AnLS onset at the age of 3 and 4, with similar lesions of clitoris and labia minora. Nine (9) out of the 12 patients (No. 1-9, table 1) were previously unsuccessfully treated with local applications of medium potency topical corticosteroids ointment, emollients, laser therapy and/or electrophoresis with lydasum, therefore we used systemic immunosuppressants.

The effectiveness of therapy was assessed on the basis of AnLS activity and fibrosis visual assessment scales in points, as well as the subjective scale of local pain sensations experienced by the child.

The activity and fibrosis scales were designed to objectify the acute inflammatory lesions in the skin and mucosa of the anogenital area, taking into account the fact that stages of inflammation and fibrosclerotic changes can be different in different anatomical parts of the genitals. Using activity and fibrosis scales, the activity index (IA) and the fibrosis index (IF) were calculated in points, which were evaluated in the dynamics of treatment.

According to the activity scale, the lesions had the following classifications:

erythema, swollen labia minora and clitoris (glans penis, foreskin);

induration (densification-thickening) of the labia minora and the clitoris (glans penis, foreskin);

erosion, ulcers of the skin and mucosa;

erythema and skin induration in the perineal suture and around the anus.

The absence of signs was evaluated as 0 point, the presence of each sign - 1 point. Thus, the maximum index of activity can be 4 points, the minimum: 0 point.

According to the scale of fibrosis, the lesions had the following characteristics:

fibro-sclerotic lesions (shiny, thinning) of the skin and mucosa of the vulva (glans penis, foreskin);

cracks, hyperkeratosis;

reduction in size of the vulva (glans penis, foreskin) due to atrophic processes;

the formation of Labial adhesion, reduction in size and / or stricture of the vestibule (phimosis, urethral stricture).

The absence of a sign was evaluated as 0 points, the presence of each sign was 1 point. Thus, the maximum IF index could be 4 points, the minimum:0 points. The scale of local pain sensations made it possible to evaluate the discomfort index in the anogenital area(ID) and included the presence of itching, burning, pain

The absence of a sign was 0 point, the presence of a sign was 1 point, thus, the discomfort index (ID) of the anogenital area could be not higher than 3 points. The above indicators of activity, fibrosis and discomfort were evaluated after 6 weeks, then 6, 12 and 24 months from the start of therapy. After 12 and 24 months from the start of treatment, a general assessment of the effectiveness of therapy was carried out, which was interpreted as a "good effect", if there was a decrease in indices of activity, fibrosis by 2 points, "satisfactory" - with a decrease in indices of activity, fibrosis by 1 point, "unsatisfactory" - with lack of dynamics of the skin process.

Patients with AnLS, performed general hygiene recommendations along with the ongoing systemic or local immunosuppressive therapy. The recommendations included: multiple daily anogenital toilet using a shower or wet toilet paper; regular change of underwear; wearing mainly cotton, "breathable", loose-fitting clothing for the lower half of the body, limited wear of trousers for girls; a ban on swimming in the pool, cycling, and other sports associated with anogenital trauma and maceration. We suggested using a diet and drugs aimed at preventing constipation; empty the bladder regularly. The long-term implementation of these recommendations accompanied by the need of attending schools and children's organizations led to resistance and negative psychological reactions in children. This was an additional stress factor, in addition to the painful pathological changes in the intimate zone. Therefore, we found it interesting to evaluate the psychological disorders associated with AnLS and we tested all children before the treatment and after 12 months.

All the children underwent the Luscher test [*Sobchik L, 2005*], which allowed to verify the psychoemotional state of the children in a short time through an objective interpretation of the sequence of color preferences. The test consisted of 8 cards of different colors: gray, blue, green, red, yellow, purple, brown, black. During the testing, the following characteristics were evaluated: emotions, motivation, communicativeness and physiological state. This point method of evaluation allowed us to objectively verify the emotional - volitional and psychophysiological levels of each child in dynamics. Analyzing the abovementioned points, we found out that the more points the children got, according to the Luscher test, the more pronounced adjustment disorders they had, i.e., the minimal number of points that the examined child could score was 4 points and this was the optimum. And the highest number of points was 16, which was a negative maximum. The Luscher test was carried out at the beginning of the study, after 6 weeks and after 12 months from the start of treatment. In addition to the Luscher test, patients underwent anxiety scale. The Children's Form of Manifest Anxiety Scale modified by A.M. Prihozhan (1994) is for children older than 8 years of age and it included 53 statements allowing measuring the degree of anxiety (ranging from complete absence to a very high level). For children under 8 years of age (5 patients), the anxiety test was evaluated using a projective method "Choose the Right Face" by R. Tamml, M. Dorki, V. Amen based on the comprehension and interpretation of 14 pictures [*Dermanova I, 2002*]. The anxiety test was implemented in degrees, from 1 to 4 points, where 1 point corresponded to a low level, while 4 points indicated higher level of anxiety.

Integrative Medicine Outcome Scale, IMOS for assessing the results (effectiveness) of treatment, which consisted of 5 points, was also used:

Complete "recovery" (CR)

Significant improvement (reduction by 50% or more of pathological indicators of a patient's objective status)

Improvement (reduction by 25% or more of pathological indicators of a patient's objective status)

Unchanged (the severity and number of pathological indicators of a patient's objective status remained unchanged)

Deterioration (new pathological indicators of a patient's objective status).

IMOS was filled out with the answers provided by the doctor participating in the study and in accordance with the data of the first and the last visit.

Results

We performed an assessment of the effectiveness of the treatment in the studied group of patients with AnLS.

The treatment varied, due to several circumstances. Patients No 1, 2, 3 were admitted to our department in 1999-2000, when we had neither experience of methotrexate treatment in morphea, nor tacrolimus ointment at our disposal. These patients received systemic treatment with oral prednisolone (Pr) (Gedeon Richter, Hungary) (0.5 *mg/kg* body weight) for 4 weeks, which was gradually withdrawn and followed by penicillamine (Cuprenil, TEVA, Poland) (8 *mg/kg* body weight/ daily) for 2 years. We made such a choice of therapy, because the previous local therapy had failed and the lesions were presented with intensive spread induration and fibrosis of anogenital zone (Fig. 2). In the first case, positive changes were seen within a month of therapy, including reduction of oedema and induration. In 12 months the fibrotic lesions significantly reduced and in 24 months changes were noted in the vulva and skin around the anus persisting in the form of slight hyperpigmentation of the skin. In patients 2 and 3 (siblings) with a long duration of the disease before treatment (8 years), the activity of the disease and its progression were stopped, but no complete remission of fibrous lesions in the vulva was achieved. The treatment effect in both cases was regarded as "satisfactory". In the follow-up period of 2 years without treatment there were no AnLS relapses and all the 3 girls presented with menarche.

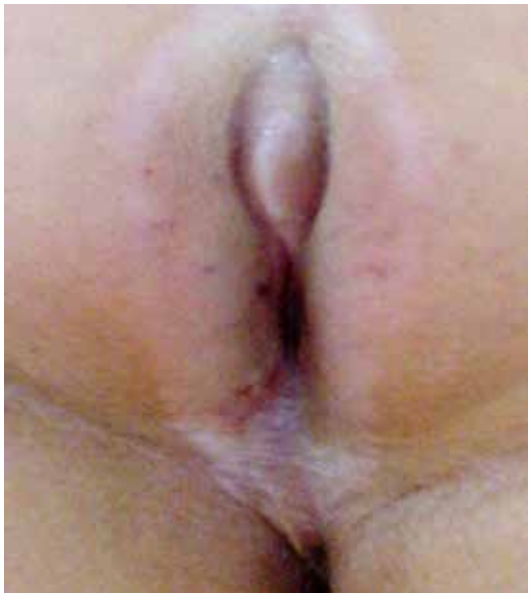

Figure 2. *Intensive induration and fibrosis of vulva before treatment.*

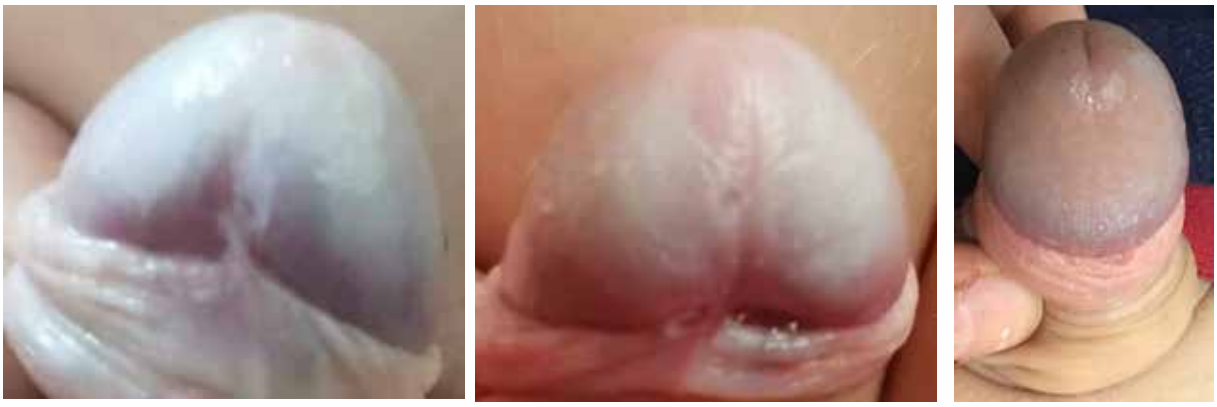

Figure 3. *Lichen sclerosus of penile before treatment (A) , after 12 weeks tacrolimus ointment treatment (B) and after 1 year (C), absence of lichen sclerosus clinical presentations.*

The other two girls (No 4.5, table 1) received oral Pr 0.5 *mg/kg* daily for 4 weeks, followed by complete withdrawal, and methotrexate 12 *mg/sq.m* per week for 24 months. This treatment choice was due to AnLS accompanied by morphea and immunologic disease activity. One more girl (No 6, table 1) with AnLS and morphea had short disease duration and obesity, so we initiated methotrexate monotherapy. In 12 months we saw intensive reduction of AnLS lesions, in 24 months she had complete remission.

In 2 girls with AnLS but without morphea, we used methotrexate (Metoject, Medac, Germany) monotherapy parenterally (12 *mg/sq.m* per week), with good result, with no exacerbations through 1-year follow-up and remission was achieved. The drug was cancelled. In patients No 10, 11, 12 (Table 1), among them 1 boy, we used local therapy with tacrolimus 0.03% ointment with success. For all the patients, this was a starting therapy and the duration of AnLS before treatment was no more than 3 months. The 13-year-old boy with LS on the glans penile received tacrolimus 0.03% 2 times a day (12 weeks) with good response and leading to a significant reduction in the manifestations (Fig. 3 A, B, C). The girls received the topical tacrolimus ointment 0.03% (Protopic 0.03%, Astellas, Japan) twice a day for 12 weeks. The effect of tacrolimus application, such as reduction of edema, induration began in 4 weeks; after 8-10 weeks we noticed the significant reverse of AnLS signs (Fig. 4 A, B). In the second year of treatment, the use of TL ointment 0.03% 2 times a day was used as anti-relapse course lasting 2 weeks, every 4 months. A good effect of therapy was maintained.

Thus, in all 12 patients with previously ineffective local AnLS therapy, a positive dynamics of treatment was obtained using treatment with immunosuppressants of various intensity. The treatment effect was confirmed by a decrease in indices of activity, fibrosis and discomfort in children. In 10 out of 12 patients, the general assessment of the treatment effectiveness after 12 months was regarded as a “good” effect; in 2 patients, it was “satisfactory”. We believe that the lack of the desired “good” effect in these patients was due to the long duration of the disease before treatment, which led to the formation of irreversible fibrotic anogenital lesions. Figure 5 demonstrates the dynamics of the parameters reflecting the pathological process in AnLS. During the treatment indices of activity and discomfort decreased significantly, IF decreased to a lesser extent, which was due to the irreversible fibrous skin changes in a number of patients, as a result of a prolonged course of AnLS. At the same time, there were no patients with gross genital defects, such as labial adhesion, urethral stricture and other disorders in our group.

The average index of activity in the group was interestingly quite high, while the average discomfort index was less than 1 point, which, as we think, reflects the specific character of the AnLS course in

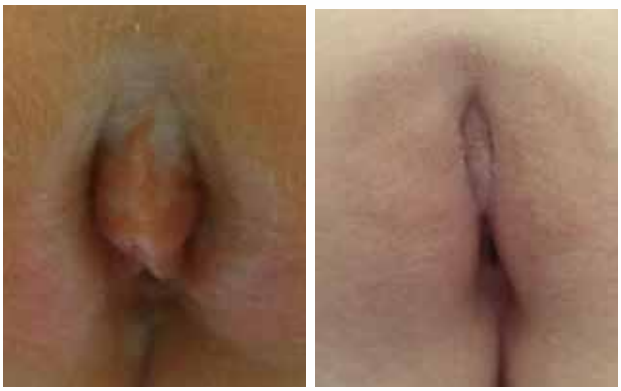

Figure 4. *Anogenital lichen sclerosus. Swollen labia and clitoris of a cyanotic shade before treatment (A). Slight hyperpigmentation of vulva after treatment (B).*

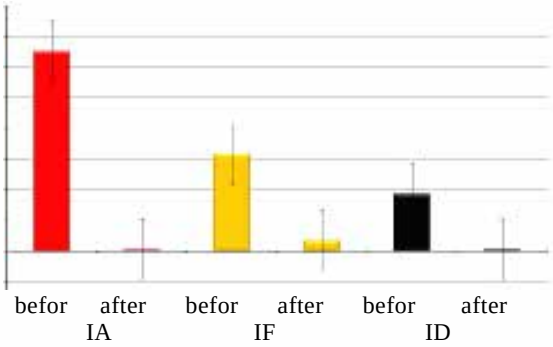

Figure 1. *The dynamics of the average values of index of activity, fibrosis index and discomfort index before and after 12 months of treatment*

childhood, namely, a low level of discomfort in the affected area. Apparently, this is due to the fact that children always make few complaints and do not concentrate on their own painful sensations, unlike adults. At the same time adolescents with AnLS are likely to be afraid to complain to parents about discomfort in the intimate area, due to the psychological characteristics of puberty age. It should be mentioned that in all the cases, the pathogenetic therapy of the disease led to the elimination of pain, without using additional medications.

The results of the psychological state assessment of the children in the studied group before and after treatment are shown in table 2. Thus, 7 patients (58.3%), not only had emotional changes and impaired motivation, but also communication problems. When analyzing the initial level of anxiety (according to the CMAS scale and the projective test), three levels of anxiety were revealed in the group - very high in a greater number of children - (75%), significantly increased (16.7%) and slightly increased (8.3%) . The obtained data indicate that, there was a rather high level of anxiety and emotional-volitional disorders in our group of children with AnLS.

Table 2.

The dynamics of the psychological state of patients with anogenital lichen sclerosus(AnLS) before and after 12 months of treatment.

Patient No.	Age (Sex)(years)	Age of disease onset	Luscher test in points		Anxiety level in points		IMOS points % of clinical improvement
			bef.	aft.	bef.	aft.	
1.	7 (F)	3	9	6	4	2	100
2.	11(F)	3	10	6	4	3	50
3.	12(F)	4	11	7	4	3	50
4.	6(F)	5	8	5	4	2	100
5.	9(F)	8	10	5	3	2	100
6.	8(F)	7	8	7	4	3	100
7.	8(F)	6	10	8	4	2	100
8.	9(F)	6	12	7	3	1	100
9.	4(F)	4	8	6	4	2	100
10.	3(F)	3	5	4	4	3	100
11.	4(F)	4	8	6	4	2	100
12.	14(M)	13	12	8	2	2	50

The further monitoring of children during the AnLS treatment showed positive dynamics of psycho-emotional state of various extent in all the patients. The nature of the changes was objectively correlated with the age of children. So, in patients under 9 years of age, there was a more pronounced positive dynamics of the Lusher test and better points on the anxiety scale. Half of the children had a decrease to insignificant levels, in 83% of patients there was an improvement. Minimal changes were recorded in a 14-year-old patient, both on the Luscher test and on the anxiety scale. Most likely, this can be explained by the negative emotional lability, not only due to somatic illness, but also puberty. The dynamics of the Luscher test and the level of anxiety during the treatment are presented in figure 6.

Hence, comparing the dynamics of AnLS as an underlying disease during treatment with the dynamics of concomitant emotional-volitional disorders and the level of anxiety, we can report that the psycho-emotional restoration of children with recovery and reduction of pain occurred to a lesser extent. There is still a lag in the improvement of motivation, emotional positivity and communication, as compared with the pronounced positive dynamics of AnLS in the same time period. The obtained data reflect deep psycho-emotional disorders of children, manifested by high anxiety, diminished emotional expression, behavioral deprivation, im-

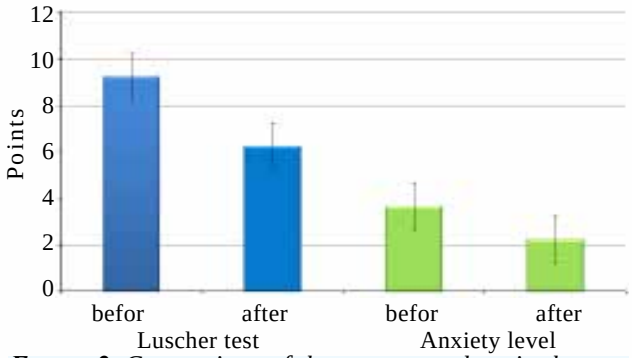

Figure 2. *Comparison of the average values in the points of the Luscher test and the level of anxiety before and after 12 months from the start of therapy.*

paired motivation caused by somatic disease.

Thus, the group of AnLS patients mostly included girls with a disease onset before puberty. In 40% of the patients, AnLS was accompanied with morphea lesions on the trunk. In the majority of cases (75%), treatment with the use of immunosuppressants was systemically prescribed in view of the ineffectiveness of the previous local therapy. Approaches to the choice of drug therapy differed due to the severity of clinical manifestations, the combination of AnLS and morphea, and the presence of the immunological activity of the disease. In all the cases of systemic immunosuppressant administration, a positive treatment effect was achieved. At the same time, in three AnLS cases with short initial duration (up to 3 months), topical calcineurin inhibitors therapy was effective without the use of topical corticosteroids. A high level of anxiety and emotional-volitional disorders, as accompanying conditions of the somatic disease, was revealed.

Discussion

AnLS is a rare condition in children, which occurs in girls more often than in boys. It has interdisciplinary character and the awareness of pediatricians, gynecologists, urologists, dermatologists and general practitioners about this rare disease is highly important. Making timely diagnosis of AnLS in the first 3-6 months after the onset allows to initiate therapy, achieve good effect from the topical immunosuppresant treatment, to avoid systemic administration of glucocorticoid and cytostatic therapy and to prevent serious complcations. Doctors should not ignore routine examination of the whole skin surface of a child, including the anogenital zone. Since AnLS often proceeds without complaints, and older children possess independent hygienic skills, can wash themselves, thus, parents often see the skin changes in the child's genitals late and consult a doctor after long-term manifestations of the disease. It is obvious that in case of morphea lesions, it is necessary to carefully examine the anogenital area, since AnLS and morphea usually coexist.

Our treatment experience of AnLS in children is modest. AnLS is normally treated by dermatologists, or gynecologists and urologists. These patients appeared in a rheumatological hospital mostly because of the ineffectiveness of the previously conducted local therapy, including topical corticosteroids. Possibly, the low efficiency of therapy was due to the long-term lack of accurate implementation of prescriptions and recommendations by the parents. Anogenital localization always causes great psychoemotional anxiety in both children and parents, fears of the outcome leading to impaired sexual function and fertility. And then parents initiate numerous consultations with various specialists, instead of accurately following the treatment recommendations.

Along with this, almost half of children with AnLS had manifestations of morphea lesions on the trunk, thus serving as a reason for referring the patient to a rheumatologist to rule out systemic scleroderma. Five out of 12 patients of the examined group received oral prednisolone treatment, which may be considered to be rather aggressive, probably influenced by rheumatology profile of our department; on the other hand, it resulted in remission in all the cases and was well tolerated, with no relapses. In the literature, there is evidential data about the positive experience of using glucocorticosteroids and methotrexate in case of topical treatment resistance.

It is obvious that the first treatment choice medication in children with AnLS without concomitant morphea should be local therapy with the use of topical corticosteroids and calcineurin inhibitors.

The data we received about the psycho-emotional disorders in children and adolescents with AnLS is of great interest. We revealed a high level of anxiety and emotional-volitional disorders persisting longer than the activity of the underlying disease. Normalization of the emotional-volitional disorders, a decrease in the level of anxiety occurs later than the clinical and subjective AnLS manifestations disappear. The so-called psychosomatic "trail" of the disease necessiates additional participation of a psychologist and neuropsychiatrist in the treatment of children with AnLS.

Since AnLS is a rare condition for children, the monitoring of patients by doctors of various specialties is highly important. It is also advisable to conduct studies in quite a large group of children and, in cooperation with doctors of different profiles to develop consensus in treatment, including agreed indications for the systemic immunosuppressant administration.

Thorough examination of skin and mucosa helps to timely diagnose a child with AnLS . Modern therapy of AnLS is stepwise, starting with local topic steroids and calcineurin inhibitors, followed by systemic steroids and methotrexate in case of local treatment resistance.

Conclusion

AnLS is a rare condition in children which can lead to severe complications and negative outcome, such as anatomical and functional disorders of the genitourinary system, and cause deep psychoemotional disorders in children and adolescents. Modern therapy of AnLS is stepwise, starting with local topic steroids and calcineurin inhibitors, followed by systemic immunosuppressants, if local treatment is ineffective, which significantly improves the prognosis and outcome of the disease. The deep psychoemotional disorders revealed in children with AnLS require including the serious work of psychologists in the complex of therapeutic measures, as well as treatment provided by a neuropsychiatrist, if necessary.

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