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Methodology Article

Dynamics of Phenotypic Manifestations of Connective Tissue Dysplasia in Children with Uroandrological Pathology in the Age Aspect

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Abstract: *Introduction*. A comparative study of the phenotypic manifestations of undifferentiated connective tissue dysplasia in children of various age groups with urological and andrological pathology is carried out in the article. *Materials and methods*. The study included 214 children aged 1 month to 17 years with clinical manifestations of undifferentiated connective tissue dysplasia, who were treated in the pediatric uroandrological department for congenital malformations and diseases of the genitourinary system. When establishing undifferentiated connective tissue dysplasia, a generally accepted table of external phenotypic markers was used with their scores. *Results*. In infants, abnormalities of the auricles and skin are most often detected. In pre-school age, craniocephalic abnormalities, pathology of the osteoarticular system, and abnormalities of the auricles were detected in the largest percentage of cases. The study found that an increase in the percentage of detection of ocular abnormalities increases with age. Moreover, 2 or more eye abnormalities were most common in older children. Anomalies of the oral cavity were diagnosed in only a quarter of infants and were manifested in them by a single sign. In older age categories, anomalies of the oral cavity were observed in more than half of patients, and often they were not single. During the examination of senior schoolchildren, it was noted that all children of this age category had some kind of abnormality from the osteoarticular system, and almost always they were multiple. *Conclusion*. Somatic manifestations of undifferentiated connective tissue dysplasia are often multi-organ in nature and often have nonspecific clinical symptoms. Identification of the patterns of formation of uroandrological pathology in patients of various age groups against the background of connective tissue failure will provide timely prevention and correction of visceral manifestations of dysplasia in children.

Keywords: Children, Dysplasia, Connective Tissue, Phenotypic Signs, Uroandrological Diseases

1. Introduction

Recently, the role of undifferentiated connective tissue dysplasia (NSTD) has been increasing in the structure of diseases of pediatric patients [1, 2]. The study of visceral manifestations of connective tissue dysplasia in children is increasingly reflected in the literature of recent years [1, 3-6]. Currently, there are indications of the chronological sequence of the formation of various somatic pathologies in children and adolescents in the age aspect [5]. The most common manifestations of dysplasia are studied by the authors in children of the school age group [1, 2]. In particular, scientific publications provide data on the state of the autonomic nervous system in schoolchildren on the background of connective tissue failure [2]. An association of kidney and urinary tract pathologies in schoolchildren has been described [1]. However, to date, there is practically no information about the characteristics of the phenotypic manifestations of connective tissue dysplasia in urological diseases in different

periods of childhood.

Obviously, in the development and course of congenital uroandrological pathology, the association of these diseases with the syndrome of undifferentiated connective tissue dysplasia is of great importance, since the negative influence of dysplastic processes on the formation of the maturity of the functional structures of connective tissue, including the urinary and genital system, has been proved [9-11]. The emerging trend towards an increase in congenital uro-adrological pathology in the population of children dictates the need for further study of this problem in the age aspect, in order to identify risk factors for the development and characteristics of the pathology of the kidneys, urinary tract and genital organs in boys if they have signs of connective tissue dysplasia. [12-15]

The aim of the study was a comparative analysis of phenotypic manifestations of connective tissue against dysplasia in case of urological diseases in different periods of childhood.

2. Materials and methods

The present study was conducted in the uroradrological department for children of the Ivanovo Regional Clinical Hospital.

The work is based on the results of examination and treatment of 214 people with various uroandrological pathologies.

The well-known classification of periods of childhood [7, 8], which includes:

The period of intrauterine (antenatal) development (40 weeks)

II. Intranatal period (the period from the onset of labor to the birth of the baby)

III. Extrauterine period:

Newborn period - from birth to 4 weeks:

from birth to 7 days - early neonatal period,

from 7 days to 28 days - late neonatal period.

2. The period of infancy (infancy or younger nursery) - from 4 weeks to 12 months

3. Preschool age - from 1 to 3 years

4. Preschool age - from 4 to 6 years

5. Younger school age - from 7 to 11 years old,

6. Senior school age - from 12 to 17-18 years,

The study included 5 periods: infancy, pre-school age, preschool age, primary school age and senior school age.

The spectrum of urological pathology included pyeloectasia, vesicoureteral reflux (PMR), communicating dropsy of testicular membranes, cryptorchidism, hypospadias, varicocele and phimosis. Below is a characteristic of uroandrological pathology in children of observation groups (table 1) by age.

When examining children, we used the standard table of phenotypic manifestations of dysplasia, which includes craniocephalic signs, eye manifestations, abnormalities of the oral cavity, bone-articular changes and external changes on the part of the skin, its appendages and muscles. When assessing the external manifestations of dysplasia, the presence or absence of a specific symptom in a child was taken into account. We also studied the percentage of two or more stigmas from this group of phenotypic manifestations of mesenchymal insolvency in each age category of patients observed.

Table 1. *Congenital uroandrological pathology in the examined children in the age aspect.*

Nosological form	The number of children examined at different age periods				
	A	B	C	D	E
Pieloectasis	45	10	7	9	7
Reflax	1	7	6	10	3
Hydrocele	1	12	12	3	-
Cryptorchidism	-	10	5	6	-
Hypospadias	-	2	3	3	2
Varicocele	-	-	-	3	26
Phimosis	-	-	10	9	2
TOTAL	47	41	43	43	40
TOTAL	214				

A - breast age, B – infant age, C – preschool age, D – primary school age, E – senior school age.

3. Results

An analysis was made of the frequency of occurrence of phenotypic manifestations of connective tissue dysplasia in the examined children at different age periods. Its results showed the following (table 2).

Table 2. *Phenotypic manifestations of dysplasia in children during various periods of childhood (%).*

Stigmas		childhood				
		A	B	C	D	E
Craniocephalic	Presence	66	88	67	79	83
	2 or more signs	23	86	72	74	58
Ophthalmic	Presence	36	58	44	42	60
	2 or more signs	18	46	42	44	37
Oral cavity	Presence	25	61	60	65	58
	2 or more signs	-	56	38	61	43
Auricles	Presence	85	76	88	88	90
	2 or more signs	35	55	53	55	50
Osteoarticular system	Presence	64	80	98	98	100
	2 or more signs	60	79	95	90	93
Skin, its appendages and muscles	Presence	70	58	65	60	68
	2 or more signs	64	71	57	81	52

In infants, abnormalities of the auricles and skin were most often detected (85% and 70%, respectively). Craniocephalic abnormalities and pathology of the osteoarticular system occurred in more than half of children in this age category (66% and 64%). In a third of children, ocular changes were detected (36%), in a quarter of cases - anomalies of the oral cavity (25%). In pre-school age, craniocephalic abnormalities (88% of children of this age group), bone-articular system pathology (80%) and auricle abnormalities (76%) were detected in the largest percentage of cases.

Craniocephalic abnormalities were most often detected in children of preschool age (88%) and schoolchildren (79% - 83%), moreover, in children of preschool age craniocephalic

manifestations were noted by two or more signs, while in infancy these stigmas were detected in lesser percent of cases (66%), and the presence of two or more craniocephalic malformations was detected only in 23% of infants.

Table 3. *Phenotypic signs of connective tissue dysplasia in children at different age periods (%).*

Phenotypic signs of dysplasia	**childhood**				
	A	**B**	**C**	**D**	**E**
Craniocephalic					
Fused eyebrows	+	+	+	+	+
Saddle nose	+	+	+	+	+
Flat nape	+	+	+	+	+
Curved nose	-	+	+	+	+
Flat face profile	+	+	+	+	+
Occipital spur	+	+	+	+	+
Two tops	+	+	+	+	+
Wide nose bridge	+	+	+	+	+
Canted forehead	+	+	+	+	+
Short neck	+	+	+	+	+
Nasal septum curvature	+	+	+	+	+
Eye					
Short palpebral fissures	-	+	-	+	+
Blue sclera	-	+	+	-	+
Narrow palpebral fissures	+	+	+	+	+
Epicant	+	-	+	-	-
Telekant	+	+	+	+	+
Hypothelorism	+	+	-	+	+
Hypertelorism	+	+	+	+	+
Mongoloid eye incision	+	-	-	-	+
Ptosis	-	+	-	+	+
Heterochromia of the iris	-	+	-	-	+
Antimongoloid eye incision	+	+	+	+	+
Improper eyelash growth	-	-	-	-	+
Myopia	+	-	+	-	+
Hypermetropia	-	-	+	+	-
Astigmatism	-	-	+	+	+
Strabismus	+	+	+	-	+
Abnormalities of the oral cavity					
Short frenum of the tongue	-	+	-	-	-
Mowed chin	+	-	-	-	+
Thick lips with furrows	-	+	-	+	+
"Gothic sky"	+	+	+	+	+
Progenia	-	-	-	+	+
Dysplasia	-	+	+	+	+
Trema	-	+	+	+	+
Malocclusion	-	+	+	+	+
Multiple dental caries	-	+	+	+	+
Abnormalities of the auricles					
Low location	-	-	+	+	-
Augmented lobe	+	+	+	+	+
Big ears	+	+	+	+	+
Protruding ears	+	+	+	+	+
Thickened ears	+	+	+	+	+
Incomplete development of the ear curl	-	+	+	+	+
Small and missing lobe	+	+	+	+	+
Soft auricles	+	-	-	-	-
Oblique direction of the auricles	+	-	+	+	+
Lack of tragus	+	+	-	-	+
Abnormal fistula	+	-	-	-	-
Parotid appendages	+	-	-	-	-
Auricle deformity	+	+	+	+	+
Anomalies of the osteoarticular system					
Dolichostenomelia	+	-	-	-	+
Moderate joint hypermobility	-	-	+	+	+
Severe joint hypermobility	-	-	+	-	-
Short pinky	-	-	+	-	+
Partial Syndactyly	+	-	-	-	-
Polydactyly	+	-	-	-	-
Thickening of the nail phalanx	-	+	+	-	-

Phenotypic signs of dysplasia	childhood				
	A	B	C	D	E
Transverse palmar fold	+	+	+	-	+
Brachidactyly	-	+	+	+	+
Arachnodactyly	-	+	+	+	+
Imbalance in finger sizes	-	+	+	+	+
Varus or hallux valgus	+	+	+	+	+
Clubfoot	+	-	-	-	+
Congenital muscular torticollis	-	-	+	-	-
Calcaneal feet	+	-	-	-	-
The predominance of 2 toes over the 1st	+	-	-	-	-
Pathological kyphosis of the thoracic spine	+	+	+	+	+
Lordosis of the lumbar spine	-	-	+	+	-
Asymmetry of standing blades	-	+	+	-	+
Symptom of a “straight” back	-	-	+	+	+
Pain in the spine	-	-	+	+	+
Funnel chest deformity	-	-	+	-	-
Keeled chest deformity	-	+	+	-	+
Severe chest deformity	-	-	-	+	+
Scoliosis of the 1st degree	-	-	+	+	+
Scoliosis 2 degrees	-	+	+	+	+
Scoliosis 3 degrees	-	-	-	-	-
Flat feet	+	+	+	+	+
Sandal-shaped slit	+	+	+	+	+
Wide short toe	+	+	+	+	+
Hallus valgus	-	-	-	+	-
"Natoptyshy" on the back surface of the feet	-	+	-	+	-
Arthralgia	-	-	+	-	+
Recurrent dislocation / subluxation of joints	-	-	-	+	-
History of hip dysplasia	+	+	+	-	+
Asymmetry of the length of the legs	-	+	-	-	-
Pterygoid scapula	+	+	+	-	+
Flat Back	-	+	-	-	+
Spina bifida	+	-	-	-	-
Anomalies of the skin, its appendages and muscles					
The skin is velvety, tender	+	+	+	+	+
Thin skin	+	+	+	+	+
Dilated vasculature	+	+	-	+	-
Skin hyperalasticity	-	-	-	+	+
Keloid scars	-	-	-	-	+
Absence or hypoplasia of the nipples	-	-	-	+	-
Hemangiomas	+	-	-	-	-
Nevuses are large	+	+	+	+	+
Multiple nevi	+	+	+	+	+
Hyperpigmentation of the skin	+	-	-	+	+
Skin depigmentation	-	-	-	+	-
Different nipple levels	+	+	+	+	+
Hypertelorism of the nipples	+	+	+	+	+
Hirsutism	-	+	-	+	+
Hyperstretching of the skin	-	-	-	+	-
Ecchymoses, petechiae, nosebleeds	+	+	-	-	+
Endothelial tests	-	+	+	+	+
Striae	-	-	-	-	+
Hypertrichosis	-	-	+	-	-
Venous expansion	+	+	+	+	+
Nail changes	-	+	+	+	+
Myatonic syndrome, diastasis of the rectus abdominis muscles	+	+	+	+	+
Hernia, prolapse of organs	+	+	+	+	+
Umbilical ring low standing	+	-	-	-	-
Sacred Sinus	+	-	-	-	-

An increase in the percentage of detection of eye abnormalities increases with age - from 36% - in infants - up to 60% - at senior school age. Moreover, we observed 2 or more eye abnormalities in a child in the group of infants in only 18% of cases, while in older ages this percentage reached 42-46.

Anomalies of the oral cavity were diagnosed in only a quarter of infants and were manifested in them by a single sign. In older age categories, anomalies of the oral cavity were observed in more than half of patients, and often they were not single.

Almost all children of senior school age (90%) had

abnormalities of the auricles, and in half of them these stigmas were multiple (50%). In infancy, several abnormalities of the auricles were diagnosed in every third child (35%), although the overall percentage of these stigmas was also high (85%).

During the examination of senior schoolchildren, it was noted that all children of this age category had some kind of abnormality from the osteoarticular system, and almost always they were multiple (93%). As age decreases, the percentage of these stigmas decreased, reaching a minimum in infants (64%).

Anomalies of the skin, its appendages and muscles in the largest percentage of cases were diagnosed in infants (70%).

The presence (+) or absence (-) of phenotypic signs of connective tissue failure in the examined patients at different periods of childhood is presented in table 3.

4. Discussion

A comparative characteristic of phenotypes of children with uroandrological pathology against the background of undifferentiated connective tissue dysplasia showed some dynamics of the external manifestations of dysplasia in the age aspect.

In infants, abnormalities of the auricles and skin are most often detected. A third of the children showed ocular changes, in a quarter of cases - abnormalities of the oral cavity. An increase in the percentage of detection of ocular anomalies and abnormalities of the oral cavity increases with age.

Craniocephalic abnormalities were most often detected in preschool children and schoolchildren, and in patients of preschool age, these phenotypic manifestations of dysplasia were noted by two or more signs, while in infancy these stigmas were detected in a smaller percentage of cases, and the presence of two or more craniocephalic developmental abnormalities were detected in a quarter of infants.

Almost all children of senior school age had abnormalities of the auricles, and in half of them these stigmas were multiple. In infancy, a few abnormalities of the auricles were diagnosed in every third child, although the overall percentage of these stigmas was also high.

During the examination of senior schoolchildren, it was noted that all children of this age category had some kind of abnormality from the osteoarticular system, and almost always they were multiple. As age decreases, the percentage of these stigmas decreases, reaching a minimum in infants.

The identification of such patterns of the prevalence of certain markers of dysplasia is relevant, since it is the basis for creating a phenotypic portrait of a child of a particular age with a given nosological form and timely correction of treatment and diagnostic measures for various uroandrological pathologies in children against the background of undifferentiated connective tissue dysplasia.

5. Conclusion

The study of the external manifestations of connective tissue dysplasia in children with uroandrological pathology in the age aspect was carried out. The regularities of the predominance of certain phenotypic markers of dysplasia in diseases and abnormalities of the development of the genitourinary system in various periods of childhood were revealed.

6. Summary

The study of external manifestations of connective tissue dysplasia in children with uroandrological pathology in the age aspect. Identified patterns of the prevalence of particular phenotypic markers of dysplasia in diseases and anomalies of development of organs of the urogenital system in different periods of childhood.

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