Journal Information Journal ID (issn): 2414-1518
Title: Galician Medical Journal Abbreviated Title: Galician med. j.
ISSN (electronic): 2414-1518
Publisher: Ivano-Frankivsk National Medical University
Article Information
Publication date: 5 September 2016
Volume: 23 Issue: 3
Electronic Location Identifier: 10.21802/gmj.2016.3.19
DOI: 10.21802/gmj.2016.3.19

Informativeness of phenotypic features of connective tissue dysplasia in children with peritoneal adhesions

MG Melnichenko
Email: marina_gm[@]i.ua
Odessa National Medical University, Odessa, Ukraine
AA Kvashnina
Odessa National Medical University, Odessa, Ukraine

Abstract

Connective tissue dysplasia can be realized with a large number of clinical variants, and accordingly, excessive postoperative adhesion formation can be considered as a manifestation of dysplastic-dependent processes. In the predominant number of surveyed children (93.8%) CTD has developed on the background of existing connective tissue dysplasia syndrome, i.e. the presence of external signs of this condition may serve as a predictor of postoperative complications of adhesions in children.

Direct correlation between the number of CTD phenotypic characters and the prevalence of intra-abdominal adhesions was determined. In our view, it allows to detect children at risk of peritoneal adhesions on the basis of external features that can be identified during general examination and do not require additional time or equipment. Accordingly, the surgical treatment of children with signs of CTD syndrome requires an integrated approach and the application of measures to prevent excessive adhesion formation, including intraoperative use of anti-adhesive gels.

Problem statement and analysis of the recent research

According to the data of different authors, postoperative peritoneal adhesions occur in 63-97% of patients after abdominal surgery [1, 3, 6]. They lead to severe complications such as adhesive intestinal obstruction, chronic pain syndromes, anatomical and topographical violation of the location of the pelvic organs and their functions. They are a risk factor for ectopic pregnancy and

tubal-peritoneal factor of reproductive disorders in girls [1, 3, 6]. Hereditary predisposition is important among risk of peritoneal adhesions as a multifactorial disease [2, 7]. Nowadays, role of connective tissue dysplasia in the development and progression of a large number of pathological conditions in children has been proved. Morphofunctional disorders of connective tissue determine the conditions for the formation of immune patological reactions [4, 7], which are the basis of pathological adhesions [3, 5, 6]. Accordingly, the presence of stigmas and severity of CTD syndrome may be an indirect sign of genetic predisposition to pathological adhesions and to assess the risk of complications in the individual patient. Identification of prognostically significant features on the basis of the data will promote the development of ways to optimize the diagnosis as a prevention of postoperative adhesions complications in children with surgical pathology of the abdomen and the pelvis.

The objective of the research was to evaluate the information content of the phenotypic clinical signs of connective tissue dysplasia in children with adhesive intestinal obstruction.

Materials and methods

62 children were involved into the study. They were treated in different departments of the Odessa Regional Children's Hospital at the age of 3 to 16 years for the period from September 2013 to March 2016. The first study group consisted of 30 children with medium and high severity stigmas of nonspecific connective tissue dysplasia (CTD) who did not have surgical diseases. The second group included 32 patients who were treated in surgical wards concerning the adhesive intestinal obstruction (AIO). The majority of children (29 - 87.5%) were hospitalized with late AIO. Complete intestinal obstruction was observed in 68.3% (22) patients. Three patients (9.4%) were hospitalized repeatedly concerning AIO during the observation period. 27 (84.3%) patients required surgical treatment. There were 19 boys (59.4%), 13 girls (40.6%). Children over 6 years (84.4%) predominated, i.e. the age contingent that underwent surgery the most often.

Clinical research method included follow-up and physical aspects: the study of past medical history, the course of the disease, general and local manifestations of symptoms. Patients' survey was conducted systematically according to generally accepted principles of patient's clinical examination. The presence and severity of phenotypic traits of nonspecific connective tissue dysplasia was evaluated additionally according to the questionnaire based on existing literature data. The questionnaire included features that could be quickly identified in the external examination and required no additional equipment for their determination.

Results and Discussion

Taking into account the variety of the phenotypic signs of connective tissue dysplasia, we considered it expedient to assess the informational content of phenotypic clinical signs according to the initial examination of the studied children. For this purpose we examined children in both groups and showed clinical signs that could be formalized for statistical analysis. According to the data analysis, significance level was determined in the distribution of the number of children with clinical signs specific gradation using Pearson criterion χ^2 ($p<0.05$). 13 phenotypic traits according to 34 gradations were identified. Not probability, but informative content of selected features was evaluated quantitatively assessing the contribution of each trait in a pathological condition among children of groups 1 and 2.

Despite the fact that all of the signs were detected more often in children with systemic connective tissue lesions, this difference was not always statistically significant. In particular,

signs pathogenetically being not a manifestation of metabolic disorders in the extracellular matrix of connective tissue detected a statistically insignificant difference ($p>0.05$). For example, epicanthal fold, fused lobe, protruding ears, webbed fingers and hypertelorism are disembriogenesis stigmas and are not based on collagen synthesis violation. Symptoms prevalent in the pediatric population are of multifactorial nature and may be a manifestation of systemic dysplasia, the result of environment factors. They also did not demonstrate a statistically significant difference between the groups for a given sample size. An example of such phenotypic traits is scoliotic posture, vision pathology, pale skin, the presence of pigmentation and so on.

The same conclusion can be drawn also in relation to signs that are rare in the population and, consequently, in the treatment group (such as carinate chest distortion, hollow foot, diastasis recti abdominis, etc.). The biggest informative statistics have signs that are the evidence of structural or functional failure of the connective tissue, such as joints hypermobility, for which the value of χ^2 criterion was 27.310 ($p<0.01$). Namely, this feature may in most cases be sufficient for determination of CTD, especially in children of older age groups. Young children are more appropriate to undergo a comprehensive assessment as hypermobility may be a manifestation of morphological and functional immaturity of connective tissue. Table 1 shows the ratio of children with certain categories of 13 phenotypic traits (34 gradations) for children of groups 1 and 2, and the importance of information measures for these signs. According to the table of critical values, criterion χ^2 larger than 3.841 is statistically significant at $p<0.05$, at a given number of degree of freedom.

Table 1.

Informative content of CTD phenotypic signs in children

SIGN	Number of manifestations		χ^2 ($p<0,05$)
	1 Group	2 Group	
Joints hypermobility	**19**	**1**	**27.310**
Asthenic figure	**18**	**10**	**6.563**
Epicanthus	5	3	0.122
Hypertelorism	5	1	2.028
Blue sclera	**11**	**1**	**8.259**
Vision pathology	8	2	2.987
Nasal septum asymmetry	6	2	1.350
Saddle nose	4	1	1.244
Gothic palate	**9**	**1**	**6.172**
Dentofacial abnormalities	**11**	**3**	**4.375**
Adherent lobe	4	4	0.216
Protruding ears	6	5	0.044
Pale skin	16	8	2.828
Severe venous pattern	12	5	2.440
Hyper elasticity of skin	**13**	**2**	**9.343**
Skin like suede	**9**	**2**	**3.988**
Skin wrinkling	5	3	0.122
Pigmented spots	7	3	0.945
The presence of “scars on the skin”	2	1	0.122
Chest distortion	**8**	**1**	**4.986**
Postural disorder	**14**	**5**	**4.644**

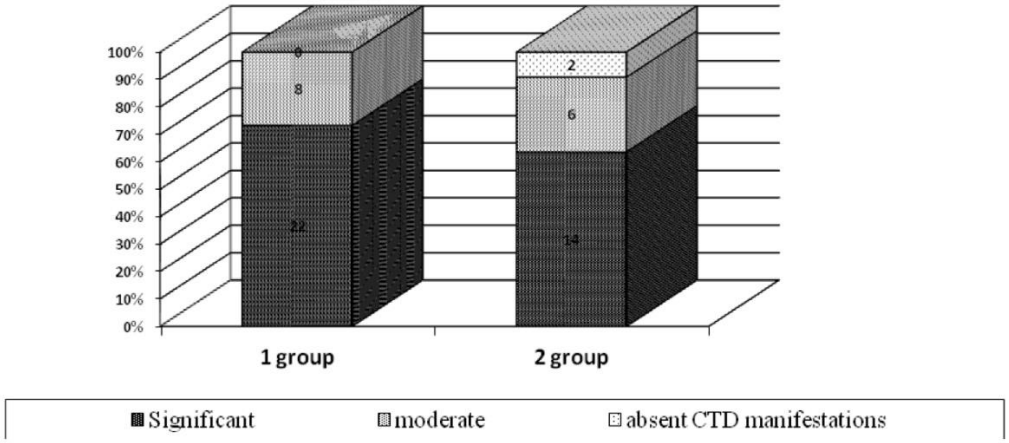
Arachnodactyly	**7**	**1**	**3.902**
Clinodactyly	10	3	3.304
Incomplete webbed fingers	2	1	0.122
Tarsoptosia	**11**	**2**	**6.374**
Hollow foot	1	0	0.772
Sandal gap	3	0	2.461
“Clavus”	5	1	2.028
Hallux valgus	1	0	0.772
Foot cross-striation	3	1	0.588
Easy bruising	**13**	**4**	**5.042**
Herniae	**9**	**2**	**3.988**
Diastasis recti abdominis	1	0	0.772
Abdominal muscles weakness	6	2	1.350

According to the Table 1, the highest χ^2 index referred to hypermobility of joints (27.310) as the main phenotypic sign of CTD. Sufficient difference was also observed between such signs as skin hyperelasticity (9.343), blue sclera (8.259), asthenic physique (6.563), hollow foot (6.374), high “Gothic” palate (6.172), tendency to easy bruising even in case of minor injuries (5.042), congenital chest distortion (4.986) and violations of posture (4.644), abnormalities of dentofacial system (4.375), presence of the carina (3.988). These phenotypic traits are the most important for screening assessment of the connective tissue failure in clinical practice. According to the estimation of informative content of phenotypic traits we divided them into significant, minor and moderate symptoms. Thus, hypermobility of joints was determined the leading sign with the maximum value of $\chi^2 = 27.310$. Secondary signs included phenotypic manifestations from χ^2 of more than 5 units (6 characters); moderate signs involved χ^2 less than 5 (7 characters). Belonging to the phenotypic characteristics of informative content may indicate the degree of systemic dysplasticity.

According to the presence and degree of severity of CTD symptoms, patients in the treatment group were distributed as follows (Figure 1).

Fig. 1.

CTD manifestations in patients of studied groups



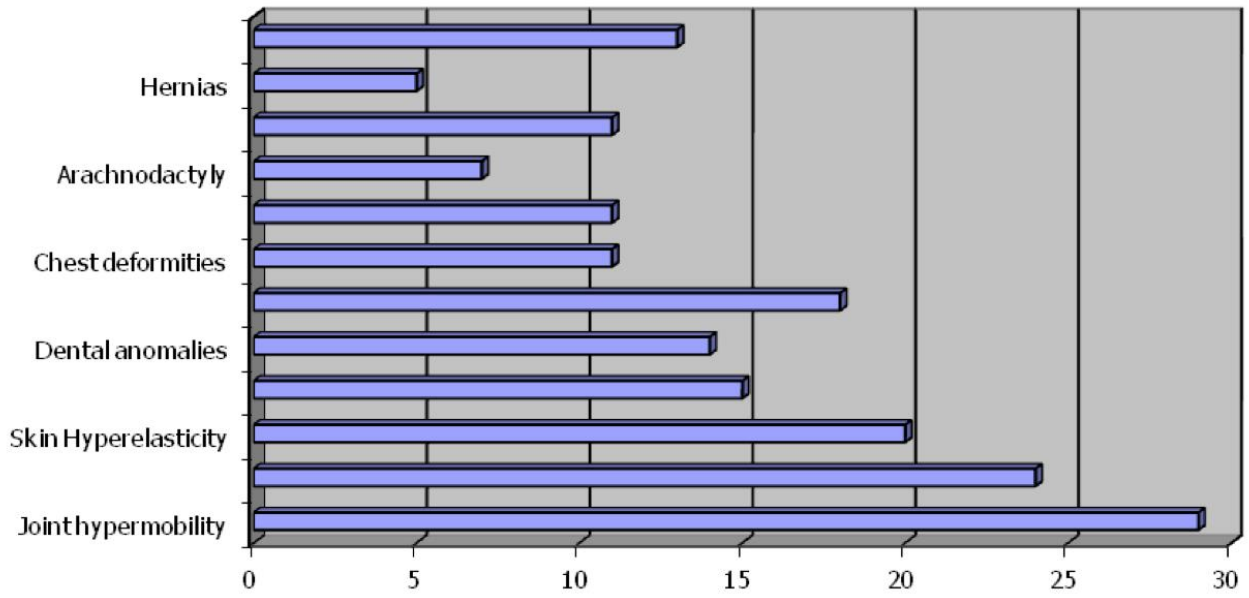
As can be seen from the chart, the first group was stratified on the basis of the presence of CTD stigmas, therefore high severity of systemic destruction of connective tissue was determined in in 22 children of the second clinical group, moderate stigmatization of connective tissue dysplasia was observed in 8 patients, absence or small number of stigmas was considered an exclusion criteria from the group.

Regarding the children in the second group consisting of patients who were treated at ORCH on CTD, signs of severe connective tissue dysplasia were detected in 14 (43.8%) patients, moderate in 16 (50%) cases; two children (6.2%) had a small number of stigmas. Thus, in 93.8% of children adhesive ileus developed against the background of connective tissue dysplasia syndrome.

Percentage of stigmatization in the first study group was much higher than the populational one. The average number of stigmas identified among children from AIO constituted 10.38 ± 4.55, which was also significantly higher than the average number of stigmas among healthy children (Student t-test: 4.40, ($p < 0.05$)). Prevalence of certain main CTD features among children with AIO is shown in the diagram in Figure 2.

Fig. 2.

The frequency of main CTD features in children with AIO



As seen from the Figure 2, the majority of children of study groups had the combination of leading dysplasticity features. The distribution of frequencies of certain dysplastic stigmas was similar to the distribution among children of the 1 group.

Two patients with CTD without clinically significant amount of phenotypic signs of connective tissue dysplasia in past medical history had indications of the prevalence and duration of intra-abdominal inflammation prior to the initial intervention. Namely, independent risk factors for

excessive formation of peritoneal adhesions involve reference to the doctor later than 2 days after the onset and spread of fibrinous-purulent peritonitis being detected intraoperatively.

We also noted the correlation between the number of stigmas of connective tissue dysplasia and the prevalence of peritoneal adhesions. In order to determine the statistical significance of the relation between the severity of adhesions and the number of external signs of CTD, Pearson correlation coefficient was calculated between index values of intra-abdominal adhesions and definitions of CTD signs for every patient in the first study group.

The correlation coefficient (r) constituted 0.699 determining a direct connection between the studied signs. The number of degrees of freedom (f) was 30. Correlation ratio according to Chedoke scale was evident; Student's t-test constituted 5.348. The critical value of Student's t-test for a given number of degrees of freedom constituted 2.042 at ($p<0.05$), respectively, statistically significant dependence of attributes.

The equation of the pair linear regression: $y = 0.30850 + 1.34097x$. The coefficient of determination r2 equaled 0.488 indicating a significant direct connection between the values of the studied signs. The average error of approximation amounted 31.7%.

The correlation between the severity of connective tissue dysplasia and time of surgery concerning AIO was also analyzed. The correlation coefficient (r) equaled 0.421. The number of degrees of freedom (f) was 30; Student's t-test equaled 2.543, dependence attributes were statistically significant ($p<0.05$). The observed connection between the studied signs was direct, Correlation ratio according to Chedoke scale was moderate, because the surgery time is a multifactorial indicator depending on many factors such as strangulation, type of intervention, the presence of peritonitis, type of surgical access, localization of the pathological process, intraoperative complications, surgeon's operating experience and so on.

The differences in the haemogram index at the time of hospitalization depending on the degree of CTD stigmatization were not statistically significant ($p>0.05$).

Conclusions

Thus, AIO developed on the background of existing connective tissue dysplasia syndrome in the predominant number of children (in 93.8%). The presence of external signs of this condition may serve as a predictor of postoperative complications of adhesions in children.

Direct correlation between the number of CTD phenotypic signs and the prevalence of intra-abdominal adhesions was identified. In our view, connective tissue dysplasia can be realized through a large number of clinical variants, and accordingly, excessive postoperative adhesion formation can be considered as a manifestation of dysplastic-dependent processes. From the perspective of clinical practice, this allows to detect children who are at risk of peritoneal adhesions on the basis of external signs that can be identified in the course of general examination and do not require additional time or equipment that is particularly important to assist this group of patients in terms of urgent service. Accordingly, the surgical treatment of children with CTD signs requires an integrated approach and the use of excessive adhesions prevention, including the use of intraoperative anti-adhesive gels.

References

1 HW Grant, MC Parker, MS Wilson, al et. Adhesions after abdominal surgery in children. J Pediatr Surg. 2008;43(l):152-156.

2 W Arung, M Meurisse, O Detry. Pathophysiology and prevention of postoperative peritoneal adhesions. World Journal of Gastroenterol. 2011;17:4545-4553. doi:10.3748/wjg.v17.i41.4545. Cited in: PubMed; PMID 22147959. PMCid: PMC3225091

3 J-J Duron. Postoperative intraperitoneal adhesion pathophysiology. Color Dis. 2007 Oct;9(s2):14-24. doi:10.1111/j.1463-1318.2007.01343.x

4 LN Russek. Examination and Treatment of a Patient With Hypermobility Syndrome. Physical Therapy. 2000:386-398. Cited in: PubMed; PMID 10758523

5 VF Demyn, SA Klyuchnikov, MA Klyuchnikova. Value of connective tissue dysplasia in the pathology of childhood age. Voprosy sovremennoi pediatrii. 2005;4 (1):50-56.

6 OV Sarkisova, VS Sukhorukov, VI Petlakh, et al. Mytohondrial violations in development of adhesive disease in children. Rossiyskiy vestnik perinatologiyi i pediatriyi. 2009;6 (54):88-91.

7 NP Shabalov, VG Arsentev. Pediatrics, National guidelines. Vol. 1. Moscow: HEOTAR-Media; 2009. Inherited tissue disease of connective tissue; p. 298-320.

Article Information (continued)

Categories:

Subject: Research Article

Keywords:

Keyword: connective tissue dysplasia

Keyword: children

Keyword: peritoneal adhesions