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Additional congenital defects in anorectal malformations

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Abstract From 1974 until 1995 a total of 264 (141♂, 123♀) patients born with an anorectal malformation (ARM) were referred to the University Hospital Nijmegen in the Netherlands. All additional congenital defects (ACDs) were registered. Special attention was paid to whether the ACDs take part in associations, syndromes, or sequences. One or more ACDs were observed in 67% of the patients. In decreasing order the defects concerned the uro-genital tract (43%), skeleton (38%), gastro-intestinal tract (24%), circulation (21%), extremities (16%), face (16%), central nervous system (15%), respiratory tract (5%), and remaining defects (5%). Associations were observed in 49% of the patients, mostly (in 44%) the Vertebral, Anorectal, Cardial, Tracheo-Esophageal, Renal and Limb association. In 5% of the patients syndromes were recognized. Sequences were seen in 2% of the patients. Remarkable is the combination of trisomy 21 and ARM without a fistula. The combination of ARM and the Zellweger syndrome has not been reported before.

Conclusion Almost all combinations of ARM and ACDs can be classified as an association, syndrome or sequence. ARM-causing agents affect males and females in equal numbers but lead to different expression in the sexes. The origin of the Omphalocele, Extrophia of the bladder, Imperforate anus, Sacral anomalies complex probably differs from that of other forms of ARM.

Key words Anorectal malformations · Additional congenital defects

Abbreviations *ACD* additional congenital defect · *ARM* anorectal malformation · *OEIS* omphalocele, extrophia of the bladder, imperforate anus, sacral anomalies · *VACTERL* vertebral, anorectal, cardial, tracheo-esophageal, renal, limb

Introduction

In the literature the incidence of anorectal malformations (ARM) varies from 1 in 1500–5000 births [5, 12, 14, 17, 23, 26]. Reported percentages of patients with one or more additional congenital defects (ACDs) vary from about 40% to 70% [2, 3, 7, 10, 24, 26, 29]. Several combinations of ARM and ACDs are expressions of known associations, syndromes, or sequences.

Here we describe a large group of patients with ARM. Special attention was paid to classification of ARM and ACDs, in particular to their combination in diagnostic categories of associations, syndromes, or sequences.

Patients and methods

All medical records of patients with ARM, referred to the Paediatric Surgical Department of the University Hospital Nijmegen

Table 1 Classification and numbers of patients

	Group A	Group B	Group C	Group D	Total
	– vesico intestinal fissure – complete ano-rectal agenesis	– persistent cloaca – vesical fistula – vaginal fistula – urethral fistula	– intermediate position of the rectal pouch* and absence of a recto-urogenital fistula – intermediate position of the rectal pouch* and transscrotal-perineal fistula	– vestibular fistula – perineal fistula – perineal fissure – covered anus – anal stenosis – anterior displaced anus	
Male	7 (44%)	48 (75%)	14 (74%)	72 (44%)	141 (53%)
Female	9 (56%)	16 (25%)	5 (26%)	93 (56%)	123 (47%)
Number of patients	16 (6%)	64 (24%)	19 (7%)	165 (63%)	264 (100%)
Survivors	8 (50%)	55 (86%)	17 (91%)	150 (91%)	230 (87%)
Non-survivors	8 (50%)	9 (14%)	2 (9%)	15 (9%)	34 (13%)

* Rectal pouch within the levator-muscle-complex, but at least 1 cm from the perineum

Table 2 Number of patients (%) with congenital anomalies in symptom categories according level of anorectal malformation. Some defects are mentioned explicitly. (*C* cervical, *Th* thoracic, *L* lumbal, *S* sacral, *VSD* ventricular septum defect, *ASD* atrial septum defect)

	Group A *n* = 16	Group B *n* = 64	Group C *n* = 19	Group D *n* = 165	Total *n* = 264
Number of patients with one or more additional congenital defects	16 (100)	58 (90.6)	17 (89.5)	86 (52.1)	177 (67.0)
Central nervous system	8 (50)	7 (10.9)	4 (21.1)	20 (12.1)	39 (14.7)
– spinal cord	–7	–5	–	–6	–18
– brain	–2	–	–	–11	–13
Uro-genital tract	16 (100)	42 (65.6)	14 (73.7)	41 (24.8)	113 (42.8)
– uropoetical tract	–16	–30	–12	–31	–79
– genital tract	–14	–17	–4	–15	–50
Skeletal	13 (81.3)	37 (57.8)	7 (36.8)	32 (19.4)	89 (33.7)
– vertebral (C,Th,L)	–7	–17	–3	–21	–58
– vertebral (S)	–8	–27	–2	–8	–42
– skeletal[a]	–8	–7	–2	–16	–33
Extremities	5 (31.3)	13 (20.3)	1 (5.3)	24 (14.5)	43 (16.3)
– radial hypo/aplasia	–	–4	–	–3	–7
– hand/finger-abnormalities[b]	–	–4	–1	–12	–17
– foot/toe-abnormalities	–5	–4	–1	–13	–15
Circulatory tract	3 (18.8)	19 (29.7)	5 (26.3)	29 (17.6)	56 (21.2)
– VSD	–	–8	–	–11	–19
– ASD	–1	–7	–3	–4	–15
– tetralogy of Fallot	–	–1	–	–5	–6
Gastro-intestinal tract	16 (100)	24 (37.5)	3 (15.8)	21 (12.7)	64 (24.2)
– oesophageal atresia/stenosis	–	–14	–2	–10	–26
– omphalocele	–10	–1	–	–2	–13
– malrotation	–5	–3	–	–3	–11
– duodenal atresia	–1	–3	–	–4	–8
Facial	2 (12.5)	5 (7.8)	7 (36.8)	29 (17.6)	43 (16.3)
Respiratory tract	3 (18.8)	3 (4.7)	1 (5.3)	6 (3.6)	13 (4.9)
Other	1 (6.3)	4 (6.3)	–	8 (4.8)	13 (4.9)

[a] Except the deformities of the vertebra and extremities
[b] Not including radial hypo/aplasia

Table 3a Overview of number of patients in associations, syndromes, and sequences

n =	♂ : ♀	A : B : C : D	Total	Survivors:non-survivors
	141 : 123	16 64 19 165	264	230 : 34
Associations[a]				
VACTERL 2	33 : 24	1 : 18 : 4 : 34	57	51 : 6
VACTERL 3	22 : 17	2 : 19 : 5 : 13	39	31 : 8
VACTERL 4	8 : 6	– : 8 : – : 6	14	11 : 3
VACTERL 5	3 : 2	– : 3 : – : 2	5	3 : 2
VACTERL 6	– : 1	– : 1 : – : –	1	– : 1
OEIS-complex	5 : 7	12 : – : – : –	12	8 : 4
Facio-auriculo-vertebral-spectrum	– : 1	– : – : – : 1	1	– : 1
Total	71 : 58	15 : 49 : 9 : 56	129	104 : 25
Syndromes				
FG syndrome	1 : –	– : – : – : 1	1	1 : –
Fanconi pancytopenia	– : 1	– : – : – : 1	1	– : 1
Kaufman syndrome	– : 1	– : 1 : – : –	1	1 : –
Townes Brocks syndrome	– : 1	– : 1 : – : –	1	1 : –
Zellweger syndrome	1 : –	– : – : – : 1	1	– : 1
Trisomy 5p	– : 1	– : – : – : 1	1	– : 1
Del 10 q26-qter	– : 1	– : – : – : 1	1	1 : –
Trisomy 18	– : 1	– : – : – : 1	1	– : 1
Trisomy 21	2 : 3	– : 1 : 4 : –	5	4 : 1
Marker-chromosome	– : 1	– : – : – : 1	1	– : 1
Total	4 : 9	– : 3 : 4 : 7	14	8 : 6
Sequences				
Klippel-Feil sequence	– : 3	– : – : – : 3	3	3 : –
Oligohydramnios sequence	– : 1	– : 1 : – : –	1	– : 1
Prune belly sequence	– : 1	1 : – : – : –	1	– : 1
Total	– : 5	1 : 1 : – : 3	5	3 : 2

b Percentage of patients in diagnostic categories

n =	♂ : ♀	A : B : C : D	Total	Survivors:non-survivors
	100 : 100	100 100 100 100	100	100 : 100
Additional congenital defects (ACDs):				
In association	50 : 47	94 : 77 : 47 : 34	49	45 : 74
In syndrome	3 : 7	– : 5 : 21 : 4	5	3 : 18
In sequence	– : 4	6 : 2 : – : 2	2	1 : 6
Not in association, syndrome or sequence	15 : 7	– : 8 : 21 : 12	11	13 : 3
Patients with ACDs	68 : 66	100 : 91 : 89 : 52	67	62 : 100
Patients without ACDs	32 : 34	– : 9 : 11 : 48	33	38 : –

[a] Number referring to the number of VACTERL constituents being present

from 1974 until 1995, were retrospectively reviewed. Four patients were excluded: three with rectal atresia and one patient who could not be classified due to lack of information (died within 24 h), leaving 264 patients 141 males and 123 females with ARM.

Details about the ARM were retrieved from the medical records, the surgical report and supplemented by data from autopsy reports of patients who died before definitive operation. Retrospectively it was difficult to differentiate between recto-prostatic and recto-bulbar fistulas and between high and low vaginal fistulas. Therefore these patients were grouped together as urethral fistulas and vaginal fistulas. For analytical purposes we classified ARM into four categories of decreasing complexity. The classification is shown in Table 1.

All ACDs were noted and categorized as listed in Table 2.

Recognized associations, syndromes and sequences as defined by Spranger et al. [27] were also noted. A frequently observed association in combination with ARM is the VACTERL-association (Vertebral, Anorectal, Cardial, Tracheo-Esophageal, Renal, Limb). VACTERL-association were diagnosed according to the definition of Weaver et al. [31]. Chi-square tests were used for statistical analysis.

Table 4 Characteristics of the patients with rectal atresia

Patient	Gender	Associated defects	Associations, syndromes, sequences
1.	Male	– circulatory tract – facial	–
2.	Male	– circulatory tract (VSD) – urogenital	VACTERL 2[a]
3.	Male	– central nervous system – uro-genital tract (uropoetical tract, genital tract) – skeletal (vertebral)	VACTERL 3[a]

[a]Number referring to the number of VACTERL constituents being present

Results

Classification and number of patients

Distribution of the ARM in four categories is presented in Table 1. The ratio of male to female was 1.15. Thirty-four patients (13%) died: 50% of the patients in group A, 14% in group B, and 9% in each of the groups C and D, most of them from sepsis, cardiac failure, respiratory insufficiency alone or in combination

Additional congenital defects

Of the patients born with ARM, 177 (67%) had one or more ACDs varying from 100% of patients in group A to 52% of the patients in group D. In Table 2 ACDs are listed according to the complexity of the ARM. In 148 (56%) patients the specific combination of ARM and ACDs could be described as either an association, syndrome, or sequence.

Compilation of associations, syndromes, and sequences

Tables 3a and 3b show the number and percentages of ACDs in the associations, syndromes or sequences.

Associations

Associations were observed in 129 patients (49%). The VACTERL-association was diagnosed in 116 patients (44%): 66 boys and 50 girls. The incidence in male and female populations was not significantly different (57% of the males and 43% of the females). Twenty patients (8%) with the VACTERL-association died, most of them from cardio-respiratory failure.

OEIS-complex (Omphalocele, Extrophia of the bladder, Imperforate anus, Sacral anomalies) was observed in 12 patients (5%): 5 male and 7 female patients. Four of them died: two due to cardio-respiratory failure, one from liver insufficiency, and one with sepsis. Of the five male patients four underwent gender reassignement and one died.

The facio-auriculo-vertebral-spectrum was observed in one girl (0.4%) with a perineal fistula. She died due to cardiac insufficiency.

Syndromes

Syndromes were recognized in 14 patients (5%). Nine patients had chromosomal syndromes and five had monogenic syndromes. Trisomy 21 was the most common chromosome defect.

Sequences

Sequences were observed in five female patients (2%). Two patients with an anterior displaced anus and one with a vestibular fistula had Klippel-Feil-sequence. Oligohydramnios-sequence was seen in one patient with a persistent cloaca. Prune-belly-sequence was recognized in one patient with complete anorectal agenesis.

Discussion

ARMs are often classified according to the Wingspread classification into high, intermediate, low, cloacas, and rare malformations [28]. This classification may be important for the operative approach, but is rather artificial. Neither the Wingspread classification nor that of Peña according to the level of the fistula [19] were useful in the analysis of our material. For analytical purposes we made four groups of patients with ARM of decreasing complexity (Table 1).

Patients with rectal atresia were excluded because we believe that the anatomy and physiology of the anal canal of these patients is completely normal [8, 16] (For comparison with other data are the characteristics of these patients shown in Table 4).

Patients in group A have anorectal malformations, but in addition the anorectum and sometimes even a part of the colon is missing in contrast to all the other patients with ARM. Most of these patients belong to the OEIS-complex. It has been suggested that the development of

ARM in OEIS differs from that in other disorders [15, 25]. Possibly patients with OEIS constitute a separate group, but we preferred to classify them within our most complex group of ARM. Patients in the groups B, C, and D have ARMs of decreasing complexity, classified just for analytical purposes more or less according to the high, intermediate, and low classification.

The male-female ratio of 1.15 is similar to that reported by Hoekstra [10], but lower than the ratios between 1.50–1.87 of other series [2, 3, 20, 24, 26, 29]. Taking into account that patients with an anterior displaced anus have minor or no problems with their defaecation and that most of them do not have to be operated on, it can be reasonably assumed that not all of these patients are referred to paediatric surgical centres. Because an anterior displaced anus predominantly occurs in females we wonder whether the true male-female distribution could be near 1.0 [18]. In this light we believe that ARM-causing agents affect males and females in equal numbers with less severe effects i.e. lower fistula levels in females.

Two thirds of our patients with ARM had one or more ACDs. Data in the literature vary between 20% and 70% [2, 3, 7, 10, 24, 26, 29]. In patients with complex ARM reported percentages vary from 75%-85%, and from 15%-35% in patients with simple forms of ARM.

Differences between series can be explained by the intensity with which the patients are investigated and the study period. Most studies were done before 1984 when more sophisticated techniques like MRI or ultrasound were not available. Other reasons explaining the differences include the definition of ACDs i.e. the inclusion of minor and/or functional defects, the length of the follow up periods with inclusion of late-appearing defects and the kind of study; i.e. whether the investigated series was population or hospital based.

Of our patients with ARM, 44% were classified as examples of the VACTERL-association. This percentage depends strongly on the definition of VACTERL-association, i.e. the number of affected organs required for the diagnosis. Table 3a shows what happens if another definition, i.e. of Czeizel and Ludányi, is used [6]. Our data resemble those reported by Rintala et al. [21].

In our series, chromosomal and monogenic syndromes were observed in 5% of patients. This figure compares well with that in other series [3, 4, 22, 24, 26, 30]. Four of the five patients with trisomy 21 had ARM without a fistula. This is in accordance with the literature [1].

The occurrence of ARM in our patient with Zellweger syndrome maybe fortuitous although one other patient with the Zellweger syndrome had the VACTERL-association [13].

Smith and Saeki [24] found 3/246 patients with the Klippel-Feil sequence, which is in agreement with the three patients observed in our series.

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