

Facial dysmorphologic and skeletal cephalometric findings associated with conotruncal cardiac anomalies

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Abstract

Anomalous conotruncal cardiac morphology and facial dysmorphism have been associated with neural crest-pharyngeal arch abnormalities. To assess these associations, 20 patients 3 to 18 years old with tetralogy of Fallot (TOF) or persistent truncus arteriosus (PTA) were evaluated by cardiologic, facial dysmorphic, and cephalometric criteria. The average number of facial abnormalities of neural crest derivation was two, while pharyngeal arch derivative abnormalities were observed with an average of five defects per subject. The total group had many more facial malformations than normal populations ($P < .00001$). The occurrence of defects was not significantly different between TOF and PTA patients.

Thirteen TOF patients 8 years, 9 months to 18 years, 10 months old ($\bar{x} = 13$ years, 4 months) had lateral cephalograms analyzed for skeletal relationships. The TOF patients exhibited higher than usual distribution of dolichofacial growth patterns (6 of 13), Class II skeletal relationships (6 of 13), mandibular retrusion (7 of 13), and maxillary protrusion (6 of 13). Trends were not absolute, since opposite patterns were individually expressed, and referencing by race tended to show more normal values for respective groups.

Introduction

Neural crest elements contribute connective tissue elements to organs developing from the first through the sixth branchial arch (LeLievre and LeDouarian 1975; Noden 1983; Kirby and Bockman 1984). These elements are critical for the development of the dermis of the face, palate, lower jaw, tongue, thymus, thyroid, parathyroids, walls (excluding endothelium) of the large arteries derived from pharyngeal arches, and the outflow tract of the heart. Research using chick chimeras as a model has demonstrated that selective ablation of neural crest elements consistently results in a concurrence of conotruncal abnormalities (e.g.: transposition of the great vessels, persistent truncus arteriosus) and pronounced deficiencies in facial development (e.g.: cleft palate, hypoplasia) (Johnson 1964; Kirby et al. 1983;

Kirby and Stewart 1983; Bockman and Kirby 1984; Nishibatake et al. 1987). Clinical reports also have recognized a multisystem linkage of facial and noncardiac abnormalities with congenital heart disease in general and cyanotic lesions of conotruncal origin in particular (Strong 1968; Kinouchi et al. 1976). Similarly, clinical evaluations of facial and cardiac anomalies in Pierre Robin syndrome (Shah et al. 1977), DiGeorge's syndrome (Huber, et al. 1967; Kretschmer et al. 1968; Van Mierop and Kutsche 1984 and 1986), Noonan's syndrome (Noonan 1968), velo-cardiac-facial syndrome (Shprintzen et al. 1978), fetal alcohol syndrome (Hanson et al. 1976; Loser and Majewski 1977), and Williams elfin facies (Jones and Smith 1975) again suggest a linkage for such malformations.

The association between cardiac and facial abnormalities in children, when considered with the experimental linkage of neural crest elements to the pathogenesis of conotruncal and facial malformations, led to the hypothesis that the abnormalities may result from a failure of the cephalic neural crest cells to translocate and interact properly with developing structures derived from the embryonic pharyngeal apparatus. In addition, the severity of the cardiac abnormalities may be related directly to the severity of the associated noncardiac anomalies. The purpose of this study was to assess a population of children with known conotruncal cardiac abnormalities in reference to facial dysmorphologic and cephalometric radiographic criteria of craniofacial structures which have significant developmental input from neural crest and pharyngeal arch elements.

Materials and Methods

Seventeen patients with tetralogy of Fallot (TOF) and three with persistent truncus arteriosus (PTA) were evaluated by subspecialists to assess cardiovascular, facial dysmorphologic, and cephalometric criteria asso-

ciated with known conotruncal abnormalities. Patient age ranged from 3 to 18 years (\bar{x} age = 10.2 years). Every patient, when appropriate, and all parents/guardians granted informed consent as required by the Institutional Human Assurance Committee.

Primary cardiovascular diagnosis was made by catheterization and confirmed at surgical correction of the conotruncal defect in every patient. Per cent aortic override and aortic root size were determined from preoperative M-code echocardiograms. General information (age, sex, race) was obtained from pediatric cardiology clinical records. Criteria for exclusion included genetic abnormalities such as Down's syndrome or other syndrome-specific dysmorphic features.

Evaluation of head and neck structures for abnormalities of facial dysmorphism used a standardized clinical checklist (available upon request). Head circumference, ear lengths, inner canthal, interpupillary, and outer canthal distances were measured according to accepted standards for age and sex (Smith 1982).

The cephalometric analysis of the skeletal relationships from standard lateral occlusal cephalograms utilized landmarks selected for their familiarity in the literature (Riolo et al. 1974). Age criteria appropriate for comparative appraisal of the skeletal relationships restricted the cephalometric group to 13 subjects 8 years, 9 months to 18 years, 10 months old (\bar{x} age = 13 years, 4 months). The cephalometric group was comprised of 11 males and two females and was distributed among nine whites and four blacks. All were in the TOF category. The normative values and study values are expressed for 9-year-old and adult populations with interpretation for age change, sex, and racial difference when appropriate for the analysis (Riolo et al. 1974).

Results

Statistical comparisons both within the groups and with overall population norms has questionable application, given the relatively small sample number, the specific nature of the population criteria, and the range of age, sex, and race distribution of the patients. Therefore, the presentation of results tends to be more qualitative in nature than quantitative, though the comparative measurements can be used to indicate trends in the group findings.

Cardiovascular

Indexed aortic root size (aortic root diameter/body surface area) was not significantly different between PTA and TOF patients. Right-sided arch occurred in one fourth of both groups. The cardiovascular findings showed no correlation between aortic override or indexed aortic root size and number or type of noncardiac malformations.

Facial Dysmorphicologic

The PTA patients demonstrated an average of six facial abnormalities of pharyngeal arch derivation, while the TOF subjects averaged four such facial abnormalities. The overall group average of five anomalies of pharyngeal arch derivation included defects of the pinnae (16 of 20 patients), nasal bridge (13/20), nares (11/20), philtrum (10/20), nasal alae (9/20), eye slant (12/20), and malar flatness (8/20).

The overall and respective PTA-TOF group averages for facial abnormalities associated with neural crest derivation was two anomalies per subject. Palpebral fissure lengths were short in 12 of 20 patients. Anomalies of eyebrow pattern were seen in 14 patients, including seven with an unusual flare or sparse eyebrows, four with synophrys, and two with short eyebrow length. Anomalies of the iris were seen in five of the 20 patients, including lacy, stellate patterns in three, anisochoria in one, and a heterochromia in one.

Head circumference and ear size, while usually within normal limits, tended to be smaller than average. Head shape was varied, though only five of the 20 subjects exhibited normocephalic form. The TOF group consisted of the five normocephalic patients plus one plagiocephalic, four dolichocephalic, and seven brachycephalic patients. All of the PTA group were brachycephalic. There was no demonstrable correlation between the average number of facial abnormalities and head shape in the clinical evaluations. The majority of the subjects did not fit into a recognized syndrome, though three individuals were diagnosed as having velo-cardiac-facial syndrome (Smith 1982).

Cephalometric

As stated previously, age criteria appropriate for comparative appraisal of the skeletal relationships from lateral cephalograms restricted the cephalometric study group to 13 subjects 8 years, 9 months to 18 years, 10 months of age, with a mean age of 13 years, 4 months. All cephalometric subjects fell into the TOF category, so no comparison between PTA and TOF patients is possible in this phase of the study. As used in the discussion, the normative values are expressed for 9-year-old and adult Caucasian populations with interpretation for age, sex, and racial differences. The cephalometric data are presented in quantitative measurements in Table 1 (next page) and as qualitative assessments of composite skeletal patterns in Table 2 (next page).

Cranial base measurements related to cranial base deflection, cranial length, ramus position, and porion location indicate 11 of 13 TOF patients exhibited values consistently within normal limits. The remaining two subjects showed a mild anterior or protrusive deflection just over one standard deviation. No specific atypical findings were noted in the overall or racial groupings.

In evaluating the maxilla positioning relative to the cranium, six subjects exhibited normal anteroposterior positioning, and six had protrusive maxillary values (two of which were beyond two standard deviations for multiple measurements). One subject was classified as having maxillary retrusion at one standard deviation below the norm. The normal to protrusive tendency of the maxilla was reflected to some degree in the numerical averages of the group with SNA = 83.3°, A-point to nasion perpendicular = +2 mm, and A-point to facial plane = +4.3 mm. While the number of protrusive maxilla suggests a tendency to forward positioning, four of these six patients were black — in which such placement is considered normal. Assessment of white subjects only resulted in subgroup values within a normal range. Therefore, no particular influence on maxillary positioning can be associated with the TOF history.

The mandible to cranial base assessment factored for age suggested a tendency toward mandibular retrusion, since seven of the 13 TOF subjects evidenced multiple measurements over one standard deviation of the normative values. Of the six remaining TOF subjects, five demonstrated mandibular measurements within normal limits, and one subject showed mandibular protrusion. The overall group averages reflect the retrusive tendency:

1. SNB = 78.7°
2. Pogonion to nasion perpendicular = -4.9 mm
3. Facial angle = 87.4°
4. Go-Gn length = 114.1 mm.

The racial distribution must be considered, since three of the four black subjects expressed the more retrusive values, again a common finding in blacks. The interpretation of a trend toward mandibular retrusion is complicated further by the variability of mandibular growth changes relative to other craniofacial skeletal elements, particularly since 11

of the 13 subjects were male with a mean age of 13 years, 4 months.

Assessment of maxilla to mandibular relationships placed the subjects into the following Angle skeletal classes:

1. Class I orthognathic = 4 subjects
2. Class I bimaxillary protrusion = 2 subjects
3. Class II = 6 subjects
4. Class III = 1 subject.

The group averages supported the Class II numbers with ANB = 4.2°, WITS = +1 mm, and maxillary-mandibular difference = 26 mm. Separate consideration of the subjects by race became necessary as subject groups more closely approximated normal values.

Evaluation of facial type suggested overall mesofacial patterns with a slight tendency toward vertical/clockwise orientations (e.g.: FMA = 28°, facial axis = 88.8°). Assessment of individual composite measurements qualitatively classified the TOF growth patterns

TABLE 1. Skeletal Cephalometric Measurements

	9-Year Old Norm $\bar{x} \pm sd$	Adult Norm $\bar{x} \pm sd$	Overall N=13	White N=9	Black N=4
<i>Cranial Base</i>					
Deflection (°)	27 ± 3	—	27.9	29.0	26.0
Ramus position (°)	76 3	—	75.1	75.7	73.5
Porion location (mm)	39 2	—	38.8	38.9	38.5
Cranial length (mm)	55 ± 3	—	59.6	60.2	58.3
<i>Maxilla to the Cranial Base</i>					
SNA (°)	81 ± 3	82 ± 2	83.3	81.0	88.5
A-Na perp (mm)	0 2	1 2	+2.0	+1.0	+4.3
A-Facial plane (mm)	2 2	0 2	+4.3	+2.7	±8.3
Co-A (mm)	87 ± 6	99 ± 6	88.3	87.7	89.8
<i>Mandible to Cranial Base</i>					
SNB (°)	76 ± 2	80 ± 2	78.7	77.7	80.8
Pg - Na perp (mm)	-6 3	-2 2	-4.9	-3.6	-8.0
Facial angle (°)	87 3	90 3	87.4	88.1	85.8
Co - Gn (mm)	105 6F	120 6F	114.1	113.6	115.3
	107 ± 6M	134 ± 6M			
<i>Maxilla to the Mandible</i>					
ANB angle (°)	4 ± 2	2 ± 2	4.2	3.2	7.8
AO - BO (mm)	—	0 F			
		-1 M	+0.5	0.0	+1.5
Mx - Md difference	20 ± 6	29 ± 3 F	25.8	25.9	25.5
		35 ± 4 M			
<i>Facial Type/Growth Pattern</i>					
FMA (°)	29 ± 5	26 ± 4	28.0	26.0	32.5
Sn - GoGn (°)	34 5	31 4	34.3	33.9	34.8
Y - Axis (°)	67 3	67 3	67.6	67.4	68.0
Facial axis (°)	90 3	90 3	88.8	89.2	88.0
Gonial Angle (°)	128 5	123 5	127.8	126.9	130.0
Mandibular arc (°)	26 4	29 4	26.8	28.7	22.8
Lower face height (°)	47 ± 4	47 ± 4	47.8	46.7	51.0

as dolichofacial-vertical = 6 subjects, orthognathic mesofacial = 4 subjects, and brachyfacial-horizontal = 3 subjects. Consideration of the subjects by race placed each group into normal value ranges. The steeper mandibular plane angles and vertical growth tendencies indicated for the black subjects are not atypical for black populations.

Discussion

In the assessment of facial dysmorphism, the total group of conotruncal patients with PTA or TOF had many more facial abnormalities than expected in a normal population (Leppig et al. 1987). The average of five pharyngeal arch abnormalities and two neural crest abnormalities in the overall study group was significant at the $P < .00001$ level when compared to normal population values. While the occurrence of facial abnormalities was not significantly different between the PTA and TOF groups, the PTA subjects showed a higher average of facial abnormalities in the assessment of pharyngeal arch derivatives. In the neural crest derivative assessment, the PTA and TOF patients had the same occurrence average. While no correlation was found using aortic override or indexed aortic root size as a measure of anatomical severity of cardiac abnormality, conotruncal lesions in PTA are felt to be more severe than TOF, since PTA involves at least partial agenesis of the conotruncal septum and TOF involves dysmorpho-

genesis of the septum. This study found a higher occurrence of pharyngeal arch derivative malformations not only in the overall conotruncal group, but also in the more severe PTA group as compared to the TOF group. The incidence rate of abnormalities in PTA vs. TOF subjects hints that facial dysmorphism is a measure of potential cardiac severity, though selection bias was present in that the study population was limited to survivors of cardiac surgery for conotruncal defects. Further selection bias was present because the patients resided in a specific geographic area, and all subjects volunteered to participate in the study.

Some tendencies in facial skeletal pattern seem to present themselves in the cephalometric appraisal of the TOF patients, though the value of statistical analysis is questionable with such a small population size. The quantitative and qualitative assessments indicate that the TOF patients as a group may show a slight tendency toward a dolichofacial-vertical growth orientation and Class II malocclusion associated primarily with mandibular retrusion. None of these trends are absolute for the group, however, since opposite patterns were evidenced by individual patients. While six subjects evidenced open bite tendencies in the cephalometric appraisal, the presence of four mesofacial and three brachyfacial patterns demonstrates that no specific growth tendencies can be attributed to the conotruncal anomalies. The inclusion of four black subjects influenced the overall cephalometric values; separate consideration by race indicated the cephalometric measurements more closely approximated normal values for each racial group respectively. Thus, no cephalometrically determined skeletal relationships observed for the TOF subjects reflect any obvious discrepancies which could be attributed to abnormalities at the developmental level. In one respect, the lack of a more definite dolichofacial/vertical growth orientation in the TOF group may speak well for the success of cardiovascular surgical techniques in normalizing respiratory demands potentially associated with cyanotic-type heart defects.

The importance of conotruncal abnormalities is that they are the most frequent type of cyanotic congenital heart disease. The complete care of children with a conotruncal malformation depends not only on proper diagnosis of the cardiac malformation, but also on an awareness of noncardiac abnormalities which provide useful data for subsequent recognition and therapeutic intervention in patient care. This study utilized just such a multidisciplinary approach in evaluating multisystem involvement in conotruncal abnormalities as a potential screening measure for complete diagnosis.

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TABLE 2. Qualitative Classification of Skeletal Relationships

	Overall (13)	White (9)	Black (4)
<i>Cranial Base</i>			
Protrusive	2	2	0
W.N.L.	11	7	4
Retrusive	0	0	0
<i>Maxilla to the Cranial Base</i>			
Protrusive	6	2	4
Orthognathic	6	6	0
Retrusive	1	1	0
<i>Mandible to the Cranial Base</i>			
Protrusive	1	1	0
Orthognathic	5	4	1
Retrusive	7	4	3
<i>Maxilla to the Mandible (Angle Classification)</i>			
Class I	4	4	0
Class I, bimax.	2	1	1
Class II	6	3	3
Class III	1	1	0
<i>Facial Type/Growth Pattern</i>			
Brachyfacial	3	3	0
Mesofacial	4	2	2
Dolichofacial	6	4	2

student, department of pediatrics; Dr. Moss is an orthodontic resident, department of orthodontics; all are at the Medical College of Georgia, Augusta, GA. Reprint requests should be sent to: Dr. Ronald A. Bell, Dept. of Orthodontics, Medical College of Georgia, 1500 Laney-Walker Blvd., Augusta, GA 30912-0200.

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AIDS-related discrimination: past, present, and future

Patterns of AIDS-related discrimination are changing as the deadly infection works its way into different populations, according to an article in the April 18, 1990 issue of the *Journal of the American Medical Association*.

In the second part of a two-part article surveying federal, state and municipal lawsuits filed that are connected with AIDS, Lawrence O. Gostin, JD, of the Harvard School of Public Health's Department of Health Policy and Management, noted that "traditional forms of discrimination, such as exclusion of children from school, refusal to rent or sell property, or refusal to provide personal services, are declining."

Gostin expects discrimination complaints in the areas of health care, nursing and social services to predominate in the future. As the epidemic moves from the homosexual community to intravenous drug users, there is a greater tendency to impede access to services for people with HIV disease.

Health care professionals have "an ethical duty" to treat HIV-infected patients, and courts are willing to enforce the professionals' legal obligation to treat patients. The courts have found that people infected with HIV, even if asymptomatic, cannot be discriminated against in the receipt of health care services.

Primary care practitioners such as internists and dentists, as well as specialists — surgeons and nephrologists — need to become familiar with the disease, because failure to maintain basic skills in relation to one disease may be grounds for the revocation of a physician's license.

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