Cytogenetic Study of Cleft Lip and Palate

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Changes in chromosome number, size, or shape can result in severe disturbances or even death as has been demonstrated in Down's syndrome, D-trisomy syndrome, trisomy 18 syndrome, and several sexual maldevelopmental syndromes. Since chromosomal abnormalities have been consistently associated with severe defects affecting several systems, one would not expect to demonstrate chromosomal changes in a condition so limited and relatively mild as cleft palate and/or lip.

However, two recent articles have suggested a possible relationship between chromosomal anomaly and clefts of the palate. Ingalls (*12*) induced cleft palate in mice by application of 6-amino nicotinamid to pregnant females and found polyploidy and fragmentation of chromosomes in foetuses affected with isolated cleft palate. Gropp (*9*) described a case of a cleft palate patient and noted nearly triploid set of chromosomes with modal number of 72 chromosomes in cells cultivated from palatal mucosa.

Furthermore, we have found in the literature an increased incidence of cleft lip and palate in several syndromes caused by chromosomal aberrations (Table 1). Complete bilateral cleft lip and palate was found to be a nearly constant finding in D-trisomy syndrome (13–15 trisomy, Bartholin-Patau syndrome) (Table 2).

Material and Methods

In order to further examine the possible relationship between clefts and chromosome abnormality, we chose 11 patients from the Clinic of Plastic Surgery in Prague. Four patients had clefts only (three lip and palate, one palate only). The remaining seven had clefts associated with some other malformations: one lip only, two palate only, four lip and palate (see Table 3). All chromosomal examinations were performed from peripheral blood samples, using the modified method of Moorhead.

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TABLE 1. Reports from the literature regarding clefts in various chromosomal syndromes.

Chromosomal aberration	*Reference*	*Cleft lip*	*Cleft palate*	*Heart defect*	*Ocular defect*	*Ears malformed*	*Extremities malformed*
Atypical chromosome 1	Patau (*22*)	×	×				
Translocation 2/3	Lee (*15*)		×	×		×	
Trisomy D	(See Table 2)						
Monosomy 16 and extra chromosome 6–12	Jennings (*13*)		×				×
Atypical chromosome 16	Sasaki (*23*)		×	×			
Trisomy 18	Holman (*11*)	×		×	×	×	×
Trisomy 18	Holman (*11*)		×	×		×	×
Trisomy 18	Van Wijck (*34*)	×	×				
Ring chromosome 18	Lucas (*17*)		×				
Extra small chrom. 21–22	Gustavson (*10*)		×		×	×	
Extra small chrom. 21–22	Gustavson (*10*)		×	×		×	
XXXXY—Klinefelter	Fraser (*7*)		×				×
XXXXY—Klinefelter	Day (*4*)		×			×	×
Translocation D/D	Jongbloet (*14*)	×	×	×	×	×	×

Results

Results of chromosomal analysis of these patients are shown in Table 3. No deviations were found either in number or in size of chromosomes. The only exception was the expected trisomy 21 in the Down's syndrome patient.

Discussion

In attempting to gain an insight into the possible relationship between cleft lip and/or palate and chromosome aberrations, we have obtained negative cytogenetic results. These data agree with Makino's (*18*) negative results from five cleft lip and/or palate patients.

The results are not surprising. The developing palate is an exceedingly sensitive area as demonstrated by the ease of experimental induction of clefts and the wide variety of agents producing them. One would expect an insult so gross as visible chromosomal alteration to affect such a highly sensitive developing structure as a part of multiple abnormality. Conversely, one would not expect congenital defects so relatively mild as clefts of the lip and/or palate to be associated with detectable changes in shape, size, or number of chromosomes in an otherwise healthy individual.

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TABLE 2. Reports from the literature regarding incidence of clefts and the Trisomy D syndrome.

Reference	*Cleft lip*	*Cleft palate*	*Heart defect*	*Ears mal-formed*	*Ocular defect*	*Extremi-ties mal formed*	*Haem-angioma*
Atkins (*1*)				×	×	×	×
Blanc (*2*)	×	×	×	×	×	×	
Conen (*3*)	×	×	×	×	×	×	
Ellis (*5*)	×	×	×	×	×	×	
Ferguson-Smith (*6*)			×	×	×	×	
Gorlin (*8*)	×	×	×	×	×	×	
Lubs (*16*)	×	×	×	×		×	×
Miller (*19*)	×	×		×	×	×	×
Miller (*20*)		×	×	×	×	×	×
Patau (*21*)	×	×	×	×	×	×	
Patau (*22*)	×	×	×		×	×	×
Scharer (*24*)		×	×	×	×	×	×
Sergovich (*25*)		×	×	×	×	×	×
Shaw (*26*)	×	×	×	×	×	×	×
Smith (*27*)	×	×	×	×	×	×	×
Smith (*27*)	×	×	×	×	×	×	×
Smith (*27*)	×	×	×	×	×	×	
Smith (*28*)		×		×	×		
Smith (*29*)	×	×	×	×	×	×	
Smith (*29*)	×	×	×	×	×	×	
Smith (*29*)			×	×	×	×	
Therman (*30*)	×	×	×		×	×	×
Therman (*30*)	×	×	×		×		×
Townes (*31*)			×	×	×	×	
Vaughn (*32*)	×	×	×	×	×	×	×
Warburg (*33*)	×	×		×	×	×	×
Yanoff (*35*)			×	×	×	×	

TABLE 3. Description of eleven patients in this series regarding type of cleft, presence and type of associated anomaly, and karyotype.

Subject	*Cleft lip*	*Cleft palate*	*Associated anomaly*	*Karyotype*
1		×	none	46/XY—normal
2	×	×	none	46/XX—normal
3	×	×	none	46/XY—normal
4	×	×	none	46/XX—normal
5		×	hypospadias, malformed ears	46/XY—normal
6	×	×	dysplasia of hips, cervical ribs	46/XY—normal
7		×	Klippel-Feil syndrome	46/XY—normal
8	×		scoliosis, torticollis	46/XY—normal
9	×	×	oligophrenia, deafness, dumbness, hypertelorism	46/XY—normal
10	×	×	pits of lower lip, eczema congen., haemangioma	46/XY—normal
11	×	×	Down's syndrome	47/XY—trisomy 21

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