Rhinology, 25, 237-244, 1987

Arhinia revisited

David Cohen and Kalman J. Goitein, Jerusalem, Israel

SUMMARY

Arhinia is a rare anomaly in which a total absence of the nose and parts of the olfactory system occurs. It is frequently associated with various multiple central nervous system (CNS) and somatic anomalies of different degrees of severity, with high mortality rate.

Twelve cases that have been reported in the literature are analyzed according to multiple criteria.

The anomalies that have been found to be associated with arhinia are: lack of olfactory bulbs and nerves, missing paranasal sinuses, high arched or cleft palate, various eye anomalies, low set ears - all in a very high incidence.

Various degrees of CNS malformations have been found in part of the cases.

Somatic anomalies have been reported in 50% of the cases. In two cases chromosome 9 anomalies have been reported.

A classification is suggested in which arhinia is classified into arhinia (total absence of the nose and rhinencephalon) and partial arhinia (partial absence of the nose), each may or may not be associated with other malformations (facial, CNS and somatic).

INTRODUCTION

The anomalies of the middle third of the face are caused by various chromosomal disorders (Lubs et al., 1961; Hunter et al., 1977; Funderburk et al., 1977; Kaminker et al., 1985) and are frequently associated with brain anomalies such as holoprosencephaly (Cohen et al., 1977) and other brain malformations (Brucker et al., 1963; Demmyer, 1967; Gruss and Matthews, 1978; Probst, 1979). The facial anomalies vary from mild nasal or eye anomalies to severe malformations, part of which are monstrous (Funderburk et al., 1977; Gorlin et al., 1976). Many of the severe cases die at birth or shortly afterwards (Dekaban, 1959) since these malformations are often incompatible with life.

Arhinia (complete absence of the nose) is only one peculiar type of these anomalies and is quite rare. We assume that only a part of these cases have been reported - probably the most isoteric and interesting. Rosen (1963) divided it into total arhinia (in which the rhinencephalon is also absent), and arhinia (in which it is present). In the literature many cases of partial arhinia (absence of part of the

nose only) are mentioned, but we will concentrate here mainly on arhinia. In the English literature we could find only 12 cases with more or less detailed reports. An attempt to identify the typical features of this anomaly is made by analizing these cases according to various criteria. Prior to this a synopsis of the relevant embryology of the nose considered from the arhinia point of view is presented.

EMBRYOLOGY

The development of the nose starts in the third week and ends in the eighth week of embryonic life. (Patten, 1971; Hamilton and Mossman, 1972; Tuchmann-Duplessis and Haegel, 1972). The frontonasal process grows in the mid-line, while the maxillary processes grow on either side. The development of the nasal cavity begins when the bucco-nasal membrane sinks posteriorly, forming the anterior nostrils and the nasal sacs, which constitutes the nasal cavity. The bottom of the sacs reach the nasopharynx leaving the bucco-nasal membrane as a septum between the two cavities. This membrane then decays forming the choanae. Failure of the bucco-nasal membrane to decay causes choanal atresia (Peebles et al., 1965; Evans and Maclahan, 1971; Hamilton, 1972).

The nasal pyramid develops from the nasal placodes on the frontonasal process. The nasal septum is the remnant of the frontonasal process in between the two nasal sacs. When these sacs fail to develop, the whole nose remains full of unorganized tissue, the major part of which tends to form a very dense irregular bone which extends from the base of the skull to the palate. This is frequently accompanied by agenesis of the rhinencephalon due to a failure in the evagination of the olfactory buds (Probst, 1979).

The paranasal sinuses, which normally start their development on the third to fourth month of embryonic life, do not develop when there is agenesis of the nasal cavity (Dekaban, 1959; Funderburk et al., 1977). The olfactory complex (the rhinencephalon) starts its development during the sixth week of gestation by the projection of the olfactory bulbs. During the next six weeks the whole olfactory system (which includes the olfactory tracts, anterior perforated space and the hyppocampus) almost completes its development (Patten, 1968).

Failure of the frontal prominence to develop causes arhinencephaly and agenesis of the corpus callosum (Marburg, 1941; Probst, 1979).

MATERIALS AND METHODS

The English literature of the 20th century was reviewed in order to find cases of arhinia. Less than 20 cases were reported and among these only 11 cases (one reported by the authors) were described in satisfactory details which might serve as adequate reference. An additional French case was found (Berger and Martin, 1969). These 12 cases are correlated according to various criteria in Table 1. Since parts of the criteria are not detailed in the case reports, we stipulated the missing

information from the case description or from the photographs. For example, when relating to IQ of a case reported by Gifford et al. (1972), and it was stated that he was a practicing attorney, we assumed that his IQ was not low. Or, when low set ears were seen in the photograph but this clinical finding was not specified in the text, we included it in the Table. Parts of the criteria have been defined by previous authors. Their prevalence is shown in Table 1.

RESULTS

Several conclusions can be drawn from the Table. The criteria will be discussed first in detail according to Table 1, and then summarized.

SURVIVAL: Eight out of the 12 cases were alive when reported. Another case (Blair, 1931) which has not included in Table 1 because of insufficient data was a teenager when reported. Thus the survival, according to these 12 cases is 66%. Dekaban (1959) and Lutolf (1976) have, however, reported a high mortality rate in these patients. We could not find data to support this contention but since the malformations are often incompatible with life we assume that many patients who died early have not been reported in the literature.

ASSOCIATION WITH OTHER MALFORMATIONS: Half of the cases reported had other malformations with varying degrees of severity.

MATERNAL DIABETES: This was found in two out of five cases. At least in a part of the other seven cases reported it would have been mentioned, if present, and, therefore, it does not seem to be consistently related.

MATERNAL TOXEMIA OF PREGNANCY, HYPERTENSION AND POLYHYDRAMNION: Although mentioned (Dekaban, 1959), toxemia and hypertension were not found in any of the six cases reported. Polyhydramnion was found in two out of eight cases. There is a well known association between polyhydramnion and fetal malformations.

PALATE ABNORMALITIES: Ten out of the 11 cases had such anomalies. Four of them had a cleft palate. The occurrence of a cleft palate implies a connection to a cavity in the nose. Thus there is evidence of a cavity in the nose in part of these cases.

SINUS CAVITIES: Seven out of seven cases in which the sinuses were examined did not develop paranasal sinuses. Few developed sphenoidal sinuses. Since the mucosal lining of the sinuses is an invagination from the nasal mucosa and since there is no mucosa in the nose of these cases, the sinuses could not have been formed. However, the bony outlines of the sinuses could be seen in case 12.

EYE MALFORMATIONS: For the simplicity of the Table we included in this category hypertelurism, small eyes, coloboma and lack of response to light. Many syndromes and malformations of the middle third of the face include eye anomalies of different degrees of severity. Ten out of the 11 cases had eye anomalies and this is typical of malformations of this kind.

Table 1. 12 cases of arhinia analyzed.

Case No.*	1	2	3	4	5	6	7	8	9	10	11	12	Total
Sex	F	F	M	M	M	M	F	M	M	F	F	M	7M/5F
Survival	–	9 days	–	inf	25 days	6 years	12 years	20 years	8 months	1 year	45 days	1 month	8/12
somatic-malform.	–	+	+	–	+	–	–	+	+	–	+	+	6/12
maternal-diabetes	–	+	?	?	?	?	+	?	?	–	?	–	2/5
toxemia	–	–	?	?	?	?	–	?	?	–	–	–	0/6
hypertension	–	–	?	?	?	?	–	?	?	–	–	–	0/6
hydramnion	+	?	+	?	–	–	–	?	–	–	–	?	2/8
palate anomal**	?	++	+	–	+	+	+	++	++	++	+	+	10/11
missing sinus	?	?	+	+	+	?	+	+	?	+	+	+	8/8
eye malform.	+	?	+	+	+	+	+	+	+	–	+	+	10/11
low set ears	?	?	(+)	?	(+)	(+)	(–)	–	(+)	+	+	+	7/9
hearing loss	?	?	?	?	(–)	(–)	?	(–)	?	+	–	?	1/4
weakness	+	+	+	–	–	–	–	–	?	–	–	+	4/11
low IQ	?	?	?	?	–	–	+	–	?	?	?	?	1/4
epil. seizures	?	?	?	?	–	–	+	–	?	?	–	?	1/5
absent:													
olfactory n.	+	+	+	?	?	?	?	?	?	+	?	+	5/5
corpus callos.	+	±	+	?	(–)	(–)	?	?	?	?	?	–	3/6
hypocampus	+	±	–	?	?	?	?	?	?	?	?	–	2/4
major brain-anomalies	+	+	+	?	(–)	(–)	(–)	(–)	?	(–)	–	–	3/10
chromosome-anomalies	?	?	?	?	?	?	–	?	?	?	9	9	2/3
operated	–	–	–	–	+	+	–	+	–	–	–	+	4/1
post mortem	+	+	+	–	–	–	–	–	–	–	–	+	4/12

\+ positive sign
– negative or irrelevant
? unmentioned
( ) our assumption from picture of text
/ number of positive cases (above line) from number of mentioned cases (below line)

** in the palate anomal: + high arched palate, ++ cleft palate

* AUTHORS (name of first author only):

1. Marburg O[27], 1943.
2. Dekaban AS[10], 1959.
3. Gitlin G[16], 1960; Rosen Z[32], 1959.
4. Berger M[3], 1969.
5. Gifford GH[15], 1972.
6. Gifford GH[15], 1972.
7. Kemble JVH[22], 1973.
8. Lutolf U[26], 1976.
9. Das Gupta HK[8], 1979.
10. Shubich I[35], 1985.
11. Kaminker CP[21], 1985.
12. Cohen D[6], 1986.

LOW SET EARS: Seven out of nine cases presented with this anomaly.
HEARING LOSS: This was found in one out of four cases. Since some of the cases died very early, and evoked response audiometry was not tested until recently, it is difficult to evaluate this finding. There may be a higher incidence of partial and total hearing loss in this anomaly.
WEAKNESS, APATHY AND LOW INTELLIGENCE: The cause of these anomalies is not clear. In some cases they may result from the associated brain anomalies. In case 12 (our patient) weakness was present without macroscopic CNS anomalies.
EPILEPTIC SEIZURES: These were mentioned in only one case.
ABSENCE OF OLFACTORY BULBS AND NERVES: In the five cases where this anomaly was reported, these parts were, as expected, missing. The strong association of their presence to the development of the nose has been previously discussed in the embryology synopsis.
BRAIN ANOMALIES: These anomalies vary from the limited absence of the olfactory bulbs and nerves through complete absence of the rhinencephalon together with major brain anomalies which are incompatible with life. Brain anomalies are also present in partial arhinia and milder nasal malformations reported (Dekaban, 1959).
CHROMOSOMAL ANOMALIES: In cases 11 and 12 chromosome 9 was found to be abnormal: in cases 11 mosiac trisomy and in case 12 inversion. In case 7 no chromosomal anomaly was found. In all the other cases chromosomal studies are not reported. Only recently chromosome 9 has been reported to be associated with phenotypic anomalies (Kaminker et al., 1985).

SUMMARY OF RESULTS

The features found to be unique, and in part different from those described in the first report on arhinia, in this survey:

1. Absence of the olfactory bulbs and nerves as the minimal degree of rhinencephalon malformations in the entity.
2. Brain anomalies of various degrees in cases that did not survive.
3. Association of somatic malformations in 50% of the cases.
4. Higher incidence of palatine anomalies whether as a high arched palate or as a cleft palate.
5. Absence of paranasal sinuses.
6. High incidence of eye malformations in various presentations.
7. Low set ears.
8. Low vitality and short survival in many cases.
9. Low association with maternal problems of pregnancy.

DISCUSSION

Arhinia is one of many presentations of middle face anomalies. It belongs to the

group of arhinencephaly. Arhinencephaly is usually associated not only with lack of the rhinencephalon (by definition), but also with various CNS anomalies, part of which are very severe. Few methods for classification of these anomalies have been suggested, (Kundrat, 1882; Dekaban, 1975; Lutolf, 1976; Probst, 1979). Arhinia is only a small subgroup of arhinencephaly which is a part of the large group of midline facial anomalies frequently associated with CNS malformations. Because of the small number of arhinia cases, it was classified together with the CNS malformations that are commonly associated with this anomaly. An example is Probst's classification (1979):

1. Pure arhinencephaly,
2. Arhinencephaly with associated malformations.

In addition, there are numerous reports on cases having only partial arhinia, such as a lack of one side of the nose, aplasia of one or two nostrils, or minor changes. Many of these cases have no associated anomalies, or have a few mild ones (Blair, 1931; Schweckendiek and Heim, 1973; Kukreja, 1973; Bakken and Aabyholm, 1976; Hunter et al., 1977; Beg, 1984; and others). The mild forms were not included in Probst's classification, since it was CNS oriented and did not detail the nasal area.

Based on the literature and the summary of the above mentioned results, an extended classification for arhinia is suggested. It includes the major forms of arhinia as well as the minor forms:

1. Partial arhinia (presence of at least one nostril and one olfactory tract):
   a. Pure (without associated malformations).
   b. With associated malformations (eye, face, CNS, ear or somatic malformations).
2. Arhinia (total, with absence of nose and olfactory nerves):
   a. Pure (without associated malformations).
   b. With associated malformations (eye, face, CNS, ear or somatic).

DEFINITIONS

Based on the published cases, definitions of arhinia and partial arhinia can be made:

Arhinia (total) is a rare anomaly in which there is an absence of the external nose, the olfactory bulbs and nerves, different degree of blockage of the nasal cavity, absence of the maxillary sinuses, high arched or cleft palate, various anomalies of the eyes and low set ears – all appearing in very high incidence. It is often associated with minimal or widely extended CNS anomalies (especially rhinencephalon) and other somatic anomalies. The anomalies are sometimes incompatible with life.

Partial arhinia is very similar to arhinia except that its anomalies are of a lesser degree.

The possible role of chromosomal aberrations in the etiology of this anomaly has not, as yet, been established.

RÉSUMÉ

L'arhinie est une anomalie présentant une absence totale du nez et de parties du système olfactif. Elle est associée fréquemment à diverses anomalies multiples du système nerveux central (SNC) et somatiques, de différents degrés de sévérité, avec un taux élevé de mortalité.

Les auteurs ont analysé selon des critères multiples, douze cas rapportés dans la littérature.

Les anomalies dont ils ont trouvé qu'elles sont associées à l'arhinie sont: manque de bulbes et nerfs olfactifs, absence de sinus paranasaux, palais fort cambré ou fendu, différentes anomalies des yeux, oreilles placées bas; toutes anomalies se présentant avec une très grande fréquence.

Dans une partie des cas les auteurs ont trouvé différents degrés de malformations du SNC.

Dans 50% des cas on a rapporté des anomalies somatiques. Dans deux cas, des anomalies du chromosome 9.

Les auteurs proposent une classification en arhinie (absence totale du nez et de la rhinencéphale) et en arhinie partielle (absence partielle du nez), les deux ne pouvant être associées à d'autres malformations (faciales, du SNC et somatiques).

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David Cohen, M.D.
Dept. of Otolaryngology
Bikur Holim Hospital
P.O. Box 492
Jerusalem 91004
Israel