The Clinic of the Department of Oral Surgery of the University Hospital and School of Dentistry, University of Michigan

ANODONTIA: REPORT OF A CASE ASSOCIATED WITH ECTODERMAL DYSPLASIA OF THE ANHIDROTIC TYPE

RONALD GRANT, M.S., D.D.S.,* AND HAROLD F. FALLS, M.S., M.D.†

THE syndrome of hereditary ectodermal dysplasia, anhidrotic type, has been reported frequently during the past few decades. Forty-five cases have been described with sufficiently accurate detail to merit acceptance. This report of an additional case is believed warranted because of the presence of two interesting associated features: (1) deficiency of the lacrimal gland secretion, and (2) congenital anodontia.

The features characteristic of ectodermal dysplasia may be grouped into the triad of (1) hypothichosis, (2) anhidrosis and asteatosis, and (3) anodontia. Intensely interesting is the frequent individual variation in the expression of the primary triad and associated secondary features. No two cases manifest the same signs and symptoms to the same degree. Conspicuous associated secondary manifestations of the dysplasia are: abnormality of the nails; hyperpyrexia; deficiency of the lacrimal, pharyngeal, conjunctival, and salivary glands; protuberant lips; depressed saddle-nosed appearance; atrophic rhinitis; and dysphonia.

Aplasia of the dental structures may be classified as (1) total anodontia, a complete absence of both deciduous and permanent dentition, and (2) partial anodontia, an absence of one or more of either the deciduous or permanent dentition but with the presence of teeth. In cases with the latter classification some patients have demonstrated only one or two maxillary or mandibular teeth. Other interesting cases have presented unilateral absence of teeth in either jaw, also partial eruption of the mandibular teeth with total absence of the maxillary teeth or a reverse situation.

Thoma[3] described the pathogenesis of anodontia as a part of the suppression of the development of the ectodermal tissue from which the tooth buds are developed. In its most severe form, it presents a total aplasia of the dental lamina and subsequent absence of development. If the ectodermal development is interfered with later in fetal life, the dental lamina may have formed and produced buds for the enamel organ of the deciduous dentition. It is possible that

From the Department of Oral Surgery, University Hospital, and Department of Human Heredity, Laboratory of Vertebrate Biology, University of Michigan, Ann Arbor, Michigan. The study was supported by a research grant from the Horace H. Rackham School of Graduate Study.

*Formerly Assistant Resident, Department of Oral Surgery, University of Michigan.

†Research Associate, Department of Human Heredity, and Assistant Professor, Department of Ophthalmology, University of Michigan.

the embryonic bud for the permanent dentition will fail to materialize. This explanation may account for the observed cases of complete deciduous development and eruption with total absence of the permanent teeth.

A normal development of the maxillary and mandibular bones has been described in the majority of the cases. A characteristic partial absence of the alveolar ridges of the maxilla and mandible is most frequently observed. This effects an appearance of underdevelopment of the bone which is not necessarily true, because the abnormal ridge is a resultant of the failure of stimulation by the erupting teeth. Several authors have reported a satisfactory development of the alveolar ridge, but do not explain the origin of the stimulation factor for its development.

The recognition of true anodontia is facilitated by its association with the triad of signs previously outlined. The marked dysplasia of the skin with maldevelopment of its secondary factors should suggest the diagnosis. A differential diagnosis must include consideration of progeria, hypothyroidism, congenital syphilis, and mongolism.

A perusal of the available literature reveals interesting variations in the associated ectodermal dysplasia in anodontia cases. A case of partial anodontia is reported by Etheridge,[5] in which the patient was totally edentulous in the left side of the mandible with complete dentition in the right maxillary and mandibular processes except the central incisor teeth. In the left side of the maxilla there was present only the first molar and second deciduous molar and cuspid. A neurotrophic etiology was postulated and was supported by the presence of hemiatrophy of the left side of the entire body associated with left side alopecia. Higgins and Kazanjian[4] demonstrated a case to Dr. Kurt Thoma of an 8-year-old boy with multiple hypertrophy of the facial structures, including the hair and bones, and with an extensive gingival hypertrophy. Clinical examination revealed total edentulism, but x-ray examination disclosed unerupted deciduous and permanent teeth.

The facial expressions and appearance of the affected individual assume an adult characteristic early in life. This is accentuated by the evident closed vertical relation of the jaw. Thoma emphasized the cosmetic changes which occur following the artificial replacement of dentition. The profile assumes a more normal proportion. This phenomenon supports the contention that normal development of the maxilla and mandible has occurred and is in proportion to development of other facial bones. The physiologic muscular function may stimulate the inherent growth factor. The maxilla is usually unaffected by total anodontia and generally assumes normal proportions unless some nasal obstructive process is present. The maxilla may be in a retrusive position in patients who have saddle noses and other facial anomalies. Alveolar ridges are generally absent as a result of loss of stimulus from eruptive dentition.

Willner[6] reviewed 125 cases of anodontia in an effort to classify the anomaly. He selected fifty of the more classic and completely described cases and arrived at a workable analysis. He was able to list twelve cases of total anodontia involving both mandible and maxilla, in only five of which the total anodontia included the absence of both deciduous and permanent dentition. It is very probable that many cases of anodontia have been misdiagnosed previous to the advent of the x-ray. It is highly probable that in some of the cases the perma-

nent teeth were unerupted and the deciduous teeth extracted in order to facilitate the eruption of the permanent ones. The patient may have been observed for only a few years with no evidence of permanent dentition and a subsequent erroneous diagnosis of anodontia made. Such cases have been reported and modern investigators question the diagnosis in view of lack of x-ray evidence.

CASE REPORT

W. R., a white boy 9 years of age, was first seen at the University Hospital Pediatric Clinic on Aug. 10, 1942. The child's chief complaint was that he had "never had teeth."

Family History.—The mother, aged 32 years, was living and well. The father, aged 39 years, was a traumatic cripple who gave a history of intermittent attacks of peptic ulcer. There were eight siblings: two girls, one aged 4 years, the other 14 years; and six boys ranging in age from 6 to 12 years. All of the siblings were living and well, all normal in appearance and in systemic development. No ectodermal dysplasia could be demonstrated in any of the siblings of the parents. There have been no miscarriages. No hereditary or chronic disease of the ectodermal system was admitted or demonstrated on either the maternal or paternal side. Syphilis by name or symptom was denied. Inheritable diseases, i.e., hemophilia, mental dyscrasias, or allergic manifestations, were likewise denied.

Birth and Developmental History.—The patient was delivered spontaneously at full term without complicating features. The mother had typhoid fever during the pregnancy. The child's health during the first few weeks of life was, in general, poor, and he was not expected to live. He always has had some ear trouble. The child sat erect, walked, and talked at normal age. The child's hair did not develop, even in poor form, until 6 years of age. As a result of a very poor appetite and lack of weight gain in infancy, the child was placed on numerous formulas. The cod-liver oil and orange juice intake was always adequate. He was never known to have sweated, and he seldom, if ever, cried tears. The teeth never erupted.

Past Medical History.—The patient had measles at 3 years of age, mumps and whooping cough at 3½ years, and varicella at an undetermined age. Frequent and rather persistent attacks of bilateral otitis media were mentioned. Pneumonia was experienced at 1½ years of age with no demonstrable sequelae.

Present Illness.—The patient was referred to the University Hospital Oral Surgery Department because of the congenital absence of teeth and a chronic nasal discharge. The mother stated that the child never had sweated or cried tears. She further remarked that it was necessary to bathe the child as frequently as five or six times a day during the hot summer months in order to keep him cool and comfortable.

Physical Examination. General.—This 9-year-old white boy was rather apathetic and small of stature for his chronological age. He was 50½ inches tall. The weight was 59½ pounds. The facial expression was that of a mature adult with pinched cheeks but very prominent and protuberant lips (Fig. 1). The child's response to conversation was noticeably limited and reserved. There was a retired indifference to his surroundings.

Head.—The skull was characterized by the prominence of the frontal bosses and the occipital process. The scalp hair was pale yellow white in color and quite thin in diameter. The individual hairs were of varying lengths and very sparse but quite uniformly distributed over the entire scalp (Figs. 1 and 2). The hair did not exfoliate very easily. The eyebrows were conspicuously thin, especially the lateral two-thirds, and were of the same yellow-white color as the scalp hair. The cilia of the lids were almost completely absent, there being only a few incompletely formed upper lid cilia.

Eyes.—The external ocular examination was negative except for moderate superficial bulbar and palpebral conjunctival injection and superficial small linear nebulous scars of the bilateral cornea. The corneal horizontal diameter was 11 mm. O.U. There was no anomaly of the iris or lens in either eye. With 2 per cent fluorescein dye there was revealed, under slit-lamp examination, a diffuse, irregular, and extensive superficial punctate staining of the cornea. The character of this staining of the cornea resembled that frequently seen in desiccation of the cornea following exposure in comatose states. There was no abnormality of the lacrimal drainage system.

The funduscopic examination revealed no abnormality in the fundus in either eye.

Repeated Schirmers' tests for the efficiency of the lacrimal secretion gave the following readings:

	Oculus Dexter	*Oculus Sinister*
6/19/43	12.0 mm.	14 mm.
6/21/43	6.0 mm.	10 mm.
6/22/43	8.0 mm.	5 mm.
7/ 9/43	3.5 mm.	5 mm.

The low readings of the above tests in combination with the history of infrequent psychic tears and the staining reaction of the cornea led to the diagnosis of congenital deficiency of the lacrimal secretion each eye.

The patient was refracted and accepted the following correction under paredrine and homatropine cycloplegia:

O.D.	+0.75 sphere	+3.00 cyl.	axis 111 = 6/9-2
O.S.	+0.50 sphere	+3.00 cyl.	axis 78 = 6/9-3

Glasses were ordered and the patient was instructed to use Ringer's solution six to seven times a day to supplant the deficient lacrimal secretion.

Nose.—The broad, saddlelike nasal base was conspicuous. The nares were large (Fig. 1). The turbinates were slightly atrophic. There was a moderate septal deflection to the left. A foul, purulent, crusted green discharge was present bilaterally. Definite atrophic changes with pus on the floor of the nares was typical of atrophic rhinitis.

Ears.—The auricles were not abnormal in shape (Fig. 3), but there was a very oblique insertion which made the ears most conspicuous. The external auditory canals were clear except for a moderate amount of cerumen. The tympanic membranes were markedly retracted bilaterally. There was evidence of a left tympanic membrane perforation. No evidence of acute or chronic otitis media was observed. No definite indication of hearing acuity loss could be demonstrated.

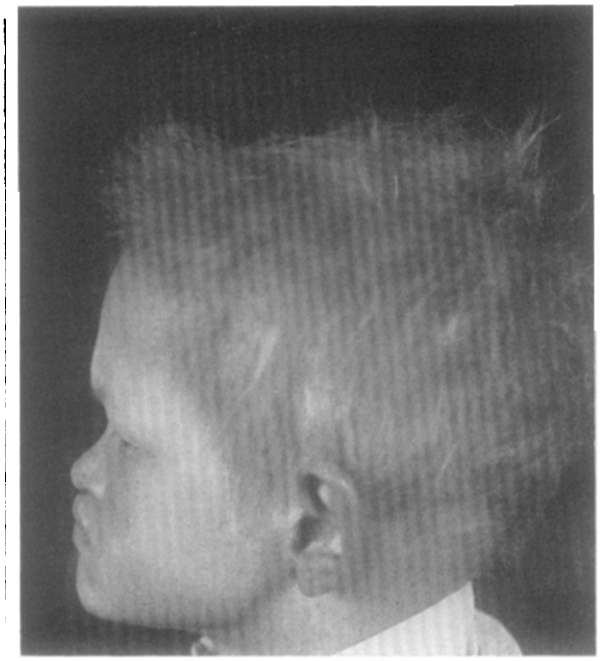


Fig. 1.—Lateral view of head showing protuberant lips and adult facies.

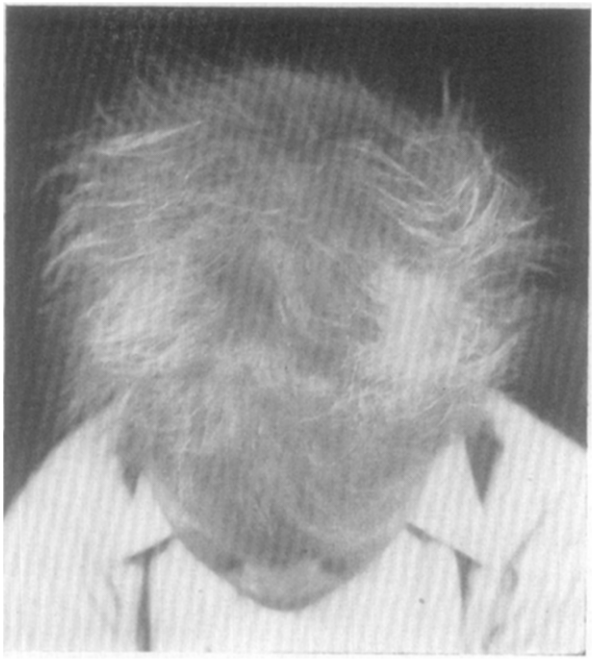


Fig. 2.—Top of head showing lanugo hair.

Sinuses.—The sinuses were normal to gross examination and transillumination.

Oral Examination.—The patient presented total edentulism. The alveolar ridges were flat, thin, and almost wanting, with sharp definition of the alveolar mucous membrane, presenting a clinical appearance of atrophy. The maxilla was broad and flat; the mucous membrane of the cheeks was continuous with that covering the alveolar ridge. The mandible appeared to be of normal size and development according to the chronological age of the patient (Fig. 4). The tongue was minimally coated. The mucous membrane of the pharynx was moderately injected, and a marked ozena was associated with a severe postnasal purulent dripping discharge. The tonsils were small and cryptic with minimal sepsis. The nasal pharyngeal adenoid tissue was minimal and coated with foul exudate. The larynx demonstrated definite atrophic changes. The salivary glands appeared grossly normal.

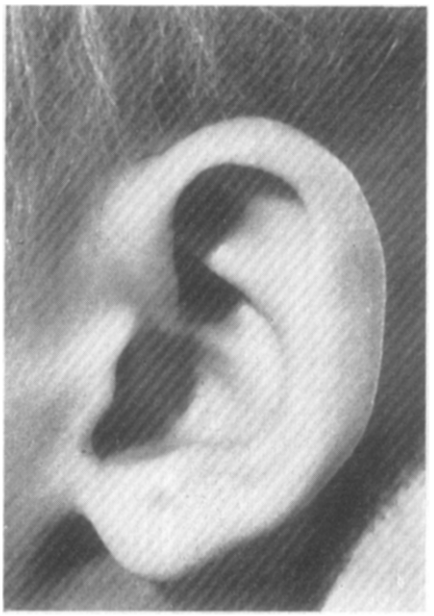


Fig. 3.

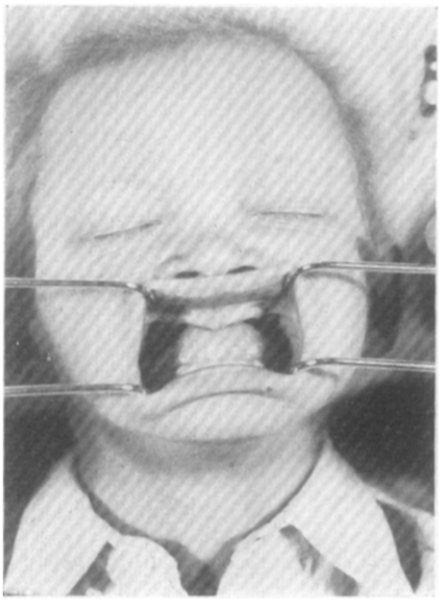


Fig. 4.

Fig. 3.—Left auricle.
Fig. 4.—Complete edentulism. Note almost complete absence of alveolar ridges.

Neck.—The neck was symmetrical and there was no gross evidence of deformities. The thyroid was not palpably enlarged. Several small, firm, nontender, anterior cervical chain lymph nodes were palpable. The mandible and chin were prominent.

Skin.—In general, the skin was smooth, thin, elastic, and minimally atrophic, as if long exposed to the elements. The superficial venous system was most conspicuous through the thin skin. The skin further presented a mild roughness and brawny desquamation. Scabietic lesions were present in the inguinal, axillary, and abdominal folds, as well as on the wrist, torso, arms, legs, and pubic area. The nails of both fingers and toes were not very unusual except that they were atrophic to a mild degree and terminated in moderate points

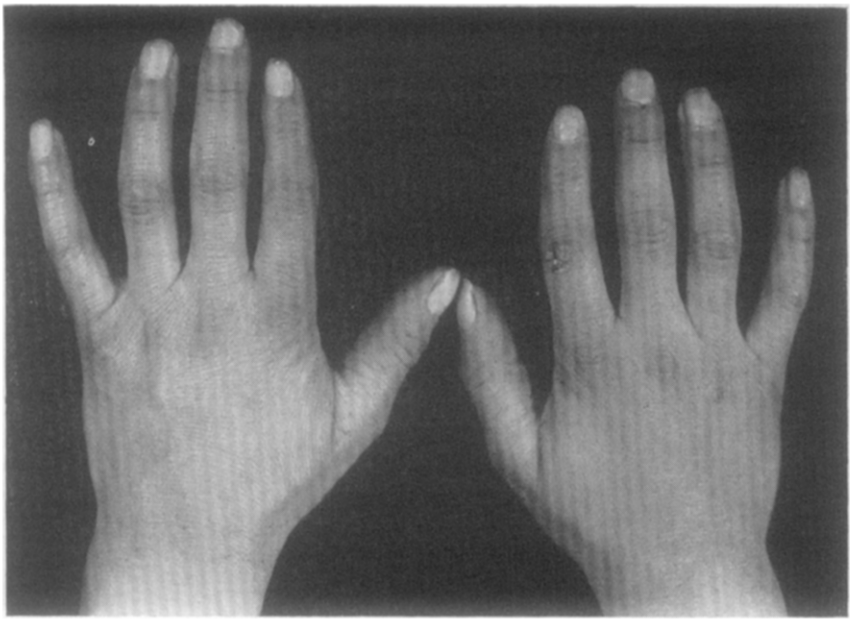


Fig. 5.—Dorsal view of hands.

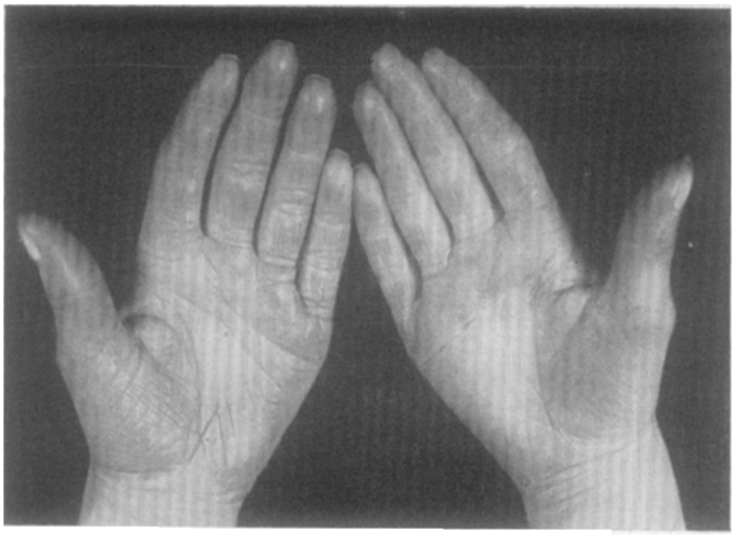


Fig. 6.—Palmar view of hands, showing atrophic changes of skin.

(like pen tips). The same atrophic skin changes were observed on the hands and were probably accentuated by exposure to the elements (Figs. 5 and 6).

Chest.—The thorax was symmetrical; no obvious anomalies could be demonstrated. The lungs were normal to auscultation and percussion. The heart was normal.

Abdomen.—The abdomen was scaphoid. The musculature was prominent and presented good tonus. There was visible peristaltic pattern beneath the somewhat thin abdominal wall. No palpable masses, no hernia, and no areas of tenderness could be demonstrated.

Genitalia.—The penis was somewhat hypertrophied, the testicles normal.

Extremities.—The skin was shiny, smooth, and thin. Numerous excoriations were observed in association with multiple small vesicles.

Spine.—The back and spine were symmetrical and straight; no gross anomalies could be observed.

Neurological Examination.—Neurological examination was definitely normal. Normal physiologic reflexes were present. The sensorium was normal.

Laboratory Procedures. Blood Studies.—Kahn's serologic examination was negative. Blood phosphorus 5.6 mg. per cent, blood calcium 10 mg. per cent, blood nonprotein nitrogen 10.5 mg. per cent, and blood phosphatase 2 n.s. In general there was no conspicious deviation from the normal levels for the various blood factors.

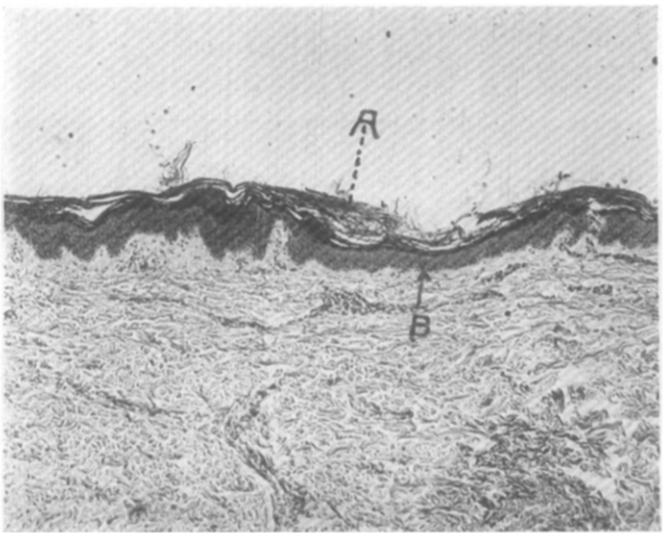


Fig. 7.—Cross section of biopsy of skin from flexor surface of right forearm.

Basal Metabolic Rate.—The basal metabolic rate, first determination, was −8. The pulse rate was 62, and the temperature 98.4° F. A reading of −8 is within the limits of normal. However, the true rate may be slightly lower when consideration is taken of the fact that the above reading is for the first determination.

Pathologic Examinations.—A punch biopsy of the flexor surface of the right forearm was taken. The specimen consisted of a portion of tissue cov-

ered by cornifying stratified squamous epithelium (*A*) without underlying accessory skin structures. The stroma was dense and there were a few perivascular infiltrations of lymphocytes. There was an increase in pigmentation of a very minimal degree (*B*) (Fig. 7).

A specimen of scalp hair was examined microscopically and was found to be unusually fine. The average area in cross section was 1,054 square microns, with a minimum of 641 and maximum of 1,838 square microns. The hair is moderately flattened as is shown by the average cross section index of 0.64 (minimum 0.55 and maximum 0.79). Furthermore the hair is unusually uniform both in size and in amount of flattening.

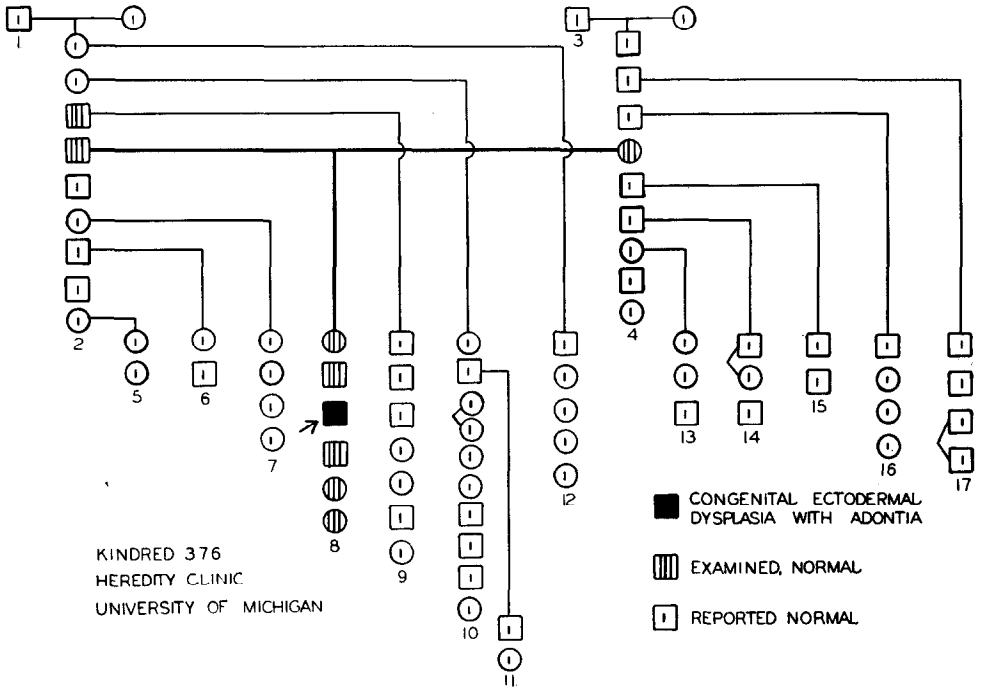
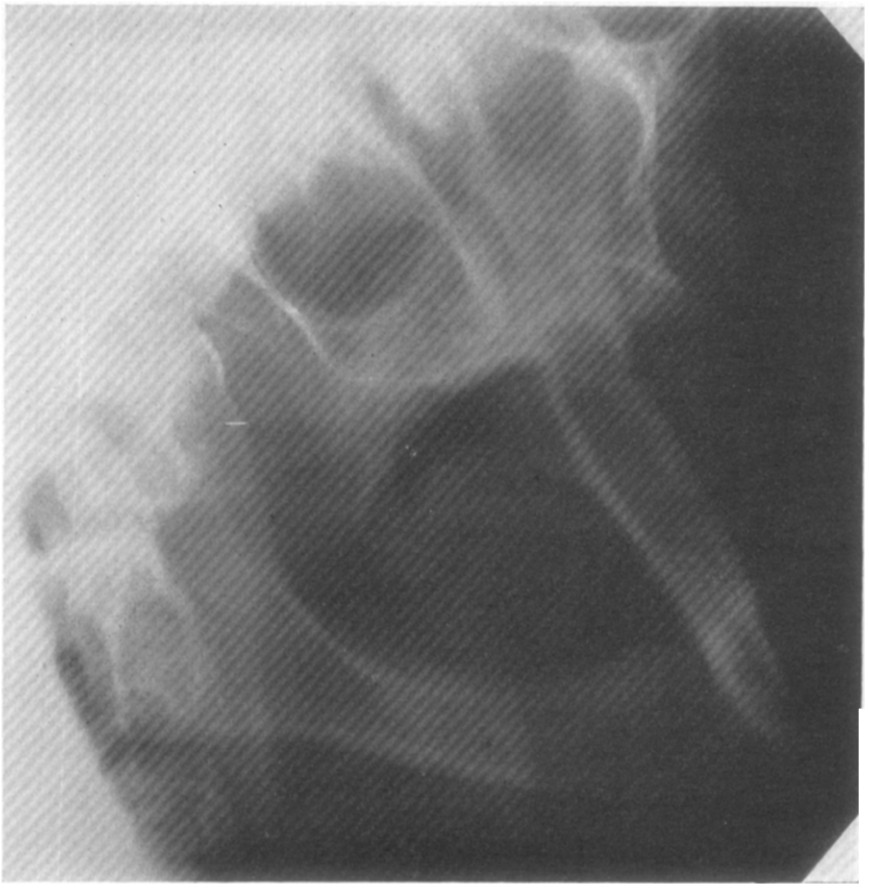


Fig. 8.—Pedigree. The patient described is indicated by arrow.

Genealogical Table.—A pedigree, based largely on hearsay evidence, is presented (Fig. 8). No living members of the family could recall any antecedent, sibling, or decendant, living or dead, who manifested changes closely or in any degree simulating those found in the patient. The pedigree differs from the conventional diagram by having the children of a single union arranged vertically rather than horizontally. The sibships are numbered 1 to 17, and a particular person will be referred to by means of the sibship number followed by a number denoting his or her position (from top to bottom, corresponding to birth order) within the sibship. Thus 8-3 refers to the propositus. Serologic tests of blood and saliva did not reveal any evidence that the legal parents of sibship 8 were not also the biologic parents.

X-ray Examination.—Examination of the paranasal sinuses demonstrated underdevelopment of all sinuses. The left frontal has budded, but there was no evidence of frontal sinuses on the right. There appeared to be a minimal

thickening of the mucous membrane lining both maxillary antra. The ethmoids were clear. Sphenoid sinuses appeared underdeveloped but were clear. A single lateral stereoscopic view of the skull revealed no evidence of abnormality of the sella turcica. The total absence of maxillary and mandibular teeth was clearly demonstrated on a single lateral jaw plate (Fig. 9).



COMMENT

The patient was referred to the Department of Prosthetic Dentistry in the School of Dentistry, University of Michigan, where, under the direction of Dr. Richard Kingery, complete artificial dentures were constucted. It was suggested to the parents that the necessity for periodic adjustment and, probably, reconstruction was obvious. Following the insertion of the denture, the boy's profile assumed more normal proportions.

The poorly defined alveolar ridge of the mandible added to the problem of construction and retention. It will be interesting to observe the effects, if any, that the denture will have toward effecting a stimulation of the ridge.

DISCUSSION

Many theories of the etiology of anodontia, associated with ectodermal dysplasia, have been proposed by various investigators. The theory of en-

docrine dyscrasia is one that has received much support. In 1928 Downs[1] completed a study of 647 patients who were affected by a wide range of endocrine disturbances and concluded that there was evidence of regularity in the appearance of dental anomalies in endocrinopathic patients. He deduced, however, that no specific dental anomaly could be considered pathognomonic of any particular type of endocrine dyscrasia. It is interesting to note that dental anomalies do occur more frequently in endocrinopathic patients than in normal individuals. Chemical and hormonal influence of maternal toxic infections on the developing fetus is easily postulated, but is proved with difficulty. One cannot, however, deny the possibility of such environmental influence.

The hereditary character of the anomaly has been generally accepted, recognition being forced by the weight of rapidly accumulating evidence. Numerous pedigrees have been reported. Anodontia associated with ectodermal dysplasia of the anhidrotic type has been commonly believed to be a sex-linked recessive character. In some pedigrees infrequent females have been known to manifest the syndrome, but this is not a fatal objection to the hypothesis, for discrepant females also have occurred in the pedigrees of other traits known to be sex-linked in inheritance. For example, heterozygous females may manifest modified pictures of color vision anomaly, hemophilia, and Leber's hereditary optic atrophy. It is not inconceivable, then, that the syndrome characterized by anodontia is sometimes incompletely dominant in the female.

An incomplete or mild form of the syndrome, namely, hypotrichosis and nail dyscrasias associated with partial anodontia, has been repeatedly reported as a simple autosomal dominant trait. A few reports have postulated a simple recessive pattern of transmission. It may well be that anodontia and its associated abnormalities is inherited through different genes in different families.

No evidence was found that the anodontia and associated dysplasias of the case here reported is inherited. No other member of this family, so far as known, exhibited any similar defect. It is therefore possible that in this family the character is not hereditary. On the other hand, it would be theoretically possible for a character of this type to be hereditary and still not to have appeared in any other members of the family known to our informants.

A sex-linked mode of heredity, such as has been postulated in some other kindreds with anodontia, might be transmitted unobserved through the females for a number of generations. Each of the sons of a carrier female should have a one to two chance of having the trait. In this kindred both the mother and the grandmother of the propositus must, on this hypothesis, have been carriers. The mother had three sons, only one of whom shows the character, and the grandmother had six sons, none of whom showed the trait. The chance that only one or less out of nine males would exhibit the trait, when each has a one to two chance of inheriting it, is 0.0195, which is one chance in about fifty. This probability would be further reduced slightly by the occurrence of a normal male in sibship 13, who, if the grandmother was a carrier, would have a one to four chance of inheriting the defect. Such a mode of heredity would therefore be possible in this kindred, though unlikely.

A hypothesis of a dominant mode of heredity with a very low penetrance seems untenable in this case. A recessive mode of heredity would be theoretically possible, but very unlikely in view of the absence of any known consanguinity between the parents. There remains the possible hypothesis that the characters shown by our patient have been produced by a mutation. Although traits to be hereditary must presumably always have originated in a mutation in either the individual concerned or in an ancestor, there is no way of proving that a mutation actually is responsible for the characters of this boy.

SUMMARY

Congenital total anodontia is relatively uncommon. The associated ectodermal dysplasia of our patient would indicate interference with the ectodermal system in early fetal life. Other cases have been reported that indicate a sex-linked heredity for the syndrome. In this kindred there is no other known instance of ectodermal dysplasia. It is theoretically possible, nevertheless, that the character may have been transmitted as a sex-linked recessive trait through the mother and grandmother.

REFERENCES

1. Downs, W. G., Jr.: Studies in the Causes of Dental Anomalies, J. Dent. Research 8: 367, 1928.
2. Cove-Smith, R.: Congenital Ectodermal Defects, Proc. Roy. Soc. Med. 23: 1407, 1929.
3. Thoma, Kurt H.: Oral Pathology, St. Louis, 1941, The C. V. Mosby Co., p. 136.
4. Higgins, H. L., and Kazanjian, V. H., in: Thoma, Kurt: Oral Pathology, St Louis, 1941, The C. V. Mosby Co., p. 139.
5. Etheridge, F. L.: A Case of Suppressed Dentition and Growth of Hair, Brit. D. J. 34: 66, 1913.
6. Willner, H.: Ektodermal Missbildungen, Deutsche Zahn- Mund-u. Kieferh. 3: 279, 1936.