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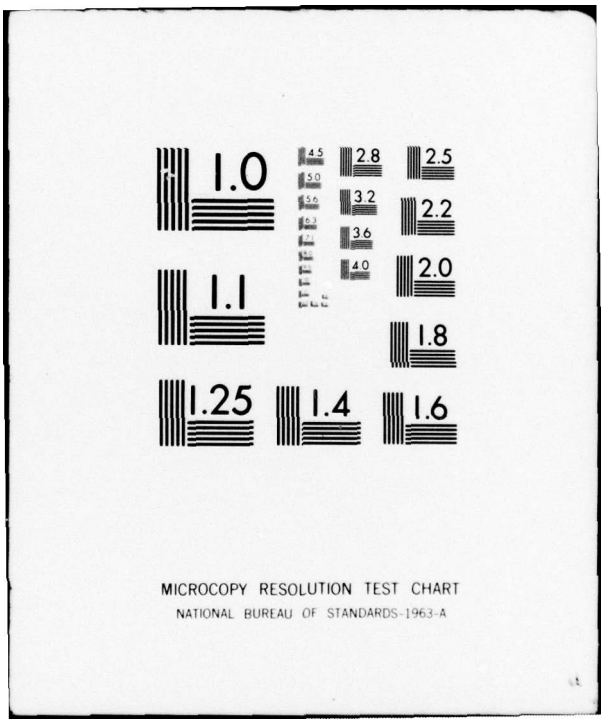
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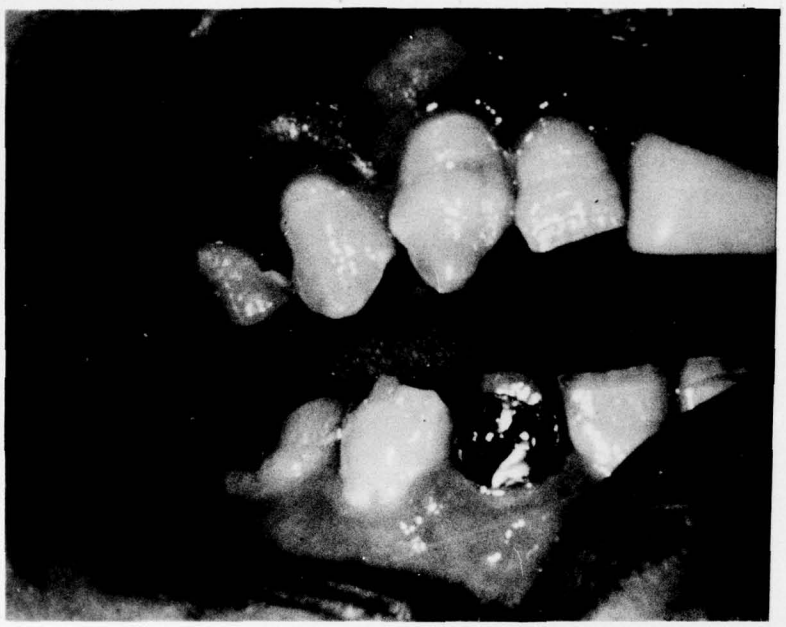
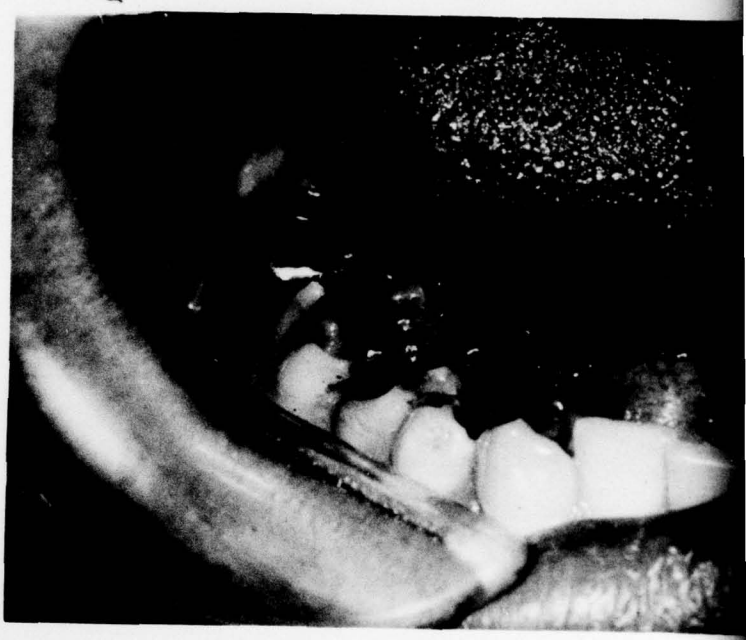
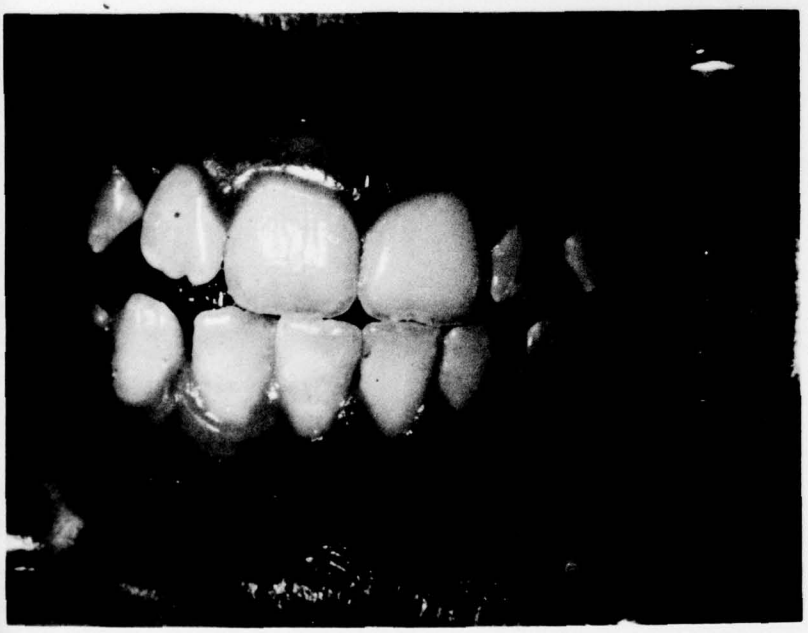
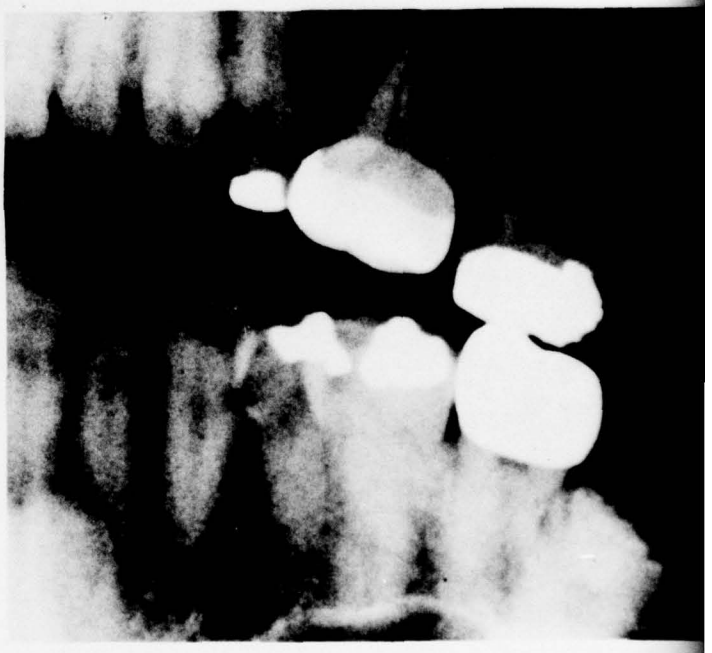
Three cases of diagnosed idiopathic hypoparathyroidism in siblings are presented. These cases are of interest due to their peculiar familial configuration and the paucity of all physically observable stigmata except those involving the teeth.









DENTAL CHANGES IN FAMILIAL IDIOPATHIC HYPOPARATHYROIDISM

John F. Nelson B.S., D.D.S.
Peter J. Tsaknis B.S., D.D.S., M.S., M.Ed.
Joseph L. Konzelman A.B., D.D.S.

The parathyroid glands develop as outgrowths from the third and fourth branchial pouches. In man they usually number four although five, six or more are not uncommon. They are small brownish-red masses usually situated within the capsule of the thyroid gland on the dorsal border of each lateral lobe.[1] These glands produce parathormone which influences calcium and phosphorous metabolism by increasing calcium absorption from the intestine, calcium mobilization from the bones and calcium reabsorption in the renal tubules. It also increases phosphate uptake in cells and enhances phosphate excretion by the kidneys.[2] Hyper- or hypoactivity of these glands result in serious metabolic defects some of which affect the teeth and supporting structures.

Hypoparathyroidism may be apparent prenatally and in children as well as in adults. The condition may occur as one of four basic types: DiGeorge's syndrome, postoperative hypoparathyroidism, pseudohypoparathyroidism (PsH) and idiopathic hypoparathyroidism (IdH).[2] In addition to these types, an entity has been described called pseudopseudohypoparathyroidism (PsPsH).[3]

DiGeorge's syndrome occurs as the result of a failure in the formation of the third and fourth pharyngeal arches and consists of a congenital absence of the parathyroid glands and thymus and anomalies of the aorta and heart. These patients present with severe immunologic deficiencies.

Postoperative hypoparathyroidism occurs as the result of accidental removal or damage of the glands usually during thyroid surgery. A history of surgery is important in diagnosis and is normally easily ellicited.

Pseudohypoparathyroidism is a condition in which the parathyroid glands are present and apparently normal with the abnormality residing in defective renal tubules. The tubules in these cases are unable to provide normal calcium reabsorption and phosphate excretion and therefore secondarily affect parathyroid activity. These patients are diminutive in stature, have round heads and faces, have dental defects, may have one or more short metacarpal bones, ectopic bone formation in the skin and fascia, exostoses, mental retardation and basal ganglia calcification. Administration of parathormone will not induce renal phosphate excretion. (Negative Ellsworth-Howard test). Pseudopseudohypoparathyroidism is a condition usually seen in relatives of patients with PsH having some of the skeletal stigmata of PsH but who respond to the administration of parathormone. (Positive Ellsworth-Howard test).[4]

Idiopathic hypoparathyroidism is a rare disease of elusive etiology. It may be congenital or appear in childhood or adolescence. Rarely, a familial pattern has been demonstrated.[2,5] Administration of parathormone or Vitamin D will result in a reversal of the hypocalcemia. Ectodermal defects of the hair, skin, nails and teeth are variable components.[5-8] Cataracts have also been reported apparently resulting directly from the hypocalcemia. A syndrome of juvenile idiopathic hypoparathyroidism, candidiasis and Addison's disease has been reported.[9-10] Basal ganglia calcification may also be present. Abnormalities of the teeth have been reported as consisting primarily of enamel hypoplasia, root blunting and concommitant dentinal defects of teeth developing during hypocalcemic episodes.[3-10]

Case #1

The patient was a 22-year-old caucasian male referred to Walter Reed Army Medical Center for a joint evaluation with two of his siblings. He was the oldest in a family consisting of seven male and three female children. The

patient was diagnosed as hypocalcemic at the age of 33 months prior to which time his parents noted that he had a tendency to walk on his tiptoes with a peculiar staggering gait. He had become progressively more clumsy and poorly coordinated with the passage of time. The patient was noted to have frequent bilateral facial grimacing and episodes of carpopedal spasm. The diagnosis was made in response to an acute episode of stiff, twitching muscles and rasping, gasping respiratory efforts. His serum calcium at that time was found to be 4.0 mg%. Intravenous calcium was administered and immediate symptomatic relief was obtained.

Since diagnosis and to the present time the patient has been managed with Vitamin D (50,000-250,000 units daily) and calcium lactate therapy. Recurrent hypocalcemic episodes have occurred periodically through the succeeding years usually as the result of a lapse in the medication regimen. Positive Chvostek and Trousseau signs have accompanied these episodes. The Ellsworth-Howard test was positive.

The patient is physically and mentally normal, being of medium stature and of considerably more than average intelligence. The physical examination failed to reveal any ectodermal defects and his eyes were normal except for a persistent myopia. Intraoral examination (Fig. 1) revealed all teeth as being present except the maxillary first premolars which had been extracted for orthodontic purposes. Enamel hypoplasia was apparent clinically primarily on the occlusal 1/3 of the coronal portions of the maxillary and mandibular premolars and molars. Five molars had received full crowns to compensate for the severe enamel defect. Other oral findings were within normal limits. X-rays revealed a supernumerary molar in the right maxilla and enamel defects on the unerupted third molars as well as erupted teeth. A radiolucent line was evident mesio-distally across the mid-coronal surface of the maxillary anteriors (Fig. 2).

No history or clinical evidence of candidiasis, thyroid malfunction or adrenal insufficiency was noted. No basal ganglion calcifications were noted on

X-ray.

Case #2

The patient was a 17-year-old caucasian male, the younger brother of the patient described as case #1. He was evaluated at Walter Reed Army Medical Center simultaneously with two siblings having similar defects. The patient was initially diagnosed as hypocalcemic at the age of three when he developed a severe tetanic crisis during his sleep which required emergency management including intravenous calcium administration. Through the years he has been managed with Vitamin D in varying dosages and calcium lactate therapy on an irregular basis usually in response to symptoms. Chvostek's and Trousseau's signs have been variable. No history of candidiasis, thyroid insufficiency or adrenal abnormality was noted.

The patient was normal on physical examination with no stigmata of dwarfism, ectodermal defects, or ocular abnormalities. He was of above normal intelligence. At the time of the evaluation his serum calcium was 6.8 mg% and his phosphorous was 10.4 mg%. A skull X-ray series was negative for defects including basal ganglion calcification.

Intraoral examination (Fig. 3) revealed no mucosal abnormalities. All teeth were present except the four first premolars which had been extracted for orthodontic purposes and a maxillary central incisor. The mandibular incisors displayed a linear enamel defect just inferior to their incisal surfaces. The maxillary cuspids likewise had mesio-distal linear defects in the mid-coronal area. X-rays revealed that the remaining anterior teeth in the maxilla had blunted root apices. Many teeth displayed enamel hypoplasia with this defect most evident roentgenographically in the nonerupted third molars.

Case #3

The patient was a 12-year-old female referred with two of her brothers for evaluation of persistent hypocalcemia. She was diagnosed initially at 8 years of

age on the basis of positive Chvostek's and Trousseau's signs and clinically diagnosed hypocalcemia. No history of other endocrine disorders or candidiasis was elicited. The patient was managed with Vitamin D and calcium lactate therapy in a similar manner to her two brothers.

On physical examination the patient was within normal limits having a normal growth pattern and no ectodermal defects. She was of normal intelligence. Intraoral examination (Fig. 4) revealed no mucosal or skeletal defects. All teeth were present with the third molars unerupted. Only minimal focal enamel hypoplasia was noted which consisted of opaque spots and concommitant transenamel pitting. X-rays revealed no pathoses.

Discussion

These cases were of interest on the basis of their familial configuration. While only three of the 10 siblings had demonstrated overt hypoparathyroid symptoms, the parents of the patients indicated that at one time or another all children had been noted to undergo facial muscle twitching. Neither parent is similarly afflicted and the family history revealed no bone, kidney, thyroid or gastrointestinal disease. There was also no history of diabetes mellitus although a maternal uncle died of pancreatic carcinoma at age 37.

Hereditary patterns have been established in PsH and PsPsH and it is generally accepted that the transmission is X-linked dominant with an expected predominance in females.[2,4] IdH has not been so clearly delineated as a hereditary disease although familial patterns have been shown.[2,5] This case is unusual, however, because of the one-generation occurrence. It is probable that all 10 siblings had the defect in a various degree, yet no evidence of similar disease in preceeding generations was apparent.

The patients did not display the ectodermal defects of the skin and eyes often seen in IdH. Further, they did not demonstrate the typical short, stocky stature and peculiar round facies or mental retardation usually seen in PsH or PsPsH.

Basal ganglion calcification has been discussed as a feature of PsH but the condition has also been seen in IdH. It may also be a feature of other syndromes with dermatological defects such as the basal cell nevoid syndrome. This feature was not noted in these cases. Cataracts are a common complication of IdH and must be ruled out on examination. Fortunately this feature was absent in these patients.

Subcutaneous calcifications are a feature of PsH and not seen IdH. These were not noted in our cases.

The response to parathormone administration of a normal phosphate diuresis (Ellsworth-Howard test) have been shown to be the dominant differentiating feature between IdH and PsH. The patients herein described were uniform in their positive responses to parathormone as well as Vitamin D.

The occurrence of candidiasis in association with IdH and Addison's disease deserves some discussion. This fungal involvement has also been noted in cases of pernicious anemia and even Hashimoto's thyroiditis.[9,11] The association of these diseases elicits the possibility of an autoimmune mechanism especally when one considers the immunological deficiency found in DiGeorge's syndrome. One cannot readily exclude the possibility that in cases of IdH with intractable candidiasis, the fungus may preceed the endrocrine disorder and be at least partially responsible for it. This disease feature was prominent in its absence in the present cases.

Abnormalities of the teeth have been seen in IdH and PsH as well as PsPsH. These defects are primarily enamel hypoplasias of varying degrees, root blunting, delayed eruption and even dentinal irregularities.[3-10] The extent and specific placement of the defects are dependent upon the chronology and degree of the hypocalcemic state. A relative lack of dental defects in case #3 is partially attributable to the later disease onset after most teeth had undergone full development. The mild defects consisted of focal opaque areas in the enamel

with minimal pitting. Findings such as these have been experimentally induced in rats by thyroparathyroidectomy.[12] Cases #1 and #2 had an earlier onset and longer time spans of hypocalcemia accounting for the greater degree of severity. The linear radiolucent bands seen in case #1 represent the results of severe hypocalcemia episodes occurring shortly after birth and have been previously documented.[3,13,14] It is difficult to determine at this point if the blunting of several maxillary anterior incisors in case #2 was due to hypocalcemia, orthodontic manipulation or a combination of both. The eruption patterns were all determined to be within normal limits.

It is of interest that the patients lacked all the other physical stigmata seen in IdH with defects confined only to the odontogenic structures. This is perhaps partially attributable to the prompt and careful medical management of these cases.

Summary

Three cases of diagnosed idiopathic hypoparathyroidism in siblings have been presented. These cases are considered to be of interest due to their peculiar familial configuration and the paucity of all physically observable stigmata except those involving the teeth.

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Illustrations

Fig. #1 Case #1 showing occlusal enamel hypoplasia and crowned second molar.

Fig. #2 X-ray from case #1 showing severe enamel hypoplasia of unerupted third molars and linear defect on maxillary lateral and cuspid.

Fig. #3 Case #2 showing linear enamel defects on mandibular incisors and maxillary cuspid. Opacities and pitting defects are visible on posterior teeth.

Fig. #4 Case #3 showing mild enamel defects consisting of pitting and concomitant opacities.