GENETICA POLONICA
Vol. 28 1987 No. 4

DENTINOGENESIS AND *OSTEOGENESIS IMPERFECTA* SYMPTOMS WITHIN FAMILY[2]

ANNA KOMOROWSKA, DANUTA ROŻYNKOWA[2]

Orthodontic Department, Institute of Stomatology, Laboratory of Human Genetics, Medical Academy, Lublin

Summary. *Osteogenesis imperfecta* symptoms were revealed in the family with *dentinogenesis imperfecta* manifesting through four generations. Out of 81 family members, 43 individuals showed hereditary developmental defect of dentin, and only 4 of them had mildly expressed bone manifestations as fractures resulted from minor trauma. However, in the fourth generation one case of *osteogenesis imperfecta congenita* could not be ruled out. It renders to conclude that it should be a rule to detect in family history any hereditary defective development (including teeth) in case of pathologic state of stillborn. Some questions regarding genetic and clinical aspects of *dentinogenesis imperfecta* are discussed on the basis of the presented family and published opinions.

It was Capdepont who in the year 1905 first described heritable discoloration opalescence and rapid attrition of dentition. The disease was known as hereditary opalescent dentin, Capdepont syndrome, *odontogenesis imperfecta* and recently is called *dentinogenesis imperfecta* (*DI*) since this developmental anomaly concerns primarily pathologic condition of the dentin.

In 1835 Lobstein recognized a disease in which fragile bones are associated in some instances with blue sclerae, joint hypermobility and otosclerosis with progressive deafness. This condition is commonly described as *osteogenesis imperfecta* (*OI*).

Dentinogenesis imperfecta — like *osteogenesis imperfecta* — belongs to a broad spectrum of various heritable disorders of connective tissue which are not mutually exclusive. V. A. McKusick wrote in the 3rd edition of his book: ... "Pedigrees in which *dentinogenesis imperfecta* was presumably an isolated anomaly inherited as a dominant are described. Some of these pedigrees are undoubtly instances of generalized disease, *osteogenesis imperfecta*, in which the dental manifestations dominate overwhelmingly" ... (1966).

Little is known about the basic molecular defect in dentin diseases. At the electron microscopic level the dentin appears to be markedly deficient in dental tubules in *DI* patients contrasted to ordered array of dental tubules laid down in normal dentin. However, in *OI* patients different protein — and gene defects have been detected:

---

[1] Received for publication: March, 1987.

[2] First author: Doc. Dr. hab.; second author: Prof. Dr. hab. Present address: ul. Kliniczna 7, 20-081 Lublin, Poland.

abnormalities of type I collagen with alteration of type I/type III ratio (Penttinen et al., 1975), amino acid substitutions, short peptide deletions, gene for alfa 1/II collagen deletion in the lethal form of *OI* (Pope, Nicholls, 1984). The extension of similar techniques to *DI* patients may be a matter of real need and time.

On the basis of the presented material some genetic and clinical aspects of *OI* manifestations dominated by *DI* symptoms within family are discussed.

FAMILY HISTORY

In 1981 the propositus A. M. was first brought by his mother to the Orthodontic Department of the Institute of Stomatology, Medical Academy in Lublin for treatment of malocclusion. Irregulary positioned, crowded incisors were grey-brown discolored and opalescent with the begining of attrition on incisal edge. Orthodontic treatment was indicated and given. After four years two other siblings and soon later their six young and three adult cousins affected by the same disease were available for examination.

The pedigree of the family of the propositus (Fig. 1) was drawn on the basis of clinical examination of 17 members and reliable information about others. Familial disturbances appear to be inherited as autosomal and dominant features. Out of 81 family members, 43 individuals had developed abnormality of dentin and 4 of them suffered bone fractures from ordinary activity in childhood.

The maternal great-grandmother (I) was the first known family member with peculiar dark teeth she had early lost. Her four sons (II) were all affected with similar dark and easily worn down teeth. Two of them had married two sisters derived from an unaffected family. Their descendants were 12 children (III) with 6 sibs in each family branch. The majority of them, i.e. 9 of 12 showed abnormal dental development. In addition, in 3 sibs (propositus' mother, her younger brother and her cousine) long bone fractures occurred in childhood. The fourth generation (IV) amounts to 25 subsequent family members with 8 children showing characteristic abnormal teeth phenotype. Among living children only the proband also experienced bone fracture at the age of six years. In one case *osteogenesis imperfecta congenita* could not be ruled out. It was IV/P. J. male child, who died of bronchopneumonia at the age of 20 months. The diagnosis of congenita form has been never confirmed, but the condition was described as intrauterine dystrophy, psychomotoric retardation (he has never walk), "rachitis" and encephalopathy probably because of skull deformation and short extremities.

CLINICAL, RADIOGRAPHIC AND LABORATORY FINDINGS

Apart from having bluish sclerae, the family members looked normal and were in good general health. No evidence of deafness were observed. However examinations toward the symptoms of joint laxity and skin changes showed both i.e. joint hypermobility and thin, translucent, hyperextensible skin.

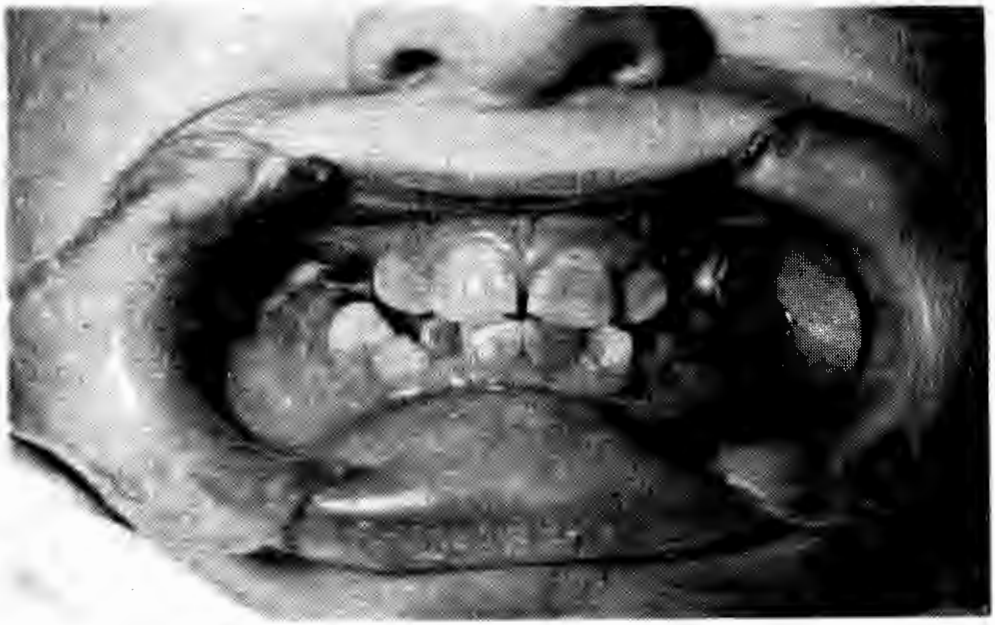

Fig. 2. Patient A. M. (propositus) at the age of 7 years and 3 months with mixed, multicolored dentition. Crowns of deciduous molars and lower right canine are dark-brown and attrited almost to the level of gingiva. Permanent incisors look greyish and opalescent. First permanent premolars at the stage of eruption are close to normal. Horizontal line divides crowns of upper incisors into white gingival margin and darker incisal part

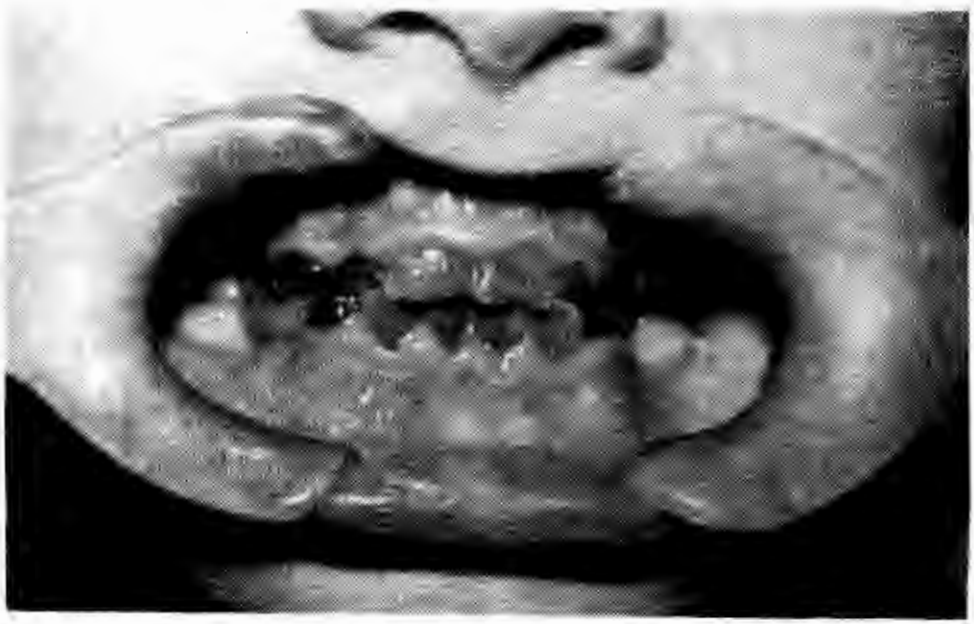

Fig. 3. Proband's brother, boy M. M. aged 8 years and 1 month. Degree of discoloration is expressed most severely among siblings. Enamel with horizontal groowing is chipped away on the incisal edge of upper central incisors and on the labial surface of the right lateral incisor. Both permanent and deciduous teeth almost equally involved, except the first permanent molars relatively unchanged

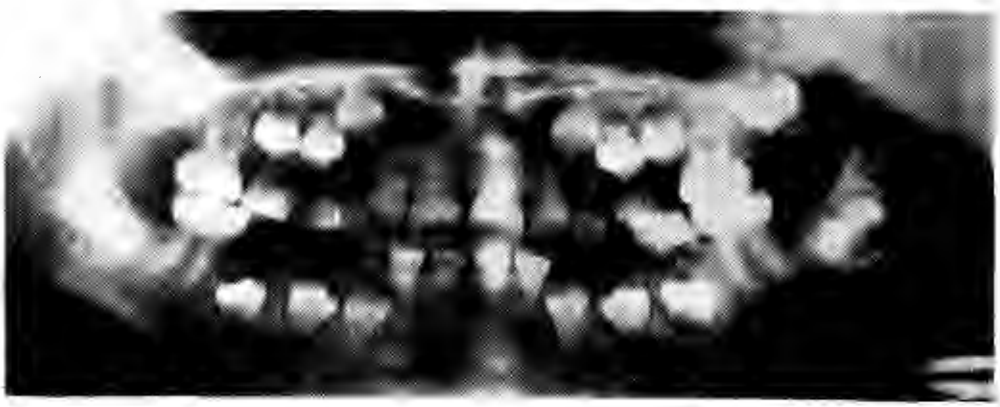

Fig. 4. Radiographic picture of dentition in the propositus A. M.

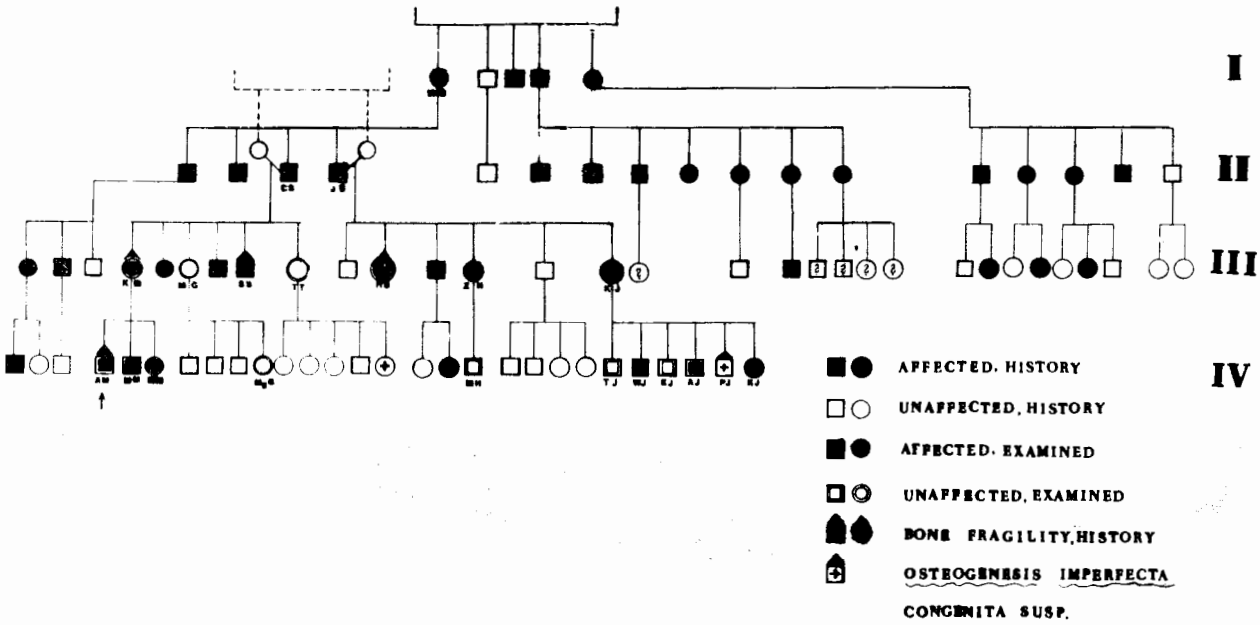

Fig. 1. Genealogy of the family with *Dentinogenesis mperfecta*, south-eastern Poland

Only the mother of the propositus and her children: two boys with their younger sister had a malocclusion. Orthodontic examination revealed that underdevelopment of maxilla with anterior cross-bite in the region of lateral incisors was a familial characteristic. The most striking clinical feature was discoloration and opalescence of teeth which soon wore down. Within the last five years the boy A. M. (Fig. 2) lost all first permanent molars and the first upper right premolar because of periapical abscesses. His mother K. M. being at the age of 22 lost her teeth except for upper incisors, left canine with premolars and lower left canine. During the last 12 years she lost only one tooth. The defect of enamel independently of the defect of the dentin was found in the present study in boy M. M. (Fig. 3).

A comparison of panoramic images indicated that some traits of the anomaly were not expressed to the same degree within the family. Furthermore, individual teeth demonstrated various states in one child. Panoramic pictures were parti-coloured due to variation in X-ray contrast of unerupted permanent teeth and their deciduous predecessors. Reduced X-ray contrast was shown mainly in the anterior teeth and in the roots of the first permanent molars, although their crowns remained better contrasted.

Obliteration of pulp chamber even before eruption was found in all cases, and radiolucency around first permanent molars' apices was also common. The roots appeared shorter than usual and constricted at the level of the cervical region. Crowns were more bulbous especially in the first permanent molars. Horizontal line at dentinoenamel junction was clearly visible on radiograph picture in the girl M. M., but less evident in her brother A. M., and almost undetectable in another brother M. M. Radiographic picture of dentition is illustrated in Fig. 4.

Usual laboratory measurements of total OH-proline excretion and plasma alkaline phosphatase level were performed in mother K. M. and her children. In one case of M. M. female child the excretion of total hydroxyproline in 24-hr urine/m^2 body surface was 96.7 mg, thus exceeding normal value range (55 - 80) for this age. Other laboratory findings were found in normal limits, even in mother K. M. and propositus A. M., who experienced bone fractures in childhood and thus were suspected to suffer from *osteogenesis imperfecta tarda*.

DISCUSSION

In the above example of *dentinogenesis imperfecta* simultaneous the occurrence of *osteogenesis imperfecta* was revealed in the family history through four generations. The genetic fitness of heterozygotes carrying the dominant *DI* gene seems not to be reduced. The segregation ratio is not very altered from 0.5 in this case (55% affected : 45% unaffected). One cannot exclude that there exists another, so far unidentified gene defect responsible for *OI* manifestations in *DI* patients. In any case, the clinical features suggest a generalized connective tissue abnormality such as blue sclerae, thin hyperextensible skin and joint hypermobility.

The presence or absence of *OI* features in patients with *DI* inclined Shields et al.

(1973) to divide *dentinogenesis imperfecta* into type I and II. The dental features and genetic relations observed in the family under investigation are similar to those described by Capdepont as hereditary opalescent dentin and correspond to the Shields type I although not very precisely. The reason is rare bone manifestation, only long bone fragility with good healing in 4 family members in early or late childhood. However, a severely affected child from the fourth generation deserves special attention. With his "intrauterine dystrophy, severe ricketts and encephalopathy" he appears to be a victim of congenital (not lethal) type of *OI*. In this respect our *DI* family reminds truly the Texas family with DI described by Heys et al. over 20 years ago (Heys et al. 1960).

The conventional types of *OI* identified by Silence et al. (1979) and modified by Pope and Nicholls (1984) are more heterogenous and contain different subgroups (Braga, Passarge 1981). When looking at this classification, the most fitting appears to be type IV of *OI*: autosomal dominantly inherited *osteogenesis imperfecta* with *dentinogenesis imperfecta*, normal sclerae, a low frequency of hearing impairment and wide variability of long bone deformities.

Patients with developmental skeletal disorders come into contact with various clinicians. *DI* patients visit first of all dentists and oral pathologists, *OI* patients come most often to orthopaedic surgeons, pediatricians or clinical geneticists. It must be remembered that certain skeletal manifestations should not be overlooked by dentist and vice versa teeth abnormalities have to be controlled by other medical specialist.

In the family under examination the need for orthodontic treatment of malocclusion was found as declared by the mother of the affected children. Traumatic bite even in normal dentition causes attrition of teeth and distinctively accelerates this process in *dentinogenesis imperfecta* cases (Ślaska, Komorowska 1973). In *DI* patients with abnormal occlusion the loss of teeth may occur earlier and — what is more important — later prosthetic restoration creates severe problem. Orthodontic appliance may protect against bite trauma when in place. The risk of possible teeth loss or fracture in *DI* children always exists, independently of orthodontic forces. In the present study three affected children were treated by monoblock and some improvement in occlusion was observed.

Regarding laboratory findings, generally used markers were unsatisfactory in determining the suggested molecular defect in both bone and dentition metabolism, which may be primarily related to collagen, calcifying matrix or mineralizing inhibitors (Bixler 1976). There is a need to continue studies on this subject.

REFERENCES

1. Bixler D. (1976). Heritable disorders affecting dentin. In "Oral Facial Genetics", Mosby Company, Saint Louis, 227 - 287.
2. Braga S., Passarge E. (1981). Congenital *Osteogenesis imperfecta* in three sibs. Hum. Genet., 58: 441 - 443.
3. Heys F. M., Blattner R. J., Robinson H. G. B. (1960). *Osteogenesis imperfecta* and *dentinogenesis imperfecta*: clinical and genetic aspects in eighteen families. J. Pediatr., 56: 234 - 245.

4. McKusick V. A. (1966). Heritable Disorders of Connective Tissue, Mosby Company, Saint Louis.
5. Penttinen R. P., Lichtenstein J. R., Martin G. R., McKusick V. A. (1975). Abnormal collagen metabolism in cultured cells in *osteogenesis imperfecta*. Proc. Natl. Acad. Sci USA, 72: 586 - 589.
6. Pope F. M., Nicholls A. C. (1984). Molecular abnormalities of collagen proteins and genes. In "Molecular Medicine" Vol. 1. IRL Press, Oxford, 117 - 175.
7. Shields E. D., Bixler D., El-Kafrawy A. M. (1973). Heritable dentine defects: dentine dysplasia type I. Arch. Oral. Biol., 18: 543 - 553.
8. Sillence D. O., Senn A., Danks D. M. (1979). Genetic heterogeneity in osteogenesis imperfecta. J. Med. Genet., 16: 101 - 116.
9. Ślaska-Nowicka M., Komorowska A. (1973). Zastosowanie protezy pochewkowej w przypadkach *odontogenesis imperfecta hereditaria*. Czas. Stomat., 2: 173 - 180.

OBJAWY *DENTINOGENESIS IMPERFECTA* I *OSTEOGENESIS IMPERFECTA* W RODZINIE

Streszczenie

W rodzinie z objawami *dentinogenesis imperfecta*, występującymi przez cztery pokolenia, wykryto cechy *osteogenesis imperfecta*. Wśród 81 członków rodziny, 43 osoby wykazywały dziedziczną rozwojową wadę zębiny, a tylko 4 spośród nich słabo zaznaczone objawy ze strony układu kostnego w postaci złamań po małych urazach. Jednakże w czwartym pokoleniu nie można było wykluczyć przypadku wrodzonej postaci *osteogenesis imperfecta*. Prowadzi to do wniosku, że powinno być zasadą prześledzenie w wywiadzie rodzinnym każdego dziedzicznego zaburzenia rozwojowego (łącznie z wadami uzębienia) w przypadku patologicznego stanu noworodka. Na podstawie własnych obserwacji przedstawionej rodziny oraz publikowanych doniesień omówiono niektóre aspekty genetyczne i kliniczne *dentinogenesis imperfecta*.

СИМПТОМЫ ОБРАЗОВАНИЯ ДЕНТИНЫ И КОСТЕЙ *IMPERFECTA* В ПРЕДЕЛАХ СЕМЬИ

Резюме

Симптомы образования костей *imperfecta* были обнаружены в семье с образованием дентины *imperfecta*, проявляющимся на протяжении 4-х поколений. Из 81 члена семьи 43 особы имели наследственный дефект в развитии дентины и только 4 из них имели слабо выраженные костные проявления, такие как переломы в результате небольших травм. Однако, в 4-ом поколении один случай врождённого остеогенеза *imperfecta* нельзя было исключить. Это приводит к выводу, что обнаружение какого-либо наследственного дефекта в развитии (включая зубы) должно быть закономерностью в случае патологического мёртвого плода.

В работе обсуждаются некоторые вопросы, связанные с генетическими и клиническими аспектами образования дентины *imperfecta* на примере представленной семьи и опубликованных мнений специалистов.