IDIOPATHIC OSTEOPSATHYROSIS

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Osteopsathyrosis is a disease of infancy and childhood characterized by a deficiency in the number and the function of the osteoblasts. The clinical features of this disease, namely frequent multiple fractures resulting from stresses which would not ordinarily produce fractures, and the resultant deformities, are the result of the production of bones which are physically and histologically unfit for stresses normally borne without difficulty.

The condition was first described by Lobstein in 1833. That form of the disease which is sometimes known as osteogenesis imperfecta was described by Vrolick in 1839. It is an exceedingly rare condition and in 1897 Griffith (8) was able to collect only 56 cases from the literature. In many of these cases the diagnosis appears to be rather doubtful. Ostheimer (11) in 1914 collected 193 cases and in 1918 Terry (13) found 119 cases of the hereditary type.

NOMENCLATURE

Great confusion exists in the literature as to the nomenclature of the disease. VanderVeer (14) uses as synonyms fragilitas ossium, osteogenesis imperfecta, and idiopathic osteopsathyrosis. Bronson (2) describes the entire clinical picture under the title of fragilitas ossium. Scudder (12) considers fragilitas ossium and osteogenesis imperfecta as synonymous. Hess (9) describes osteogenesis imperfecta as of two forms: osteogenesis imperfecta congenita and osteogenesis imperfecta tarda, the latter corresponding to idiopathic osteopsathyrosis. Conrad and Davenport (4) call the disease hereditary fragility of bone. Brittle bones, and hereditary hypoplasia of the mesenchyme (10) have also been used in describing it. Of these various terms, osteopsathyrosis is the one which is most applicable. As its roots signify "bone" and "crumbling," it is a fairly descriptive appellation. Fragilitas ossium, which is possibly the most commonly employed name, is equally applicable to other conditions which render a bone fragile, e.g., bone cysts, metastatic carcinoma, and the like.

Clinically, there are three entities which may be fairly well distinguished one from another, namely: osteogenesis imperfecta, hereditary osteopsathyrosis, and non-hereditary idiopathic osteo-

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There appears to be no unanimity of opinion as to whether these are separate diseases or simply three forms of the same disease, and it may be debated whether the term osteopsathyrosis should include osteogenesis imperfecta. The name "fetal osteopsathyrosis" has been suggested, and, if the conditions are really identical, may be accepted as a sufficiently descriptive name. Terry (13) suggests that osteogenesis imperfecta may be only a more severe form of osteopsathyrosis. Osteogenesis imperfecta, however, has at least three features which seem to distinguish it to some extent from osteopsathyrosis. These are: (1) imperfect development of the membranous bones; (2) the occurrence of intra-uterine fractures; (3) a high degree of mortality (early death of patient). Colby (3) adds a fourth distinguishing feature: frequent fractures of the cranial bones.

These features are not present in the typical form of idiopathic osteopsathyrosis, in which disease the membranous bones are seldom, if ever, affected, in which fractures do not usually occur before the middle of the second year, and in which the patients do not die of the disease. As to the hereditary and non-hereditary forms of the disease, these are rather sharply differentiated by one phenomenon, namely the occurrence, in the hereditary form, of blue sclera as a dominant characteristic. According to Conrad and Davenport (4), osteopsathyrosis associated with a blue sclera is a definitely hereditary disease, being one of the best demonstrations of the hereditary transmission of a pathological condition. The blue sclera must not, however, be confused with the blueness of the sclera which is common in small children. When present, it is unmistakable, the sclera having a very pronounced deep china-blue color. However, one case which I shall report (Case No. 8493) is an exception to this statement as to the hereditary nature of the condition, there being a definite blue sclera with no family history of multiple fractures or fragility of bone. It may be, then, that we are dealing with two, or possibly three, conditions which, while related, are not identical, i.e., osteogenesis imperfecta, hereditary osteopsathyrosis (brittle bones with blue sclera), and a non-hereditary idiopathic osteopsathyrosis.

Etiology

The etiology of osteopsathyrosis remains absolutely unknown. Various theories have been advanced, but none of them has been well substantiated. The condition is variously regarded as a primary defect of the bone-forming tissue, as a disease of nutrition, and as a disease of the ductless glands. According to Foote (6) foreign investigators have found fragility of bone following re-
moval of the thyroid and parathyroid in dogs. Thymus deficiency has also been considered and Gorter, quoted by Fairbank (5), has reported definite improvement following the feeding of fresh pigs' thymus. It is evident, however, that functional disabilities are not transmissible and the glandular theory of etiology must be limited to the hereditary form of the disease, or that associated with blue sclera. A more important objection to this theory is that post-mortem studies have never revealed any pathological process of any significance except in the bones themselves. It is often stated that there is an actual deficiency in the inorganic salts in the diseased bone, but this is not borne out by chemical analysis, which always discloses the normal salts in their usual amounts. Nor does there appear to be any significant variation in the blood calcium or phosphorus. In our cases the blood calcium, as Ca, varied from a minimum of 9.3 mg. to a maximum of 12.6 mg.

Fig. 1. Case 1905: Girl of Eighteen Years, Showing Typical Head, Protruding Abdomen and Deformity of Right Leg and Thigh

The first fracture occurred at five years. Multiple fractures of the right femur and leg have occurred since.
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Bookman, quoted by Foote (6), says that in active cases calcium retention is somewhat or very much below normal. He thinks that variations in the course of the disease have a tendency to change the calcium balance, and adds that calcium retention is favorably influenced by the administration of cod-liver oil and phosphorus, and still more strongly by calcium lactate. None of our cases has shown any response whatever to these agents.

Syphilis does not appear to be a factor, and is found among these patients no more frequently than in any group of the same size. Nor does rickets appear to be a factor. The majority of the children in our series were not rachitic. Griffith (8) says that 27 per cent of the cases collected by him showed hereditary features, and heredity was a factor in 28 per cent of the cases collected by Fairbank (5). It is evident that these percentages are based on the entire number of cases of fragility of bone observed. I believe that it may be stated definitely that osteopsathyrosis which is not associated with blue sclera is a non-hereditary disease.

CLINICAL FEATURES

Clinically, osteopsathyrosis is characterized by extreme deformity of the extremities resulting from the occurrence of multi-
ple fractures. The slight degree of violence which will produce fractures in psathyrotic bones is astonishing. Fractures result from such slight stress as accompanies arising from a chair, turning over in bed, or throwing a ball. They are comparatively painless, which, Bronson (2) suggests, may be due to the slight trauma to the soft tissues. Pain is so insignificant a factor that the fractures are often times unnoticed. Union is nearly always rapid, but

![Image of a child and an X-ray with a star and a bone highlighted.](image)

**Fig. 3. Case 2682: Multiple Deformities of Both Lower Extremities and Left Arm**

The photograph shows the typically shaped head. The roentgenogram shows the gross deformities of the bones of both legs, with a rather recent fracture of the left fibula.

the number of fractures which may occur in a single bone is so great that extreme deformities are common.

A fairly constant feature of the disease is the peculiar and rather typical shape of the head, which exhibits a bilateral increase in its diameter and unusual prominence of the frontal and occipital bones, but without the square-headedness of rickets.

Hess (9) describes attacks of profuse sweating and a protruding abdomen as characteristic features, and these seem to be
present in a fair proportion of the cases. He also believes that these children are usually under-developed mentally, but this is not substantiated by our series of cases, all of our patients being of average intelligence.

Fractures may occur in any of the long bones. In our experience, nearly 50 per cent of all fractures occurred in the humerus, while the second most common location was the femur. Foote

![Image of a child with deformed bones]

(Fig. 4. Case 2063: Typical deformities and characteristically shaped head)

The roentgenogram shows the extreme deformities of the bones of the right arm and forearm and an ununited fracture of the ulna.

(6) reverses this order and gives the femur as the most common location of fracture and the humerus second. The typically shaped head was observed in 6 of the 11 cases here reported. Two patients had attacks of profuse sweating and two exhibited the characteristic protruding abdomen.

The disease is, to some extent, self-limited, subsiding at about the age of puberty. After this fractures do not ordinarily occur and, if the patient has survived (as is usually the case), he is no longer subject to fracture in any greater degree than an average person. This is one of the reasons for believing that osteogenesis imperfecta and osteopsathyrosis may not be identical, the former disease being almost invariably fatal.

The onset of the disease is early in life. In our experience
the first fracture occurred at an age varying from five days to nine years. The average age at first fracture was 2.4 years. The diagnosis is based upon the typical history of multiple fractures occurring without reasonable or adequate violence, the comparative painlessness of the fractures, and the x-ray findings. Supporting these findings are the rather typical deformity of the head (which, however, is not always present) and sometimes the protruding abdomen and a history of attacks of sweating. There are no char-

![Characteristic Gross Deformities](image_url)

acteristic laboratory findings. The blood calcium and phosphorus content are usually normal. The cellular blood picture is not affected. The urinary findings are unimportant, although Bowcock and Lewis (1) have reported a case associated with glycosuria, and acetone was found in the urine of five patients in our series. We obtained no important family history in any case, even including one with a typical blue sclera.

**Roentgen Findings**

The x-ray findings are fairly characteristic. The most striking feature is the great disproportion in the size of the epiphysis as compared with the diaphysis of a long bone. The epiphyses are normal, which at once differentiates the condition from rickets. The diaphysis is slender and usually very irregular. The cortex is thin. There is a general decrease in the density of the bones, and they have a fibrous appearance. Usually there are marked deformities, and one or more fractures are seen.
Pathology

In one of our cases (Case 1905), an osteotomy was performed, and some bone was obtained for study by the pathologist. The material was found to be composed of a vascular connective tissue in which were numerous areas of bone formation. There was no evidence of a medulla. The cortex was thin. Foote (6) describes the psathyrotic bone as having a thin shaft, a thin cortex, scanty cancellous bone structure, and a large medulla. Microscopically he found the cambium layer of the periosteum to be thin and abnormal, with irregularly distributed osteogenetic cells. The Haversian systems were either absent or poorly developed. Large lacunae in the cortex were filled with spongy bone. Wagoner (15) describes a thin porous cortex, and isolated areas of new bone within the medulla. He calls attention to the fact that the fragility is due not to insufficient organic elements, which are always found in normal amounts on analysis of the bone, but to the inelasticity caused by a deficiency of the fibrous tissue and to im-
pairment of the strength of the bone by the absence of the tubular structure of the Haversian systems. This is also Terry's impression, and both Terry (13) and Ostheimer (11) find a tendency for new bone to be formed by direct metaplasia or cartilage cells.

FIG. 6. CASE 5979: SHOWING TYPICAL BONE STRUCTURE AND EASE WITH WHICH UNION OCCURS

This child had a large number of fractures of both legs

This, Terry believes, accounts for the rapid repair so often observed. The most complete study of the pathology of this condition is that given by Key (10), from whose classical description I quote freely.

On gross examination he found the bone to be very hard and brittle. The periosteum was friable. The cortex was unusually
thick and very hard. (All other writers have found thinness of the cortex a constant feature.) On staining, the cortex resembled embryonic bone, in which were a great number of wide canals running parallel to the long axis of the bone and communicating freely with one another. In the dense bone between the larger canals a few typical Haversian canals were seen. In some areas were dense masses of bone in which no canals were found. The large canals were filled with a very vascular tissue. In most places the walls of the larger canals were lined with one or more layers of osteoblasts, resembling the osteoblasts of normal bone, but present in greater number. The Haversian canals were not lined with osteoblasts. A few osteoclasts were seen. The structure of the matrix of the bone was similar to that of normal bone except for the irregular arrangement of the lamellae. The organic matrix, like that of normal bone, was made up of alternating sheets of coarse collagenic fibers. An occasional elastic fiber was found. Bone cells were about as numerous as in normal cortical bone.

The following is a typical case history, serving as a fair example of most of these cases:

**Fig. 7. Case 5070: Fracture Resulting from Throwing a Ball**

The first fracture in this case was at eighteen months. A total of eleven fractures occurred.
CASE NO. 8493: A boy, aged ten, was admitted to the Orthopedic Hospital complaining of multiple and repeated fractures.

Past History: The patient had walked normally at the age of two years. At that time he began to suffer frequent fractures from very slight injuries and on admission had deformities of the entire skeleton except the arms. He had had numerous operations, apparently open reductions, for fractures. He had had no fracture within the past year. He had had no childhood diseases except whooping cough and mumps.

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CASE 7220: CHILD FIVE DAYS OLD WITH MULTIPLE FRACTURES AND MULTIPLE DEFORMITIES

This is the type of case often described as osteogenesis imperfecta.

Family History: The father and mother were living and well. There was one brother, aged eight, who was a normal child.

Examination: The patient could not walk. On examination the head showed the broad diameter between the parietal regions characteristic of osteopsathyrosis. There were a slight left lumbar, right dorsal scoliosis and a marked curved deformity of both scapulae. Both arms were fairly straight; both forearms markedly curved, the curve being somewhat more pronounced on the right side than on the left. There were marked lateral bowing of both thighs and anterior bowing of both legs, the tibiae appearing as sharp bony crests in the mid-shin on both sides. The knee joints were well developed and the child had about twenty degrees of motion on the left side and ten degrees on the right. His eyes showed the characteristic china-blue sclera. Blood calcium was 12.7 mg. per 100 c.c. of blood.
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X-ray Findings: An antero-posterior view of the chest and both shoulders showed exaggerated curvature of both clavicles. The ribs were extremely delicate and the right seventh rib had been fractured. The humeri were fairly normal. There were marked curvatures of both bones of the left forearm and the radius had evidently been fractured at its neck. The carpus and the metacarpus were about normal. There was extreme bowing of both bones of the right forearm, probably due to multiple fractures which had healed. The right carpus and metacarpus appeared normal.

Antero-posterior views of both femora and the hip joints showed extreme outward bowing of the right femur, the bowing being so marked that the shaft of the bone formed an arc of a circle which would have a diameter of perhaps 8 or 9 inches. Fractures had evidently occurred through the condyles and the midportion of the shaft, where there was extensive new bone formation. The left femur was bowed markedly outward, but not quite so much as its fellow on the opposite side. There was an incompletely united fracture at the junction of the lower and middle thirds of the left femur and apparently there had been multiple fractures between this point and the condyles.

Antero-posterior and lateral views of the left leg showed extreme forward and inward bowing of the tibia and fibula. The fibula was poorly developed and almost thread-like in appearance. There was extreme thickening of the shaft of the tibia at the junction of its lower and middle thirds, where the bowing was most pronounced and where there had probably been fractures at various times.

Antero-posterior and lateral views of the right leg showed a bowing similar to that observed on the opposite side. The bones of the tarsus were greatly decalcified. The changes had the x-ray characteristics of osteopsathyrosis.

TREATMENT

A multiplicity of remedial measures have been proposed, but have proved to be of little or no value. High calcium content diets (to compensate for the probably low calcium retention, and thus to maintain the calcium balance) with viosterol and heliotherapy are indicated in all of these cases. Calphiomin and calcium lactate are often given, and it is believed that the calcium of calcium lactate may be utilized in the metabolic processes. Endocrine therapy has accomplished little, although one of our patients sustained no new fracture during one year of endocrine treatment. The use of fresh thymus of pigs is reported by Gorter as having effected a cure. Thus far we have not been able to obtain any fresh thymus for therapy.

The fractures must be treated as any other fractures. Constant watchfulness on the part of the parents is necessary to prevent injury, though even under ideal conditions fracture will occur, since it is practically impossible to guard against the very slight trauma needed to break these fragile bones.

CONCLUSIONS

1. Osteopsathyrosis and osteogenesis imperfecta are probably two phases of one disease, although a fair case can be made out for the existence of osteogenesis imperfecta as a separate entity.
2. That form of the disease occurring without blue sclera is definitely non-hereditary.

3. That form of the disease occurring with blue sclera is considered a definitely hereditary disease, the blue sclera being a dominant characteristic. One non-hereditary case having a blue sclera is here reported. It is possible that this child’s descendants will have osteopsathyrosis.

4. The clinical and x-ray findings are quite characteristic.

5. There is no adequate treatment.

BIBLIOGRAPHY

12. Scuttar, Robert: In Tice's Practice of Medicine, Chapter 1, Sect. VI, Vol. VI, W. F. Prior Co., Inc., Hagerstown, 1921.

DISCUSSION

Dr. W. H. McGuffin (Calgary, Alberta): Dr. Goin's excellent presentation brings to my mind two cases of a similar nature. One patient is a girl who is now about seventeen years of age. She was afflicted in infancy with multiple and recurring fractures and is now so crippled from deformities that she is almost totally incapacitated. Recently I examined a new-born baby. Multiple fractures involved nearly every bone of the body. The attending surgeon corrected the malalignment of the fragments. Within three weeks callus formation was present and union established. The skull presented a very unusual appearance. The shadows were irregular in the roentgenogram, there was a loss of density, and the head was very large. On palpation it felt like a large membranous bag with islands of bony substance scattered here and there.

It has always been my understanding that these cases, which I have termed “osteogenesis imperfecta,” were due to a calcium deficiency, like rickets in children and osteomalacia in adults. But how are we to account for the rapid calcium
deposit in the regions of the fractures? That is the question. It would seem to indicate that there is no loss of calcium in the blood nor any loss in the production of calcium. The fact that the fractures in the two cases referred to were seen almost simultaneously with birth would indicate a possibility of calcium metabolism disturbance during intra-uterine life, the calcium deficiency in the infant’s osseous system being of maternal origin, while the other condition, fragilitas ossium or “osteopsathyrosis,” occurring later in childhood, is due to defective calcium metabolism of the child.

DR. J. N. SISK (Madison, Wis.): I would like to call attention to the present condition of twins, whom I described two years ago before the Wisconsin Radiological Society. These children are four years old, sisters of three normal children. They presented practically symmetrical fractures in the femurs, the humerus, the ribs bilaterally, and one clavicle.

About six months ago, one of the children suffered another fracture of the femur. We put her in bed and hung the heels to the fracture frame. Abundant callus formed at once. Within a few weeks, however, the callus surrounding the new fracture began to thin to such an extent that we feared that if the child stood the bone would crumble. Later the picture changed. Union was strong and complete function was established.

DR. GOIN (closing): I might say that, although I have seen few cases under five years of age, one child whom I did see had fractures, evidently uterine, which were already reunited.

The repair of the bone, which is very prompt, is one of the characteristic features of the disease. I have had one case in my service in which there were five known fractures of one tibia. Although at present the tibia shows a very thin cortex and all the usual changes, there is absolutely no evidence of fracture. The bone contour is perfectly normal, and the fracture has healed with ideal results.

One case has been under my observation for eleven years. During that time, the girl has grown up. At the age of nineteen years she married, became pregnant, and had a normal child by Cesarean section. Thus we have in one family four generations living, only one generation of which presents this disease.