OSTEARTICULAR CHANGES IN A CASE OF ESSENTIAL OSTEOLYSIS

An Anatomical and Radiological Study

R. LAGIER and E. RUTISHAUSER, GENEVA, SWITZERLAND

From the Institute of Pathology, University of Geneva

These observations were made on a youth who died at eighteen years of age and who during his life time developed a progressive condition corresponding to that of essential osteolysis. A clinical and radiological study of his condition was made in 1956 by Neyroud, Baumgartner and Lenoir and was recently completed by Humair and Koralnik (to be published).

SUMMARY OF CLINICAL AND RADIOLOGICAL FEATURES

The condition appeared early in life as a severe degree of pes planus, and led gradually to shortening of the feet. In the upper limbs it appeared as club hand and limitation of elbow movement. It was accompanied by considerable atrophy of the muscles of the forearms and legs.

The patient was the only child in a family with no known history of osteoarticular disease. There was no past history of trauma. He had had difficulties in adapting himself to school life, but neurologically nothing abnormal was noted and he had had no endocrine disorder.

Radiographic examination eight months before death revealed fairly symmetrical lesions of the wrists, hands, elbows and feet. The carpal and midtarsal bones had disappeared. Epiphysial osteolysis affected the elbows, the distal end of the ulna, the metacarpal and metatarsal bases, the heads of the fourth left metacarpal and the first right metatarsal, and the ends of some of the phalanges of the hands and feet. The distal phalanges of the hands were intact, the proximal epiphyses of the affected phalanges of the feet had undergone osteolysis. The metacarpals, metatarsals and phalanges were remarkable for the reduction of their diaphysial diameter as well as for the atrophy of the cancellous bone of the epiphyses, which were spared by the osteolytic process. Their cortical bone showed no osteoporotic thinning, nor did that of the other long bones.

The hips were normal. In the shoulders and knees the only noticeable feature was coarse lattice-work atrophy of the cancellous bone of the epiphysis, clearly demarcated by the epiphysial line. Also observed were depression of the cranial vault of the bathrocephalic type in the parieto-occipital area, asymmetry of the articular processes of the atlas with slight platybasia, and thoracic scoliosis.

The patient died from hypertensive nephropathy with uraemia, the signs of which seem to have become evident a year and a half earlier. When the patient was in hospital for the terminal illness the sedimentation rate and the electrophoretic pattern of serum proteins, both of which had been normal in 1954, were altered. The sedimentation rate was in the region of 30 millimetres in the first hour (Westergren); electrophoresis supplemented by immuno-electrophoresis showed a fall in γ-globulins and a rise in α₂ globulins corresponding to a very great increase in haptoglobin. The serum levels of calcium and inorganic phosphorus were altered by the renal insufficiency, and that of the alkaline phosphatases was 3-4 Bodansky units.

GENERAL NECROPSY FINDINGS

The necropsy A113/63, confirming the results of an earlier needle biopsy, showed chronic glomerulo-nephritis with special features. These findings will be the subject of a separate study by Chatelanat and Simon. Sclerosis of the intima was noted in the coronary arteries.
and some atheromatous plaques were found in the aorta. The parathyroid glands contained clear but not hyperplastic cells. No lesion was found on examination of the brain and cervical medulla (Dr E. Wildi).

Radiological examination of the skeleton provided results similar to those found in the examination six months previously (Figs. 1 to 4). Arteriography of the lower limbs revealed no abnormalities of the blood supply.

The dental radiograph showed numerous pulp stones and a tendency to caries, hypercementosis, and lysis of the roots. The lamina dura had not disappeared. These findings are described in a paper to be published shortly (Dr A. J. Held).

Examination of serum taken two hours after death revealed the following features. Immuno-electrophoresis gave results analogous to those observed during his last hospitalisation (Dr J. J. Scheidegger). The latex test was negative. The seromucoid level of the serum, determined by the tyrosin content, was 10.3 milligrams per cent—about three times the normal level. The levels of hexosamines and protein-bound hexoses were respectively 122 and 116 milligrams per cent—that is, approaching normal limits (Dr F. Infante). On high voltage paper electrophoresis (Antener and Buri 1963) of the serum and of urine collected at the same time neither proline nor hydroxyproline could be identified (Miss I. Antener). The amount of glycuronic acid and aldose in the skin (indicating the content of acid and neutral polysaccharides) was found to be within the normal range (Lagier and Exer 1960) (Dr G. Bührer).
ANATOMICAL AND RADIOLOGICAL EXAMINATION OF THE SKELETON

The left foot and knee, the vertebral column (including the occipito-cervical junction) and some portions of the cranial vault and of a rib were examined.

LEFT FOOT

The left foot showed slight valgus deformity without equinus, and its shortening gave it the appearance of a tabetic foot, like that of the right foot. The pulps of the second and third distal phalanges were thickened and widened on their plantar surfaces. The radiological appearance (Fig. 4) provided the basis for an anatomical study.

Tarsus and tibio-tarsal joint—The midtarsal bones had disappeared. The calcaneus and the talus were deformed, the latter being tilted vertically and medially (Fig. 4). Histologically the cortical bone in both presented in places an irregular outline indicating a process of erosion identical with the one to be described in the metatarsal bases. The same indented outline was seen in the distal extremity of the tibia and fibula. The lower extremity of the tibia on certain sections showed a flattening of its anterior border without erosion. The cartilaginous surfaces
of the tibio-tarsal joint were normal, with slight superficial fibrillation in relation to a small anterior synovial expansion that was vascular but not inflammatory (Fig. 8).

**Metatarsal bases**—Radiologically the metatarsal bases all showed resorption of the bone. While the outline of the cortex could be distinguished in the fifth and especially in the first metatarsal (Fig. 5), erosion of the others was indicated on the lateral radiographs by the chamfering (Fig. 14).

Anatomically these bony stumps were covered with fibrous tissue, and that of the first metatarsal was dislocated superiorly and anteriorly. Histological examination revealed a similar process in all five metatarsals (Figs. 10 and 18). The covering of cartilage had disappeared. The erosion was shown by the irregular outline of the external cortical bone, which had on its outer surface a thin layer of fibroblastic connective tissue lined with a fibrous mass that in some places was in direct contact with the bone. This fibroblastic connective tissue sometimes contained capillaries and osteoclasts, but the rarity of the latter was striking. In some areas erosion of the cortex was part of a positive remodelling of the bone, indicated by the presence of osteoblasts or of metaplastic bone apparently of long standing. Near the base of the third metatarsal we noted a small area of basophil necrosis of the adjacent connective tissue.
Metatarso-phalangeal joints—Radiologically the only metatarso-phalangeal joint that was the site of an osteolytic process was the fifth. The others were remarkable for the considerable atrophy of the cancellous bone of the epiphysis. There was also side-to-side deformation of the heads of the third and fourth metatarsals.

Metatarsal joint surfaces—The first four metatarsal joint surfaces had preserved their smooth, pearly-white appearance, but they were irregular and in places their cartilaginous covering had disappeared and given place to a thin covering of fibrous tissue (Figs. 9 and 13).

Histologically they were the site of a regressive process indicated by the substitution of either a fibrocartilaginous or fibrous connective tissue structure for that of hyaline cartilage. In the former case the substitution was either complete, involving a vast area of the cartilaginous covering (Fig. 16), or partial, in a zone of chondrocytic necrosis, and it then produced a picture similar to that seen in the base of a proximal phalanx. In the latter case connective tissue
replaced the hyaline cartilage either by superficial exposure of fibrils (with disappearance of the acid polysaccharides on staining with Alcian blue) or including some islands of cartilage, or covering it like a pannus in continuity with non-inflammatory synovial membrane. It could also be in direct contact with the subjacent bone, either at the margin, where it was attached to the erosive periosteum of the epiphysis, or centrally, where it isolated cartilaginous areas. This isolation of separate areas was especially marked in the third toe. In a median sagittal section the plantar segment appeared to consist of hyaline cartilage replaced in parts by connective tissue; the dorsal segment was represented by cartilage of the "fibrous" type covering a foundation of remodelled bone (Fig. 16).

The head of the fifth metatarsal, lysed radiographically, appeared as a vertically flattened sheet of pearly-white colour. Microscopy showed that it was covered with a fibrous tissue clothing a reshaped stump of bone (Fig. 19).

Phalangeal joint surfaces—The phalangeal joint surfaces were smooth and flat. That of the second toe, however, had a small crater in the centre (Fig. 9) and that of the fifth had borders which in places terminated abruptly.

Histologically, regressive phenomena similar to those just mentioned were found, but the areas where fibrous cartilage replaced the joint surface were localised (Fig. 7). The crater in the second toe was occupied by vascularised connective tissue accompanied by superficial fibril exposure in the adjacent cartilage (Fig. 11). The dorsal marginal region of the third toe showed considerable pannus containing blood vessels covering the hyaline cartilage (Fig. 17). On the surface of the fifth toe the area of replacement of hyaline cartilage by fibrous tissue corresponded to the dissection out of a small isolated nucleus (Figs. 19 and 20). There was not necessarily any similarity between the changes in the metatarsal head and those in the phalangeal base (Figs. 15 and 19).

The synovial membranes were smooth and histologically showed no signs of inflammatory hyperplasia. Exceptionally, there were some congested fringes in relation to the joint spaces similar to those shown in the tibio-tarsal joint (Fig. 8).

The cancellous bone of the epiphyses was remarkable for considerable simple atrophy, not arising from resorptive endosteal activity (Figs. 15 and 19). The external outline of the epiphysial and metaphysial cortical bone most often presented an irregular appearance indicative of resorption histologically akin to that shown in the metatarsal bases (Fig. 19). The marrow was fatty, and the only area of vascular connective tissue reticulum that we saw, a very small one, formed part of the remodelling process affecting the surface of the head of the fifth metatarsal (Fig. 19).
OSTEOARTICULAR CHANGES IN A CASE OF ESSENTIAL OSTEOLYSIS

Left foot. Fifth metatarsal and fifth toe. Figure 19—Head of the fifth metatarsal, horizontal median section. (Haematoxylin and eosin, × 9.8.) The cortical bone of the epiphysis is remodelled and covered with a layer of connective tissue; that of the metaphysis appears to be eroded. Scarce trabeculation in the epiphysis. On the right, phalangeal surface with a cleft of connective tissue isolating a small marginal islet of bone (below on the figure). Figure 20—Base of the proximal phalanx. (Haematoxylin and eosin, × 42.) On this section, cut differently from that in Figure 19, the marginal islet of bone is continuous with the phalangeal epiphysis. Figures 21 and 22—Joint covering of the proximal phalanx; edges of the cleft of connective tissue in a section near that shown in Figure 19. (Haematoxylin and eosin, × 74.) Figure 21—The marginal islet of bone with a fibrous pannus covering some islets of hyaline cartilage. Figure 22—The main segment, with a persisting islet of hyaline cartilage overhanging the cleft.
Interphalangeal joints—The interphalangeal joints of the second and third toes were radiologically normal, the only notable feature being the atrophy of the epiphysial cancellous bone. In the first interphalangeal joint, however, signs of osteolysis were observable (Fig. 5) and they were also visible on the proximal joint of the fourth and on both of the fifth.

In the joints where the epiphysial outline was radiologically intact the cartilage covering was smooth and pearly-white but to a greater or lesser extent thinned. Microscopically it appeared of uneven thickness and showed changes of a regressive nature similar to those already described for the metatarso-phalangeal joints: chondrocytic necrosis, superficial fibril exposure (Fig. 12) and replacement of hyaline cartilage by non-chondrified connective tissue, which could assume the character of a pannus covering remnants of the cartilage or be at times in direct contact with the bone at the edge of the joint surface. In the marginal areas the plates of cartilage frequently showed loss of substance in depth, this being replaced by connective tissue (Fig. 12) or presenting a clearly demarcated free border. These appearances can be related to those of epiphysial bone erosion (Fig. 12).

In the interphalangeal joint of the big toe the proximal epiphysis was represented by a small sphere of fibro-hyaline connective tissue covering eroded bone. The cortical bone of the distal phalanx—like the remains of the other epiphyses appearing lysed in the radiographs—was eroded. The synovial membranes, the cancellous bone and the marrow presented the same features as in the metatarso-phalangeal joints.

Diaphyses: distal extremities of the distal phalanges: soft parts—The cortical bone of the shaft of the tibia, the fibula and the metatarsals presented no signs of erosion externally, but this was not always the case with the phalanges, which were shorter. The striking feature of the cortical bone of the tibia was the extent of the osteocytic necrosis.

Wherever they could be examined the distal extremities of the distal phalanges presented in places a denticulate appearance, but to an extent that was within the range of the normal.

There were no signs of inflammation of the soft tissues. The distal pulp of the second and third toes, however, presented a striking appearance. It corresponded in development to a fairly cellular desmoid connective tissue, the fibrils of which were embedded in a metachromatic mass of acid polysaccharides and were in part argyrophil. The enlarged pulp was traversed by numerous venous capillaries with a dilated lumen, but was lacking in arterioles. This decrease in the arterial network was a feature also found in the remaining periphalangeal soft tissue, where it was not accompanied by involutional sclerosis of the digital arteries (Fig. 31). In the pulp, close to the proximal border of desmoid tissue, we observed some round-cell aggregates disposed around a central vascular lumen; these aggregates differed from a normal glomus by the irregular arrangement and the staining characteristics of their cells (Fig. 33).

LEFT KNEE

The left knee contained 5 millilitres of a transparent and colourless liquid which clotted rapidly and gave a normal response to the mucin test. The various regions of its synovial and cartilaginous coverings were macroscopically and histologically normal, with the exception of a tuft of connective tissue on the lateral femoral condyle. This tuft consisted of a non-chondrified fibrous tissue continuous with the subjacent hyaline cartilage and did not present the characteristics of fibrillation of the Weichselbaum type of degeneration. The superficial part of this hyaline cartilage on the lateral border of this condyle and on the lateral edge of the intercondylar notch was covered with a sheet of connective tissue like a pannus but not vascularised (Figs. 23, 25 and 26).

Radiographs showed atrophy of the epiphysial cancellous bone; histologically this was of simple type, without endosteal activity; it did not extend beyond the epiphysial line and there were no remnants of endochondral ossification cartilage. The epiphysial and metaphysial cortical bone of the femur and tibia was the site of a process of erosion histologically similar.
to that observed in the feet, and it was in juxtaposition with several islets of hyaline cartilage, as, for example, on the anterior surface of the lower extremity of the tibia (Fig. 24). This process of erosion, however, did not show macroscopically or on the radiographs.

Under the thinned cortical bone of the medial aspect of the left anterior tibial tuberosity there was a vascularised nodule of connective tissue in the middle of an isolated area of fibril formation in the marrow (Fig. 29). Its vessels were partly filled with contrast medium; its histological characteristics gave the impression that it was a matured form of a reticular proliferation similar to that we described for a cervical vertebra. Silver stain showed its close relationship with the surrounding areas of fibril formation, in the middle of which other isolated capillaries could be observed. It had a small arteriole beside it, and this permits the hypothesis that it was a vascular nodule inserted between the arteriole and the intercellular sinuses.

CRANIAL VAULT, RIBS AND VERTEBRAE

No cortical or cancellous bone erosion was observed in the spinal column, ribs, or cranial vault. The thinning of the bone in the area of the depression at the junction of the occipital and parietal bones was principally due to a decrease in the volume of the diploe.

In the spinal column the epiphyseal cartilage plates had on the whole disappeared, the few persisting remnants displaying no endochondral activity. The dens [odontoid process], however, was in great part replaced by a fibrous mass, but the basilar part of the occipital
Various vascular patterns observed. Figure 27—Erosion surface of the cortical bone of the base of the fourth left metatarsal. Capillaries within fibrocytic connective tissue, in an area of osteoclast and osteoblast activity. (Haematoxylin and eosin, × 174.) Figure 28—Fatty marrow under the reshaped surface of the head of the fifth left metatarsal (detail of Figure 19). Slight vascular network of connective-tissue fibres with dilated venous sinuses injected with Indian ink. (Haematoxylin and eosin, × 69.6.) Figure 29—Isolated nodule of vascularised connective tissue under the cortical bone of the left tibia (medial aspect of the anterior tibial tuberosity). Below and on the right, part of an arteriole, the lumen of which is full of Indian ink. (Haematoxylin and eosin, × 248.) Figure 30—Pericapillary cuff of reticular cells at the periphery of the area shown in Figure 34 and in the vicinity of a bony arch. (Haematoxylin and eosin, × 277.5.) Figure 31—Segment of a plantar artery with a tortuous course in the proximal phalanx of the third left toe, seen in longitudinal section. The walls are unchanged. The lumen has been injected with Indian ink. (Haematoxylin and eosin, × 42.) Figure 32—Dissociation of arteriolar wall surrounded by arches of bone, at the periphery of the area shown in Figure 34. (Haematoxylin and eosin, × 207.) Figure 33—Modified glomus near the proximal border of the fibrous area of the enlarged pulp of the extremity of the third left toe. (Haematoxylin and eosin, × 186.) Figure 34—Isolated patch of vascular connective tissue in the body of the seventh cervical vertebra. Vascular nodule attached to a dilated arteriole in the vicinity of newly formed bone. (Haematoxylin and eosin, × 126.4.)
bone was not eroded. In the body of the seventh cervical vertebra there was an area of fibril
formation in the marrow, surrounded by a trabecular framework thickened where it came
into contact with it by metaplastic and lamellar bone formation. The following curious
vascular changes were observed in this area: a vascular nodule was attached to a dilated
arteriole, whose wall displayed smooth muscle dissociation; the lumen of the capillaries
contained some red cells and stood out in a mass of reticular cells with a rounded or spindle-
shaped nucleus and abundant cytoplasm, but externally poorly defined (Fig. 34). Secondly,
an isolated capillary was surrounded by a cuff of reticular cells, some of whose nuclei were
pyknotic and whose cytoplasm was confluent (Fig. 30). Thirdly, a dilated vessel was caught
within a bony trabecula and its wall resembled a swarm of ill-defined and swollen leiomyocytes
(Fig. 32).

DISCUSSION

Relation to other osteolytic conditions—The term osteolysis is sometimes used in histology to
define certain resorptions of bony tissue, especially relating to osteocytic activity (Kind 1951,
Bélanger et al. 1963). It has also been adopted in gross anatomy and particularly in radiology
to designate the total or partial disappearance of one or several bones. It is most often used,
though its limits are then rather poorly defined, when the process is not obviously infective
or neoplastic, and this is the sense in which we use the term.

Such a process may be manifested in certain pathological conditions presenting,
nevertheless, different radiological pictures; this is so in tabes, syringomyelia, scleroderma
and Raynaud’s disease. There are, however, three special conditions which we wish to mention:
1) post-traumatic osteolyses, of a regional nature (Mouchet 1943; Nicod 1945; Crasselt 1961);
2) ulcero-mutilating acropathy, which typically involves the feet, is of a heredo-familial
character, and is accompanied by skin ulceration and sensory disturbances (Thévenard 1953;
Lièvre and Gama 1957); and 3) mutilating forms of rheumatoid arthritis, which fall within
the category of inflammatory rheumatisms (Eisenstadt and Eggers 1955; Lièvre and Gama
1957). Our case is undoubtedly distinct from these, but it is none the less striking because
of certain radiological similarities that suggest the possibility of common links in
pathogenesis.

When a form of osteolysis cannot be linked with a cause it is called essential, a term
that is sometimes also applied to some forms in whose origin a traumatic factor might
reasonably be invoked. From the point of view of classification the group of essential
osteolyses should be broken up, although this does not mean a priori exclusion of pathogenic
links. In some cases the condition is one of “acro-osteolysis,” affecting the phalanges of the
hands and feet, especially the distal phalanges (Harnasch 1950; Lièvre and Gama 1957;
Joseph, Nezelof, Guéraud andJob 1959). In others, considerable areas of bone disappear,
particularly in the shoulder and pelvic girdles (Gorham and Stout 1955; Branco and da Silva
Horta 1958; Hambach, Pujman and Malý 1958; Johnson and McClure 1958; Jones, Midgley
and Smith 1958; Weiss 1960). Gorham and Stout (1955) linked these “massive osteolyses”
with haemangiomatosis, which has also been found by other workers in identical cases. There
are, however, accounts of other osteolytic processes radiologically similar to our case, and
likewise associated with skeletal abnormalities; some of these record a familial character
(Thieffry and Sorrel-Déjerine 1958). Two of these cases are akin to ours in that there is no
known hereditary past history and especially in that a delayed hypertensive nephropathy with
uraemia developed (Déro, Rathy, Rosselin and Catellier 1961; Mahoudeau, Dubrisay,

Essential features of the case presented—In placing this anatomical analysis in its clinical and
radiological context we are led to certain conclusions.

In the bone the chief features of the erosion of the cortex are as follows: Except in some
of the phalanges the process of erosion spared the shaft. It often, but not necessarily, affected
the bones of the tarsus and epiphyses and metaphyses of the foot and knee. In the tarsus and in several metatarsal and phalangeal extremities it caused total or partial osteolysis; on the other hand, it did not affect the outline of the bones of the knee, as seen on the radiographs, or that of the lower extremity of the tibia and fibula or of some of the metatarsal and phalangeal extremities.

Histologically it appeared as a process developing very slowly. It was characterised by the denticulate appearance of the external outline of the cortical bone and the relative lack of osteoclasts in the adjacent connective tissue. The latter characteristic has been indicated as occurring in "massive osteolysis" (Gorham and Stout 1955). Remodelling of the bone was sometimes completed by signs of osteogenesis.

The process of erosion was associated with trabecular rarefaction of the cancellous bone of the epiphyses, and sometimes with the presence of osteocytic necrosis (especially on the tibial shaft, which showed no erosion).

Apart from some vascularised areas of connective tissue of negligible size in certain places where the continuity of the cortical bone was broken (tarsus, head of the fifth metatarsal) no pathological endosteal activity was observed. Nowhere were any signs to be found of renal osteopathy or of osteodystrophy of the Sudeck type. The alveolar ridges of the jaw were radiologically preserved.

The process of erosion was not accompanied by inflammation of the adjacent soft tissues. In none of the bones examined, except for some inactive plaques in certain vertebrae, were any remnants of epiphyseal cartilage observed.

In the joint cartilages different changes were seen. When osteolysis was observable radiologically the joint cartilages had disappeared and the bone was covered directly with fibrous tissue. This tissue generally formed part of a mass of connective tissue in which the extremity of the bone was buried, but it sometimes appeared as a sheet covering a mobile and remodelled portion of the joint.

When the bone outline was preserved as seen on the radiographs, different regressive changes were noted; they were not always visible macroscopically. Thus on the metacarpal and phalangeal surfaces different transformations could be observed: partial or total replacement of the "hyaline cartilage" structure by one of "fibrous cartilage"; superficial fibril exposure; chondrocytic necroses; partial replacement by connective tissue that sometimes assumed the form of a pannus; complete disappearance of the cartilage, the cortical bone being covered by a thin connective-tissue sheet with no signs of erosion. On the lateral femoral condyle there was a small fibrous tuft, not chondrified, the fibrils of which were prolongations of those on the subjacent hyaline cartilage. It should be stressed, however, that the cartilage of the epiglottis showed no histological changes.

As regard to the general features it was found that the affection was associated with non-osteo lytic skeletal abnormalities, dental lesions and a hypertensive nephropathy of late onset producing uraemia. It does not seem to have the familial character noted by Thieffry and Sorrel-Déjerine (1958), though not by other workers. However, cases of epilepsy were mentioned as having occurred in the mother's family.

There were no neurological disorders. The parathyroid glands, the brain and the cervical cord showed no anatomical changes.

The data derived from immuno-electrophoresis did not suggest an immunological process. The methods used revealed no alterations in the polysaccharide level in the dermis.

On the other hand, examination of serum taken after death showed a large increase in the seromucoids and failed to reveal the presence of proline. Neither proline nor hydroxyproline was found in a specimen of urine collected at the same time.

Considerations on the nature of the process—This exceptional form of essential osteolysis is thus characterised by certain changes in the osteoarticular connective tissue; these changes are more diffuse than could have been expected clinically or from radiographs. The process

---

The Journal of Bone and Joint Surgery
of erosion of the bone affected essentially the epiphysial and metaphysial cortical bone, but did not always lead to osteolytic resorption visible macroscopically and radiologically. It developed extremely slowly, concurrently with simple atrophy of the cancellous bone and with regressive changes in the structure of the cartilage. It cannot be linked with familial illness; but it is associated with skeletal abnormalities.

These changes in bone and cartilage, when not accompanied by macroscopic and radiological indications of osteolysis, undoubtedly present histological features that in themselves can be found in other conditions. In young subjects, a qualitatively analogous metaphysial moulding erosion is normally found, but it does not yield such a markedly tattered appearance of the cortical bone. The fibrillar change in the hyaline cartilage and its partial replacement by connective tissue can be observed near the joint margin from a certain age onwards and especially in various pathological conditions; here we would stress their size and extent, and their appearance in such a young subject. For this reason we consider that these manifestations, though themselves non-specific, should be regarded as a minor degree of, or a preliminary stage in, the changes that lead to fully developed osteolysis. The cause of this development is not known to us.

Our observations do not give us ground for concluding that the condition is of vascular origin. We found no evidence for the haemangiomatosis described by Gorham and Stout (1955) and confirmed by several workers in subjects showing "massive osteolysis" (Gorham and Stout 1955; Hambach et al. 1958; Johnson and McClure 1958; Jones et al. 1958), but our case is clearly distinguished radiologically from these—which shows that in the field of essential osteolysis caution is needed in extrapolating findings (Crepsi 1962).

Nevertheless, in the histogenesis of lesions indicating a process of osteolysis, the importance of the vascular factor should not be underestimated. It is a factor that frequently obtrudes itself in the development of the osteoarticular anatomical changes (Rutishauser 1956). In the fibroelastic zones in contact with the eroded cortical bone (Fig. 27), in the pannus covering the cartilage (Fig. 17) and in the vascular reticular tissue on the surface of the reshaped bone (Fig. 28), vascular manifestations were minor in comparison with the extent of the anatomical changes, and especially with the amount of fibrous tissue laid down. Yet this very discrepancy, along with the scarcity and small size of the osteoclasts responsible for the erosion of the bone, reflects the sluggish and very slowly progressive nature of the condition. The renal lesions had the same features of sluggishness and slow progression (Chatelanat and Simon 1965).

The above vascular components were part of a tissue transformation. It might be worth mentioning that peculiar vascular aspects independent of such tissue transformation were also observed (Figs. 29, 30, 32, 33 and 34). In the foot the arterial trunks were tortuous but their walls were unchanged (Fig. 31). Smooth muscle changes were present in a vessel in the body of the seventh cervical vertebra, associated with proliferation of vascularised reticular tissue (Figs. 30, 32 and 34). Under the cortical bone of the upper epiphysis of the left tibia could be seen a capillary nodule similar to that already noted in vascular dysfunction in bone (Fig. 29) (Rutishauser 1963). Noticeable in the enlarged pulps of the toes was the reduction in the arteriolar bed and the presence of perivascular cellular cuffs that did not present the appearance of the normal glomus (Fig. 33). Although these were exceptional observations they emphasise the general nature of the vascular dysfunction in the subject under study. The scarcity of such aspects is also explained by the slow course of the process.

Although, then, we cannot attribute to it the causal role postulated in other forms of osteolysis, in our case a vascular factor was implicated, which was not limited to the areas where the osteoarticular structures had disappeared. We think that it played a part in the histogenesis of the condition.

As regards the neurotropic factor postulated for the origin of some osteolyses (Crasselt 1961), we have no evidence to present. Whereas we cannot exclude a priori the possible existence
of common links in pathogenesis, we must state that we did not observe any histological evidence for Sudeck's dystrophy.

We were impressed by the absence of proline and hydroxyproline in the urine and serum. If this were confirmed in other cases there would be justification in postulating a disturbance in the metabolism of proline, which is a precursor of hydroxyproline in collagen synthesis.

The increase in the seromucoids, along with a normal level of hexosamines and protein-bound hexoses, suggests the existence of a ground substance depolymerisation differing from that of an inflammatory state (Dr F. Infante). It seems to indicate progressive destruction of connective tissue substance. The possibility of a link between this phenomenon and the nephropathy of late onset might be raised.

Independently of the problems mentioned above, this observation brings us back to some of the chief constants of non-specific change in joint surfaces, in conditions that clinically and radiologically do not correspond to the criteria of "rheumatic disease." In cartilage the replacement of "hyaline" by "fibrous" structures, or partially by connective tissue sometimes of pannus type, is an important element in the histogenesis of arthritis and arthrosis. It is interesting to note that the cartilaginous changes and remodelling of the bone on the dorsal segment of the head of the third metatarsal (Fig. 16) present features that are observed in the histogenesis of the osteophyte of arthrosis (Rutishauser, Lagier and Grasset 1959).

SUMMARY

1. A case of essential osteolysis is presented, occurring in a young man of eighteen with no known family history and developing progressively from early childhood. The condition was radiologically evident in the elbows, hands and feet, and was accompanied by atrophy of the cancellous bone of the epiphyses of the shoulders and knees. It was also associated with certain abnormalities of the skull and vertebrae. The patient died from a nephropathy of late onset.

2. Examination of the left foot revealed on the radiologically "lysed" bony extremities a very slow process of erosion affecting essentially the epiphysial and metaphysial cortical bone, of a non-inflammatory nature and accompanied by disappearance of the hyaline cartilage. The extremities not radiologically "lysed" showed signs of erosion that were histologically similar but not macroscopically evident; they were accompanied by regressive changes in the hyaline cartilage.

3. There were no signs of renal osteodystrophy or of Sudeck's dystrophy.

4. Post-mortem tests revealed an increase in the seromucoids and failed to reveal the presence of proline in the serum or of proline and hydroxyproline in the urine.

5. The authors discuss the place of this condition among osteolyces in general.

The authors express their thanks to Professor G. Bickel, Director of the University Medical Clinic, Geneva, for providing them with the clinical history of this patient. They also thank Miss I. Antener (Nestlé Research Laboratories, Vevey), Dr F. Infante and Dr J. J. Scheidegger (Surgical Clinic and Institute of Hygiene of Geneva University) for the analyses they carried out; and Miss J. Merlo for photographing and Miss E. Neumann for preparing our sections.

A paper published after completion of the present manuscript describes several cases of osteolysis observed in the same family, involving especially the carpal and tarsal bones; some of these were accompanied by nephropathy (Shurtleff, D. B., Sparkes, R. S., Clawson, D. K., Guntheroth, W. G., and Mottet, N. K. (1964): Hereditary Osteolysis with Hypertension and Nephropathy. Journal of the American Medical Association, 188, 363.)

REFERENCES


OSTEOARTICULAR CHANGES IN A CASE OF ESSENTIAL OSTEOLYSIS


HUMAIR, L., and KORALNIK, O. Ostéolyse essentielle avec néphropathie hypertensive urémigène. (To be published.)


