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Histology of Kashin-Beck lesions

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Abstract There are few papers in existence describing the histopathology of Kashin-Beck disease. The few existing papers mention chondronecrosis within the epiphyseal primodium and metaphyseal cartilage. In the present study, two series of samples were available for histology: supernumerary fingers removed from young subjects and intra-articular bodies collected in more advanced cases of the disease. The prevailing characteristic of the samples is the absence of vascularisation within the proximal cartilage end plate of the phalanx associated with an alteration of the epiphyseal bone formation. These observations suggest that Kashin-Beck disease could develop from an alteration of the angiogenesis of the metaphyseal cartilage resulting in degeneration with consequent joint dysplasia, which may be associated with a decrease in growth of the diaphyseal bones.

Résumé Très peu de publications décrivent l'histopathologie de la maladie de Kashin-Beck. Elles mentionnent essentiellement la présence de nécroses des chondrocytes au sein des cartilages métaphysaires et articulaires. Dans notre étude, un examen histologique a été réalisé sur deux types de prélèvements: des doigts surnuméraires

provenant de trois sujets jeunes et des souris articulaires provenant de cas plus âgés. La caractéristique la plus marquante est l'absence de vascularisation de la couche terminale du cartilage épiphysométaphysaire des phalanges entraînant une perturbation de l'ossification épiphysaire. Ces observations suggèrent que les manifestations cliniques de la maladie de Kashin-Beck soient dues à un trouble de l'angiogénèse au niveau du cartilage métaphysaire entraînant sa dégénérescence et secondairement des dysplasies articulaires associées ou non à une diminution de la croissance de la diaphyse des os longs.

Introduction

The main lesions of Kashin-Beck disease involve the growth plate and the articular cartilage. However, few publications exist that describe the histology of these alterations or try to explain their pathogenesis [3, 5, 6, 8].

Mo [5, 6] gives the most detailed histological description. Following his observations, the cartilage involved shows dystrophic changes, such as atrophy, degeneration and necrosis with repair and adaptive changes, leading to disturbance of endochondral ossification. In the case of atrophy, the chondrocytes are reduced in size and number. The affected articular and growth plate cartilage appears thinner than normal. In the joints, the degenerative changes observed in the cartilaginous matrix are similar to those that occur during the natural process of ageing, with fissure formation, fibrillation and degenerative alteration. In growth plate and articular cartilage chondronecrosis seems to be the prevailing manifestation. In the necrotic areas chondrocytes die, lose their nuclei and become ghost cells. The intercellular matrix remains for a period, then the ghost cells disappear and necrotic areas gradually become disorganized. These necrotic areas are multifocal; they affect different bones in different locations and do not show a strictly bilateral symmetry. The chondronecrosis is located in the deep zone of the cartilage almost always close to bone and bone marrow. The maturing chondrocytes show cellular vacuolization and condensation with

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slight degenerative changes in the cytoplasm. After the chondrocytes die, secondary changes appear. The surviving chondrocytes adjacent to these necrotic areas soon proliferate and even form chondrocyte clusters. Eventually the necrotic areas heal with scarred bone tissue.

Patients and methods

Two series of samples were available for examination: supernumerary fingers removed from two children and an adolescent boy, and intra-articular loose bodies collected along with synovial tissue in more advanced cases of Kashin-Beck disease. The specimens were fixed in formaldehyde solution (8%), and decalcified in a solution of ammonium chloride (70 g), formic acid (50 ml) and hydrochloric acid (14 ml) in water (1000 ml). The specimens were then rinsed in ethanol and processed for paraffin embedding. The histological sections were cut at 5 μ m and were stained with hematoxylin and eosin.

The fingers for which we knew the ages comprised a supernumerary thumb from a 4-year-old girl (Fig. 1), two fingers from a 13-year-old boy (Fig. 2), and a supernumerary toe from a 17-year-old boy.

Fig. 1 Cartilage end-plate of the phalanx of a 4-year-old girl characterized by a complete absence of blood vessel penetration and no epiphyseal ossification ($\times 6.25$ hematoxylin and eosin)

Fig. 2 Cartilaginous subperiosteal formation on the diaphyseal bone cortices of a 13-year-old boy showing delayed ossification ($\times 20$ hematoxylin and eosin)

Results

All these fingers, removed during the development period of Kashin-Beck disease, were characterized by complete absence of penetration of blood vessels within the proximal end-plate of the phalanx, and thus were devoid of epiphyseal bone formation. This is a very abnormal condition, because it is well-known from radiological findings [2] that epiphyseal ossification is well-established in the phalanges before the age of 3 years. Under such abnormal conditions, the cartilage end-plate is found to contain enlarged chondroplastic lacunae and cleavage of the matrix is suggestive of incipient fragmentation. In the same phalanges, the presence of a cartilage sheath between periosteal and diaphyseal bone is further proof of deficient vascular supply.

The loose bodies found during the examination ($n=5$) were chunks of degenerate cartilage. They differed from common articular loose bodies by their abnormal thickness, and by the scarcity of chondrocytes within their partly necrotic matrix.

The samples of synovial tissue ($n=2$) were characterized by absence of leucocyte infiltrates, and the presence of small pieces of bone at the surface of their hyperplastic villi. Signs such as these are characteristic of advanced-stage osteoarthritis.

Discussion

The pathology of Kashin-Beck disease may be explained by deficient penetration of blood vessels in the epiphyseal end-plate, followed by degeneration and fragmentation of the epiphyseal end-plate. Deprived of its blood supply, the diaphyseal bone is unable to grow in length and develops precocious osteoarthritis.

Indeed, our histological findings on supernumerary fingers are consistent with radiological findings (Perlmutter et al., personal communication) that have been observed in other fingers of children suffering from Kashin-Beck disease. The volume and condition of the loose intra-articular bodies reported in this paper may be a further proof of this pathogenic mechanism.

Our histological findings point to a deficit of blood vessel penetration into the epiphyseal end-plates as an initial factor inducing Kashin-Beck disease. Unfortunately, our findings do not designate the factor(s) responsible for such a deficit. Along the limb the proximal-distal gradient of the altered joints, frequently observed in clinics [4] and on X-rays in full skeleton examinations [Hinsenkamp et al., personal communication], reinforces the hypothesis of the interaction of external factors (cold, microtrauma, hypoxia) affecting the peripheral joints most often. Local deficiency of the blood supply could result from vasoconstriction due to sustained exposure to the cold in winter, particularly in school classrooms where children do not move very much; poor thyroid response to the cold due to deficiency in iodine and pos-

sibly selenium [7]; a possibly vasoconstrictive effect of mycotoxins; or a more specific effect of mycotoxins on epiphysial ossification [1].

References

1. Chasseur C, Suetens C, Nolard N, Begaux F, Haubruge E (1997) Fungal contamination in barley and Kashin-Beck disease in Tibet. *Lancet* 350:1074–1075
2. de Roo T, Schröder HJ (1977) *Atlas de l'âge osseux*. Maloine, Paris, 1
3. Kolsteren P (1992). Kashin-Beck disease. *Ann Soc Belg Med Trop* 72:81–91
4. Mathieu F, Begaux F, Lan ZY, Suetens C, Hinsenkamp M (1997) Clinical manifestations of Kashin-Beck disease in Nyemo Valley, Tibet. *Int Orthop* 21:151–156
5. Mo DX (1987) Pathology and selenium deficiency in Kashin-Beck Disease. In: GF Combs, JE Spallholz, OA Levander, JE Oldfield (eds) *Selenium in biology and medicine*. 3rd symposium. Van Nostrand Reinhol, New York, pp 924–933
6. Mo DX (1990) Advances in the pathology of Kashin-Beck disease and its relationship with selenium and other elements. In: Chinese Academy of Preventive Medicine (CAPM). *Proceedings of the international workshop on Kashin-Beck disease and non-communicable diseases*. WHO, Beijing, pp 42–55
7. Moreno-Reyes R, Suetens C, Mathieu F, Begaux F, Zhu D, Rivera MT, Boelaert M, Nève J, Perlmutter N, Vanderpas J (1998) Kashin-Beck osteoarthropathy in rural Tibet in relation to selenium and iodine status. *N Engl J Med* 339:1112–1120
8. Nesterov AI (1964) The clinical course of Kashin-Beck disease. *Arthritis Rheum* 7:29–40