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Distribution of insulin-like growth factors in condylar hyperplasia

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Summary

Condylar hyperplasia (CH) is a local overgrowth of the condylar process of the temporomandibular joint (TMJ) of unknown etiology. Probably, growth factors like the insulin-like growth factors (IGFs) are involved in its pathogenesis. Specimens from 12 patients were investigated histologically and immunohistochemically to obtain the distribution of the IGFs-I and -II and the IGF1 receptor. The results revealed juvenile and adult subtypes. While generally IGF-II could only be detected weakly, in the juvenile cases strong immunostaining for IGF-I in cartilage and bone supposes an influence on pathological growth processes.

Introduction

Hyperplasia of the condylar process of the temporomandibular joint (TMJ) is a rare disease of unknown etiology and pathogenesis and is often characterized by enlargement leading to facial asymmetry and chin displacement. Unilateral condylar hyperplasia (CH) is the most frequent subtype (Obwegeser, 2001). Usually, CH begins during the childhood or early adult life, where the condyle is in its growth phase or has just ceased growth activities. Histopathologically, an increased thickness of specific layers of the condylar cartilage and the occurrence of cartilage rests in the subchondral condylar bone are described (Obwegeser, 2001). The insulin-like growth factor (IGF) system

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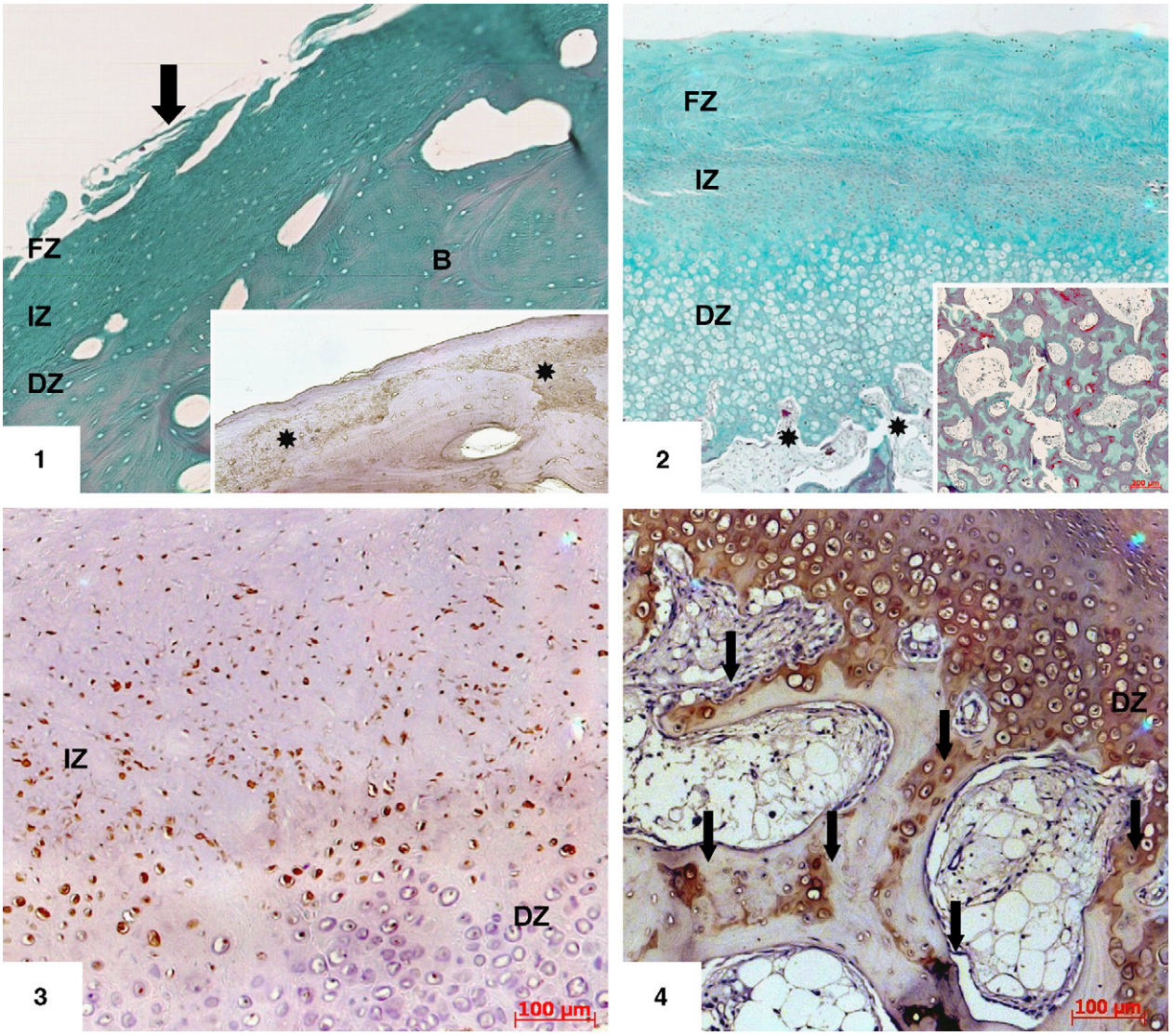
represents a growth factor family consisting of the ligands IGF-I and -II, two receptors (IGF1R, IGF2R) and six binding proteins. It controls pre- and post-natal development and growth and is also involved in the development, physiology and pathology of bone and cartilage (Schmidt et al., 2006). IGFs are important factors for the neonatal and growing condyle and may play a role in mechanical transduction and osteoarthritis of the TMJ (Götz et al., 2005). Considering CH as a local post-natal overgrowth syndrome, IGFs could play a role since overexpression of IGF-II is implicated in the etiolgy of different overgrowth syndromes (Ambler, 2002).

Materials and methods

Archived paraffin blocks of condyles used for histopathological diagnosis representing 12 patients (9 female, 3 male, 14–44 years) with clinical



Figures 1–4. 1. Condyle, male, 35 yrs, control specimen, cartilage with superficial fibrous zone (FZ), intermediate zone (IZ) and deep zone (DZ), B = subchondral bone, arrow: surface fibrillation; trichrome staining, original magnification × 10; *Inset*: same condyle, IGF-II immunohistochemistry, immunostaining in subchondral bone and cartilage (asterisks); DAB, original magnification × 10. **2**. Condylar hyperplasia, male, 16 yrs, cartilage with superficial fibrous zone (FZ), intermediate zone (IZ) and deep zone (DZ), asterisks: erosion zone; trichrome staining, original magnification × 5; *Inset*: subchondral spongiosa structure of the same condyle; trichrome staining, original magnification × 5. **3**. Condylar hyperplasia, female, 21 yrs, IGF-I immunohistochemistry, staining of chondrocytes in the intermediate zone (IZ), DZ = deep zone; DAB, original magnificatiion × 10. **4**. Condylar hyperplasia, female, 14 yrs, IGF-I immunohistochemistry, staining of the lower part of the deep zone (DZ) and calcified cartilage, rests of calcified cartilage in subchondral bony trabeculae (arrows); DAB, original magnification × 10.

unilateral CH having undergone high condylectomy were evaluated. Additionally, a healthy left condyle of a 35-year-old male, resected for forensic reasons, was investigated as a control specimen. Selected 5 μm sections were deparaffinized and stained with hematoxylin–eosin (HE), Masson-Goldner's trichrome, PAS and alcian blue. Immunohistochemistry using antibodies against IGF-I, -II and IGF1R (Biomol, Hamburg, Germany), indirect immunoperoxidase or DAKOEnVision® (Dako, Corpinteria, USA) with DAB detection was done on sections according to recent protocols (Götz et al., 2006) including positive and negative controls.

Results

In the control specimen, a thin adult condylar cartilage consisting of a superficial fibrous zone (FZ), an intermediate (IZ) and a deep zone (DZ) with few hypertrophic chondrocytes was visible (Fig. 1). Signs of beginning cartilage degeneration, but a normal subchondral bony structure could be seen (Fig. 1). Histologically, the CH specimens could be divided into two groups: 5 specimens (14–21 years) showed typical growth stage cartilage structures with a fibrous FZ, a subjacent proliferative IZ and a broad DZ consisting of hypertrophic hyaline cartilage and calcified cartilage (CC), and an erosion zone (Fig. 2). Subchondrally, cartilage remnants (CR) were also visible in different quantities reaching into the spongy bone (Fig. 4). The condylar spongiosa consisted of a network of thickened trabeculae (Fig. 2, inset). Osteoid seams and large numbers of osteoblasts were visible in most cases. The older patients showed the adult type of condylar cartilage comparable to the control case, but with a persisting hypertrophic DZ in some cases and a spongy bony structure resembling the one seen in the younger cases. Also, remnants of CC could be observed in most cases.

In the juvenile-type CH specimens strong IGF-I immunoreactivity (ir) was found in the cells of the IZ and upper DZ (Fig. 3), in some cases also in osteoblasts and bone marrow matrix. Extracellular ir appeared in the CC including all CC remnants located in the subchondral bone (Fig. 4). IGF1R was mainly found in IZ chondrocytes and osteoblasts. IGF-II ir was weak and limited to the FZ. In general ir was reduced in all adult-type CH and was comparable to the adult control specimen. In the only one instance IGF-II was observed in IZ cells. In contrast to the CH cases, IGF-II could be observed in the cartilage matrix and cells of the DZ as well as in subchondral bone of the control condyle (Fig. 1, inset). Stronger staining for all components investigated appeared in degenerated cartilage areas.

Discussion

Analysis of the CH cases investigated revealed the classical histopathological signs for the juvenile and adult types (Obwegeser, 2001). Some features ascribed to the juvenile CH could also be found in the adult type, e.g. spongy bone hyperplasia and CC islands within the bone. Osteoarthritis was also common. It can be speculated that the weak or missing IGF-II ir in the CH cases means that this growth factor is probably not involved in the pathogenesis of CH. In contrast, the occurrence of IGF-II could be demonstrated in the cartilage and bone of an adult healthy condyle. Strong ir for IGF-1 and IGF1R in the cartilage and bone of the juvenile CH cases suppose an auto- or paracrine influence on growth processes. Especially in the IZ, IGF-I might promote cellular proliferation due to its anabolic function (Laron, 2004). Thus, the weak or missing IGF-I and IGF1R ir in the adult CH specimens may be a sign of downregulation. The appearance of IGFs in degenerated cartilage areas indicates an involvement in osteoarthritis as known for other joints or the TMJ of other species (Götz et al., 2005).

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