特別講演

Factors that Affect Growth and Deviation of the Nasal Septum

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There are many factors influencing the normal and pathological growth of the nasal septum, for instance, race, family, hormones, nutrition, injuries, infections, tumours, surgery, and orthodontic treatment. Most of them are not investigated in a concluding manner.

The ideal subject for studying some of these factors are identical twins, one of them had different environmental conditions or a midfacial trauma during the growth period. But there are only a few cases incompletely documented in literature which allow no conclusions.

By the life-long research of Ryo Takahashi¹⁰⁾ some fundamental knowledge is now available concerning some of these factors. He demonstrated that septal deviation first appeared in the Neanderthal man due to structural alterations between brain skull and facial skull. Takahashi's findings are based on the examination of skulls in animals and hominids, and on clinical observations of the Japanese population.

I would like to support some of Takahashi's concepts and to add a few new data based on our clinical and radiocephalometric studies of patients, and on findings about the metabolic and proliferative behavior of the human septal cartilage in different age groups.

Clinical observations

We studied the natural history of 50 adult patients with a carefully documented history of untreated midfacial trauma in childhood. By means of photographs, facial development could be followed over the years of growth. This, together with the pre-operative set of data, allowed the following conclusions: deformity of the nose some months after mid-

facial injury may look unimpressive and is often not recognized by the family. Alterations of the bony pyramid and the premaxillary region are rarely visible in the first decade. Rapid and remarkable changes appear during the pubertal growth spurt, the onset of which varies between 11 and 14 years.

From these findings, we concluded that the long-term effect of even minor trauma to the nose in childhood is not predictable before the end of pubertal growth spurt. If such an injured nose is surgically treated during growth it is impossible to separate the influences of the original injury and of the surgical manipulations after the end of puberty.

Septal abscess during childhood with destruction of the septal cartilage results in a growth inhibition not only of the septum, but in some cases, too, of the upper lateral cartilages and the bony pyramid. We could conclude from several own cases⁵⁾ that the growth inhibition of the nasal structures is more pronounced the earlier the septal abscess had destroyed the septal cartilage. In the young children the nasal bones are positioned on top of the not yet resorbed cranial parts of the upper lateral cartilages.

Thus the partial destruction of the upper lateral cartilages by abscess leads to an inhibition of growth of the nasal bones, too.

In one study we determined the distribution and activity of Cathepsin D, a necrolytic and autolytic collagen degrading enzyme with optimum activity in the acid pH range. This enzyme is distributed all over the septal cartilage with nearly equal activity. This finding may help to explain the rapidity of cartilaginous destruction in many cases of nasal

Fig. 1 : Proliferative potential of the human septal cartilage in three age groups. The numbers in the 5 areas represent percent of colony-forming chondrocytes /100 inserted cells in comparison to fetal chondrocytes which form 100%. We distinguish 5 areas within the septal cartilage (compare numbers of the middle age group): anterior or caudal end (59); central area (35); posterior area (9); suprapremaxillary area (30); caudal prolongation (20)(from 13).

septal abscesses⁵⁾.

Besides injuries and infections of the nasomaxillary complex surgery in early childhood can inhibit nasal development and cause septal deviations. We conclude this from some catastrophic long-term results of nasal tip correction in infants with lip-palate-clefts within their first year of life. Especially incisions of the alar base and incisions through the columella produce an underdevelopment of the nasal lobule which becomes apparent in its real extent after the pubertal growth spurt. We have some examples where the nose of a cleft patient was not corrected before adulthood: these patients have normal dimensions of their nasal structures which only show cleft-

typical deformities. The suture of the upper lip along in early childhood leads to a minor growth inhibition of the maxilla as we know from comparison with not operated cases.

Since 18 years we have performed reconstructive septorhinoplasty in children because of flexed nasal deformities due to trauma. The long-term results after their pubertal growth spurt vary from poor to normal growth of the injured and surgically treated nose^{4,6,7)}. We can not explain in each case why a good or a poor result was registered at follow-up, but we found some techniques which will end up in some types of growth inhibition when practiced on the growing nose: resection of the central area as it is done by Killian's submucous septal resection, or the caudal end of the septum (fig. 1); separation of the upper lateral cartilages from the septal cartilage; scarification of the septal cartilage; not replacing cartilaginous struts into sites of cartilaginous defects; transposition of posterior cartilage to more anterior sites; exposure of the lower lateral cartilages by the external approach through a columella incision; destruction of blood vessels which are adjacent to the cartilage, in the mucoperichondrial flaps by traumatic preparation of tunnels or by incisions in the septal mucosa.

Furthermore our long-term follow-ups demonstrated that there was a rare of recurrent septal deviations after septoplasty in about 25 per cent of the operated children, and that this rate increased when septoplasty was performed in the period of the pubertal growth spurt. On the other hand our examinations showed that osteotomies of the nasal bony pyramid did not inhibit nasal development⁶⁾.

Thus in conclusion certain surgical techniques performed on a child's nose may disturb further nasal development, but we are far away from an understanding of the reasons why we obtain failures or satisfying long-term results.

For the surgical intervention of a child's nose it is necessary to know whether there are special zones or sites in the septum and surrounding nasal structures that are more concerned with growth than

others. The controversial discussion of these "sites of growth" in the nose induced a series of experiments which will briefly be reviewed in the following pages.

Microcosmos septum

The septal cartilage is a unique cartilage because it is a result of sequential inductive interactions from cephalic mesoderm and neural tube and neural crest ectoderm. To learn more about the metabolic and proliferative potential of this cartilage, a group at the University of Ulm studied biopsies of the septal cartilage of patients between 5 and 65 years of age whose only pathology was a deviated septum¹¹⁻¹⁷.

Cell replication was measured by in vitro incorporation of labelled thymidine, which represents DNA synthesis, while the extent of matrix synthesis was measured by in vitro incorporation of labelled sulfate into cartilage, representing the last step in proteoglycan synthesis^{11,12}.

In two other experiments, chondrocytes were isolated from five different areas of the human septal cartilage to measure cell density and to determine the capacity of isolated chondrocytes for clonal proliferations¹³.

In addition, metabolic pathways were assessed by measuring such enzymes as Cathepsin B and D, β -hexosaminidase, acid, and alkaline phosphatase in septal cartilage of endocrinologically healthy persons and in patients with acromegaly^{14,17}.

Cathepsin B activity, a neutral thiol proteinase degrading both the nonhelical and helical region of the collagen molecule was not different in acromegalic patients and controls. However, Cathepsin D activity, a lysosomal proteinase degrading proteoglycans, and β -hexosaminidase activity a chondrocytic enzyme breaking down glycosaminoglycan side chains of the proteoglycans were significantly augmented in acromegaly. Activity of alkaline phosphatase, an enzyme linked to cartilage mineralization, was recognized in large areas of the septal cartilage whereas in healthy controls its activity could only be detected in the chondroosseous junction.

These various studies demonstrated that the human

septal cartilage is a very complex part of the midface and is built up of five areas (fig. 1) displaying partial age dependency, strict local distribution and predominance of either matrix synthesis, cell replication, and proliferative capacity.

The complicated pattern of distribution of enzymes in the five areas is different in septal cartilage of patients with acromegaly. Contrary to previous suggestions, the posterior area of the septal cartilage adjacent to the perpendicular plate cannot be considered a growth zone, but is rather an area in which, until age 40, chondrocytes are transformed into bone by enchondral ossification.

A variety of hormones and growth factors are influencing the growth of septal cartilage. The stimulatory effects of insulin (BHI), growth hormone (GH) and insulin like growth factor I and II (IGF I and II) were assessed in an in vitro culture system that measures the proliferation of single chondrocytes to cell clones in a semi solid medium. Mesodermally derived human fetal epiphyseal and postnatal articular and ectodermally derived human nasal septal chondrocytes could be investigated and compared^{15,16}. IGF I stimulated clonal growth of fetal chondrocytes, but IGF II was significantly more effective. In contrast IGF I was more effective in adult articular chondrocytes than IGF II. GH and BHI did not affect clonal growth of fetal or adult articular chondrocytes. IGF I and IGF II both stimulated clonal growth of nasal septal chondrocytes without any significant difference.

In addition BHI stimulated effectively the clonal growth of septal chondrocytes. In contrast to mesodermally derived articular chondrocytes septal chondrocytes did response to the stimulatory action of epidermal growth factor (EGF).

The results of this study^{15,16} show that IGF I is the predominant growth factor for skeletal growth. Presently the finding that IGF II is as active in stimulating clonal growth of septal chondrocytes as IGF I and the fact that EGF is an effective stimulus only for the clonal growth of ectodermally derived chondrocytes is difficult to explain.

However it must be mentioned that high concentrations of IGF II and EGF can be found in the brain. It must remain speculative if the neural crest origin of the septal chondrocytes therefore influences their responsiveness toward growth factors. In another experiment we could show that Glibenclamide (Euglucon) increased clonal growth of human chondrocytes from the septal cartilage. Glibenclamide appears to be the first non-hormonal agent to augment growth of chondrocytes. The somatomedins may be involved in its action²⁾.

Acromegaly is an endocrine disease due to growth hormone excess originating from a somatotrophic adenoma of the pituitary gland. Excessive growth hormone levels lead to high insulin like growth factor concentrations, which are known to stimulate cartilage growth in vivo and in vitro.

Septal cartilage was obtained from acromegalic patients during transnasal hypophysectomy and from healthy adult during septoplasty to analyse the type of Collagen, the intracellular glycogen, several intracellular enzymes, and the capacity of septal chondrocytes to grow in cell colonies¹⁷⁾.

Both in acromegalic patients and controls type II collagen was the major collagen and type I collagen (15% of total collagen) was additionally found in the chondro-osseous junction, the zone of cartilage mineralization. In contrast to controls no minor collagens as type X collagen were detected in acromegalic cartilage. These minor collagens are believed to be important for biomatrix stabilization. Intracellular glycogen, the major source of energy of chondrocytes, was found to be drastically reduced in acromegaly.

The activity of biomatrix degrading enzymes is enhanced in acromegalic septal cartilage, while its clonal proliferation capacity is reduced. Some of these findings can be explained by the raised growth hormone and IGF concentrations in acromegalic patients, which needs further investigations¹⁷⁾.

All these numerous findings about the metabolic and proliferative pathways in the nasal septal cartilage of healthy subjects and acromegalic patients underline the concept of the septal cartilage to be a

special type among the cartilages in the body: it is really a microcosmos concerning its metabolic features, and we start to understand why this cartilage—opposite to others—is able to grow even in the aged persons. Takahashi had shown¹⁰⁾ that there is a permanent increase of people with septal deviation during life, and we tried to present here some of the findings which may help to explain Takahashi's clinical observations.

The preliminary surgical implications of these findings are that so-called centers or sites of growth cannot be detected within the human septal cartilage, but that areas of differing mitotic and metabolic capability partly depend on age. The caudal end the central area, which usually is excised in radical submucous resection, are important even in the elderly, while the suprapremaxillary area is important for nasal growth in children. No conclusions were reached as to the effect of resection of the ethmoidal-septal junction, the site of enchondral ossification in children.

Interrelationship of growing nasal skeletal units

The nasal region is built up of 24 bony and cartilaginous units originating from the frontonasal segment and from the paired branchial arches. The interrelationship of these skeletal units has not yet been investigated in humans. What will happen to these different units if one or some of them are destroyed during growth? For instance, one nasal alar is underdeveloped by trauma, surgery, tumour or congenital, does this influence the healthy nasal alar of the other side? Or: if the premaxilla is destroyed, does this inhibit the growth of the septal cartilage?

We were especially interested to obtain information on the interrelationship of the nasal septum, the premaxilla, and the maxilla, because these informations are of importance for the technique of septoplasty in childhood. This topic is surrounded by a plethora of divergent data from human pathology and from animal experiments. Scott's hypothesis⁹⁾ which implicates the nasal septum as the determinant of the midfacial growth, is opposed by Moss's opinion³⁾ "of the relative developmental independence of the

nasal septum and maxilla".

In cooperation with our Maxillo-Facial Department adult patients with midfacial deformities induced by mechanical trauma in childhood were studied, therefore, by means of a thorough ear-nose-throat and orthodontic examination, anterior rhinomanometry, facial photographs, dental casts, lateral radiocephalograms and orthopantomograms. The radiocephalograms were evaluated according to the recommendations of Haase^{1,8)}. To obtain data on the pathogenesis of the midfacial deformity, old photographs were analyzed as well as the reports of nasal and maxillary surgery to find the sites of traumatization within the nasomaxillary complex. The evaluation of the various data in each patient led to the conclusion that midfacial trauma during childhood may induce alterations in growth leaving uni- and /or bilateral deformities of single skeletal units of the nasomaxillary complex in the adult. Using exact measurements the following parts of this complex could be demonstrated to grow nearly independently from each other: nasal bones, septal cartilage, lower lateral cartilages, premaxilla, and maxilla.

To find out rules about the interrelationship of septal cartilage and maxilla/premaxilla we used two different groups of our 185 investigated patients with midfacial trauma in childhood: one group demonstrated huge noses in combination with compressed or shortened maxillae. The other group was characterized by small noses and normal or very large maxillae and premaxillae. Patients from the last group often had a history of septal abscess in childhood with loss of septal cartilage, but with normally developed premaxilla and maxilla. Patients of the first group often had a history of injury to their premaxillary region with frontal teeth impression and compressed maxilla, but their noses showing normal or large dimensions in comparison to our control group. From the data of these groups we can conclude that there are patients with normal or large nose in connection with arrested growth of the maxilla/premaxilla and, vice versa, patients with inhibited nasal growth and normal maxilla/premaxilla.

These findings strongly support the opinion of Moss that there is a relative developmental independence of the two adjacent skeletal units, nasal septum and maxilla/premaxilla. The clinical conclusion drawn from this study support those who advocate conservative surgery on the septal cartilage of the child and minimizes the fear of interfering with the growth of the adjacent nasomaxillary structures by septoplasty.

Our radiocephalometric studies demonstrated, furthermore that all investigations of the growing nose must include a thorough orthodontic examination and that the classic anthropological measurements of the nasal dimensions are of no great help to find out trends of midfacial growth. There are many shortcomings of the radiocephalometric measurements, too, for the evaluation of data of the growing midface⁸⁾, but until now this method is the only fairly exact technique to gain some reproducible data.

The nasal septum is a fascinating structure in our midface, determining the beauty of the face with its dimensions, representing a unique cartilage of our body as to its life-long lasting growth potential and a microcosmos of mostly unknown metabolic pathways which will attract our scientific interest.

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