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Arrested pneumatization: Witness of paranasal sinuses development?

S. Kuntzler, R. Jankowski *

Pôle neuro-tête et cou, service d’ORL et de chirurgie cervico-faciale, hôpital Central, université de Lorraine, CHU de Nancy, 29, avenue du Maréchal-de-Lattre-de-Tassigny, 54000 Nancy, France

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ABSTRACT

Objectives: Recent radiological studies have demonstrated that formation of the sphenoid sinus is preceded by a phase of fatty transformation of the bone marrow, and then by a phase of fat involution prior to the appearance of an aerated cavity and that this process can sometimes be interrupted, resulting in the persistence of images of arrested pneumatisation. The objective of the study was to confirm the existence of arrested pneumatisation in the sphenoid bone, and to investigate the presence of similar images in the maxilla, frontal and ethmoid bones.

Material and methods: In this single-centre, retrospective study, 207 CT scans with no signs of mucosal opacity or sinus retention performed for assessment of septorhinoplasty or chronic nasal dysfunction were reviewed according to Welker’s criteria to detect images of arrested pneumatisation.

Results: Twenty-two patients presented 30 images suggestive of arrested pneumatisation of the maxilla (13/30), sphenoid (10/30) and frontal (7/30) bones. No images of arrested pneumatisation were observed in the ethmoid bone.

Conclusions: The results of this study question the classical mechanisms of formation of the paranasal sinuses. According to the hypothesis of postnatal bone cavitation resulting from bone marrow involution and centripetal gas production, paranasal sinuses would constitute distinct organs that develop independently of the ethmoidal olfactory organ, which is formed from the embryonic cartilaginous olfactory capsule.

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1. Introduction

The development of paranasal sinuses has been essentially investigated by postnatal radiological studies. Standard radiographs classically visualize the maxillary sinus by the first year of life, the sphenoid sinus at the age of 4 years, and the frontal sinus only at the age of 7 years [1]. These classical findings were radically modified by the advent of CT and MRI, which allow more detailed analysis of the early stages of development [2–4]. Classically, development of the sinuses is complete, or at least remains apparently stable, by early adulthood. Development of the sinuses varies according to size and gender and marked variations in shape and size can be observed from one individual to another.

The ethmoid first appears during the period of embryonic organogenesis (first trimester of pregnancy) at the 7th week of foetal life, in the form of a rudimentary M-shaped cartilaginous capsule in the mesenchyma surrounding the two olfactory pits, formed by invagination of the olfactory placodes towards the embryonic brain. The central limb of the “M” forms a midline sep-

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* Corresponding author. Tel.: +03 83 85 11 52; fax: +03 83 85 22 58.
E-mail address: r.jankowski@chu-nancy.fr (R. Jankowski).

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Recent MRI studies have shown that formation of the sphenoid sinus is preceded by a phase of bone marrow fat transformation and a phase of fat involution before the appearance of air [2,9,10]. This process can sometimes be interrupted for unknown reasons, leaving persistent radiological images described as central skull base arrested pneumatisation (basisphenoid, pterygoids, clivus and occiput). Imaging of central skull base arrested pneumatisation reveals important radiological features that are useful for the differential diagnosis with fibrous dysplasia or chondrosarcoma [11].

The objective of this study was to confirm the existence of arrested pneumatisation images in the sphenoid bone, but also to identify similar images in other usually pneumatised facial bones, i.e. the maxilla and frontal bones. Arrested pneumatisation images were also systematically investigated in the ethmoid bone.

The working hypothesis of this study was that images of arrested pneumatisation may be observed in all bones in which bone marrow fat involution should precede the formation of pneumatised cavities. The results of this study provide elements of discussion concerning the mechanisms of formation of the paranasal sinuses.

2. Materials and methods

In this single-centre retrospective study, CT scans performed over a consecutive 6-month period in the context of assessment of septorhinoplasty or chronic nasal dysfunction without mucosa opacity or sinus retention were searched in the Radiology Department database and retrospectively reviewed looking for images of arrested pneumatisation.

Radiological criteria suggestive of arrested pneumatisation were defined by Welker et al. in the central skull base [11]:

- incidental discovery on CT-imaging;
- zone of asymptomatic abnormal ossification;
- in a site of usual pneumatisation of the central skull base.

Patients likely to present bone metastases, osteomyelitis, fibrous dysplasia or with a history of major facial trauma were excluded.

The zone of abnormal ossification had to present at least 2 of the following 4 criteria:

- well-circumscribed, sclerotic margins, with narrow transition zone;
- regions of internal fat density zones;
- regions of internal soft tissue density;
- curvilinear internal calcifications.

Welker’s criteria were used to detect images suggestive of arrested pneumatisation of the maxilla, frontal, sphenoid and ethmoid bones.

3. Results

A non-consecutive series of 207 CT examinations with no signs of mucosal opacity or sinus retention were randomly extracted from the Radiology Department database.

Welker’s criteria were used to detect 22 patients (11 males, 11 females) between the ages of 16 and 64 years (mean: 39.5 years, median: 38 years) presenting images suggestive of arrested pneumatisation of the maxilla (Fig. 1), frontal or sphenoid bones (Fig. 2).

Images of arrested pneumatisation in 2 different sites were demonstrated in 8 patients, resulting in a total of 30 affected bones (Table 1):

Fig. 1. Example of arrested pneumatisation of the left maxilla. The peripheral sclerotic condensation of the zone of abnormal ossification, curvilinear internal calcifications, fat density zones, and soft tissue density zones are visualized. The left maxilla appears to be smaller than the right maxilla with an appearance of intussusception of the anterolateral wall (canine fossa) and evagination of the orbital floor (the left orbital volume appears to be greater than the right orbital volume). These images resemble those observed in silent sinus syndrome, but the present study did not assess the similarity or possible differences between arrested pneumatisation and silent sinus syndrome.

Fig. 2. Example of arrested pneumatisation of the left sphenoid bone on a coronal CT section with bone window settings. The zone of arrested pneumatisation is situated in the triple junction zone: base of the greater wing/base of the pterygoid process/basisphenoid. The external morphology of the sphenoid bone appears to be normal.

| Table 1 |
| CT scan sites showing signs suggestive of arrested pneumatisation in the paranasal mesenchymal bones (n = 30) and the ethmoid (n = 0) in 22/207 patients. |
|----------|----------|
| Maxilla only | 6 |
| Sphenoid bone only | 5 |
| Frontal bone only | 3 |
| Maxilla + sphenoid bone | 3 (2 ipsilateral/1 contralateral) |
| Frontal bone + sphenoid bone | 2 (2 ipsilateral) |
| Frontal bone + maxilla | 2 (1 ipsilateral/1 contralateral) |
| Bilateral maxillae | 1 |
| Ethmoid bone | 0 |
Table 2
Distribution of CT scan signs suggestive of arrested pneumatisation as a function of gender (M = male, F = female) and side (R = right side, L = left side).

<table>
<thead>
<tr>
<th>Gender Side</th>
<th>Maxilla</th>
<th>Sphenoid bone</th>
<th>Frontal bone</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>9 M F</td>
<td>4 M F</td>
<td>3 M F</td>
<td>16 M F</td>
</tr>
<tr>
<td>F</td>
<td>4 F</td>
<td>6 F</td>
<td>4 F</td>
<td>14 F</td>
</tr>
<tr>
<td>R</td>
<td>5 R L</td>
<td>8 R L</td>
<td>1 R L</td>
<td>14 R L</td>
</tr>
<tr>
<td>L</td>
<td>1 L</td>
<td>2 L</td>
<td>6 L</td>
<td>8 L</td>
</tr>
</tbody>
</table>

Table 3

<table>
<thead>
<tr>
<th>Welker’s CT criteria</th>
<th>Maxilla (n = 13)</th>
<th>Sphenoid bone (n = 10)</th>
<th>Frontal bone (n = 7)</th>
<th>Total (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>10</td>
<td>7</td>
<td>30</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>6</td>
<td>7</td>
<td>23</td>
</tr>
<tr>
<td>3</td>
<td>13</td>
<td>10</td>
<td>7</td>
<td>30</td>
</tr>
<tr>
<td>4</td>
<td>11</td>
<td>5</td>
<td>5</td>
<td>21</td>
</tr>
</tbody>
</table>

- 3 patients presented arrested pneumatisation of the maxilla and sphenoid (2 ipsilateral, 1 contralateral);
- 2 patients presented arrested pneumatisation of the frontal bone and maxilla (1 ipsilateral, 1 contralateral);
- 2 patients presented arrested pneumatisation of the frontal bone and sphenoid bones (2 ipsilateral);
- only 1 patient presented arrested pneumatisation of both maxillae.

The maxilla was the most common site of arrested pneumatisation (13/30), followed by the sphenoid (10/30) and frontal (7/30) bones.

No predominance was observed according to gender (16 males, 14 females) or side (14 right sides, 16 left sides) (Table 2) with ipsilateral associations in 5 cases and contralateral associations in 3 cases.

The frequency of Welker’s radiological criteria in each bone is reported in Table 3. Criteria #1 (well-circumscribed, sclerotic margins, with narrow transition zone) and #3 (regions of internal soft tissue density) were constantly observed on all images, regardless of the site. Criteria #2 (regions of internal fat density zones) and #4 (curvilinear internal calcifications) were associated with the above two criteria in more than two-thirds of cases.

No arrested pneumatisation images were observed in the ethmoid bone in this series of 207 patients.

4. Discussion

This study shows that images of arrested pneumatisation were observed in the sphenoid bone and in the maxilla and frontal bones, but not in the ethmoid bone.

The results of this study cannot confirm that arrested pneumatisation does not occur in the ethmoid bone, but support the working hypothesis that images of arrested pneumatisation should be observed in all bones that develop pneumatised cavities after bone marrow fat involution. This mechanism was demonstrated in the sphenoid bone in 1989 by Aoki et al. [9], and was subsequently confirmed by several studies [2,10,12]. This same mechanism was demonstrated by Scuder et al. in formation of the frontal sinus [2], but has not been described in the maxillary sinus and ethmoid.

However, the presence of signs of arrested pneumatisation in the maxilla tends to suggest that this same mechanism is involved in the formation of the maxillary sinus. On the other hand, the absence of signs of arrested pneumatisation in the ethmoid is not surprising, as the mechanism of formation of the ethmoid is very different from that of the paranasal sinuses.

The ethmoid is already present at birth and, due to its connection with the airways and adaptation of olfactory function to life in air, it becomes an aerated organ. The mechanism of bone pneumatisation, as it is currently understood, is probably not involved or only constitutes a secondary mechanism in the formation of the ethmoid sinus.

The pioneer work by Aoki et al. [9] on bone marrow fat involution of the sphenoid was based on knowledge of bone pneumatisation in birds. Pneumatisation of a bone is due to replacement of trabecular bone and bone marrow by pneumatised cavities [13]. MRI has furthered our understanding of bone pneumatisation due to its tissue differentiation capacity. In a retrospective MRI study of 401 children under the age of 15, Szolar et al. showed that the sphenoid sinus had a uniform low signal intensity on T1-weighted sequences, similar to that of red bone marrow up until the age of four months. Signal intensity then gradually changed from hypointense to hyperintense: the sphenoid sinus showed high signal intensity in 48% of children between the ages of 4 and 6 months, 87% of children between the ages of 7 and 9 months, and 93% of children between the ages of 10 and 12 months. This signal change reflects red bone marrow fat involution, which precedes the appearance of pneumatisation. The first aerated cavities of the sphenoid are small and appear in the anterior part of the bone, while images of fat involution are still observed in the periphery. These cavities appear in 8 to 14% of children between the ages of 15 and 21 months, 25% between 22–24 months (2 years), 38% between 25–30 months, 60% between 31–36 months (3 years), 85% between 43 and 72 months and 100% at the age of 109–120 months (10 years) [10].

The formation of an aerated cavity in the sphenoid bone therefore appears after a phase of bone marrow involution, and the signs of arrested pneumatisation described by Welker correspond to persistence of zones of bone marrow involution that are not aerated.

Formation of the sphenoid sinus therefore appears to occur intrinsically as a result of a primary bone cavitation phenomenon. These findings tend to invalidate the 100-year-old theory proposed by Zukerkandl [14], attributing expansion or even bone colonisation properties to ethmoidal air cells. Some authors have tried to demonstrate an “osteoclastic front” on “ethmoidal epithelial diverticula” to explain aeration of facial bones [15], but the physiological mechanisms inducing and regulating this behaviour of the ethmoid mucosa are difficult to infer from its primary nature.

The ethmoid arises from the M-shaped cartilaginous capsule surrounding the primary olfactory organ arising in the embryo from invagination of the olfactory placodes towards the primary cerebral vesicle [5]. This cartilaginous olfactory capsule is derived phylogenetically from the prechordal placodes of the first marine vertebrates (agnatha), in which its function was already to form a protective skeleton around the olfactory mucosa [16].

This structure has been conserved, although modified, during the course of species evolution leading to mammals and man, to form a key bone of the skull base, the ethmoid [8]. In mammals, the ethmoid forms two blind paramedian sacs entirely lined by olfactory mucosa, the surface area of which is increased in proportion to the number and degree of folding of the ethmoturbinates. In man, the ethmoid is divided on each side of the midline septum into an olfactory cleft, in which the olfactory mucosa persists in the olfactory fossa underneath the cribiform plate, and an ethmoidal labyrinth in which the olfactory mucosa has been replaced by vestigial mucosa. The formation of the human ethmoidal labyrinth probably results from intertwining of ethmoturbinates following remodelling of the face related to acquisition of bipedal stance [7].

Formation of the ethmoid therefore appears to be very different from that of the sphenoid, frontal and maxillary sinuses; sufficiently different to suggest two independent organs. The ethmoid, as an
olfactory organ, is already formed at birth and its natural opening in the nasal airway (also acquired during evolution [7]) results in its aeration. Paranasal sinuses are only formed when the bone metabolism of the maxilla, frontal and sphenoid allows bone marrow involution and secondary cavitation.

The superior situation of the maxillary ostium underneath the orbital floor and the sphenoidal ostium underneath the cribiform plate, as well as their very small dimensions compared to the volume of the sinus cavities, are indirect arguments suggesting that the cavitation phenomenon may correspond to evacuation via the nasal airway of gas resulting from bone marrow involution. In contrast with the hypothesis of Zukerkandl, the paranasal sinus cavities are not formed centrifugally by expansion of the airways, but centripetally by evacuation of gas derived from bone marrow fat involution into the airways. Nitric oxide (NO) plays a central role in bone metabolism [17], particularly in the mechanisms of bone remodelling [18], and continuing production of NO by the paranasal sinuses [19] could be a remnant of the NO production responsible for the formation of the sinuses. The ostium remains the chimney allowing evacuation of the sinus production of NO, as indicated by a study showing that improvement of nasal (and probably ostial) patency in polyposis in response to corticosteroids increases the rate of expired NO [20].

According to the centrifugal hypothesis of Zukerkandl, the paranasal sinus mucosa is the same as the ethmoidal mucosa, as it is derived from evagination. According to the centripetal hypothesis, these two mucosae may be different. An example of this difference has been demonstrated by immunohistochemical studies and in situ hybridization of mRNA, which showed that the enzyme NO synthetase is intensely expressed at the summit of the sinus epithelium, whereas this enzyme is only weakly present in nasal epithelium. This difference is responsible for the very high levels of NO measured in the paranasal sinuses, close to the maximum thresholds of atmospheric pollution [19].

5. Conclusion

In conclusion, signs of arrested pneumatization may possibly represent a marker of the mode of formation of the paranasal sinuses. According to the hypothesis of postnatal bone cavitation resulting from bone marrow involution and centripetal gas production, paranasal sinuses would constitute distinct organs independent of the ethmoidal olfactory organ. The pathophysiological consequences of this identification of two distinct organs have yet to be studied.

Disclosure of interests

The authors declare that they have no conflicts of interest concerning this article.

References