REVIEW ARTICLE

Craniosynostosis. I. Biological basis and analysis of nonsyndromic craniosynostosis

Fernando Chico Ponce de León

ABSTRACT

Craniosynostoses are defined as closure, ossification and sclerosis of one or more cranial sutures. This condition causes different grades of brain compression, intracranial hypertension and detriment of intellectual coefficient and vision. In the first part of this review article, an overview of the history of craniosynostosis is presented from prehistorical times through the subsequent centuries, to the French School, and culminating with the experiences of the Hospital Infantil de México Federico Gómez. Following this, the biological bases are summarized including embryogenetic, epidemiological and etiological features, as well as pathophysiological, clinical and imaging aspects. Finally, seven different types of nonsyndromatic craniosynostoses are analyzed including those with one or more sutures.

Key words: craniosynostosis, scaphocephaly, plagiocephaly, trigonocephaly, brachycephaly, oxycephaly.

INTRODUCTION

Craniosynostosis is a condition where one or more cranial sutures present closure, ossification and sclerosis producing different brain compression levels and intracranial hypertension as well as intellectual and visual deterioration.[1-3] This entity can be present at skull base or at cranial vault and is frequently accompanied by cranial and facial dysmorphic features that require surgery. Craniosynostosis can be nonsyndromic or may be associated with a syndrome.

HISTORY

Cranial surgery dates from prehistoric times with expressions found both in the American and Africa-Eurasian continents. Evidence of the above are trepanned crania found in southern Europe as well as in South America (Peru). In Mexico, there are trepanned crania associated with Zapotec and Aztec cultures. Indian Sutra techniques are well-known for rebuilding nasal features.[4-12]

Galen made formal reference to craniosynostosis in his cranial anatomy treatises although they contain no illustrations.[13,14] During the Renaissance, both Vesalius' *Fabrica* as well as illustrations from Leonardo da Vinci and Durer and della Croce's editions show a number of craniosynostoses. Vesalius and della Croce drew malformed crania, whereas da Vinci and Durer illustrated abnormal facies and heads.[7,12]

The first references to cranial sutures in American literature are found in works by Alonzo López de Hinojosos and Agustin Farfán (1578 and 1579, respectively) although there is no specific reference to craniofacial malformations.[4,5,15,16]

The study of malformations in general was structured by the end of the 18th century, with special emphasis on malformations in internal organs, brain, thorax and abdominal cavities, genitalia and limbs. The 19th century was especially important in the study and classification of craniosynostosis. Becker and Virchow studied them and established laws where the cranium will develop in the same direction of the stenosed suture.[17] By 1890, surgery for these conditions began. In France, Marie-Lannelonge published

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De la craniotomie dans la microcéphalie in *L'Académie des Sciences.*[18] At the same time, Lane published a private work describing surgery of a microcephalic cranium in the U.S.[9] This type of surgery was resumed in 1927 according to interventions carried out by Faber and Towne in "oxycephaly" cases, as craniosynostoses were called at the time, with better results than their preceding colleagues.[18]

The development of new techniques from the French School led by Tessier, Marchac and Renier firmly settled the need to provide surgical treatment for craniosynostoses.[18-28] Specific techniques were refined to deal with a certain type of craniosynostosis such as Dhellemmes' technique used for trigonocephaly.[29-31] In Mexico, Fernando Ortiz Monasterio Garay and Antonio Fuente del Campo became international references on this type of surgery.[32-37]

The experience from Hospital Infantil de Mexico Federico Gomez (HIMFG) is presented here. We hope publications in regard to series about these conditions gradually appear from large pediatric centers both from Mexico as well as Latin America because at the present time few quality studies have been published (Esparza et al., Ferreira et al. and others), which are bibliographic reviews.[17,38-45]

CRANIAL AND FACIAL EMBRYOGENESIS

The cranium develops from two embryogenic origins: 1) cranial vault, jaw and face develop from neural crest; 2) cranial base develops from mesoderm as well as vertebral column (Figure 1).

Formation of growth cartilages from cranial base bones starts at approximately the 5th gestational week with condensation of mesenchymatic cells in cartilaginous foci, which will take place at the occipital plate on each side of the notochord to form parachordal cartilage where the occipital scale will develop. The ethmoid bone will develop from trabecular cartilages, whereas nasal bone processes will form from nasal capsules. According to Testut, the sphenoid bone presents 18 ossification centers.[46] This description has been simplified recently with pedagogic purposes, including only six ossification centers with three centers at each side: a central part with sella turcica is formed by hypophyseal cartilage, one center for lesser wings of sphenoid from orbitosphenoidal cartilage and another center for greater wings of the sphenoid from alisphenoid cartilage. Towards the 6th and 7th gestational weeks, paired cartilages are already fused and will have contact with each other towards the 12th gestational week. At the same time, the temporal bone develops from otic capsule chondrification.[47,48]

Experiments carried out in animals have demonstrated cranial vault origins are linked to ectomesenchyme from neural crests. In human beings, this origin is yet to be demonstrated. Khonsari and Català propose parietal bones and base bones as mesodermal derivates and consider that definitive arguments on their mesodermal or ectomesenchymal origins are difficult to confirm for the time being. The interparietal bone would be derived from neural crests as well as temporal, pterion and facial scales.[49] Ogle located frontal, parietal, interparietal and temporal scale origins from ectomesenchyma of neural crests.[48] The authors agree that certain conditions must prevail so that sutures remain permeable and, when these conditions fail, craniosynostosis can take place (Figure 2).

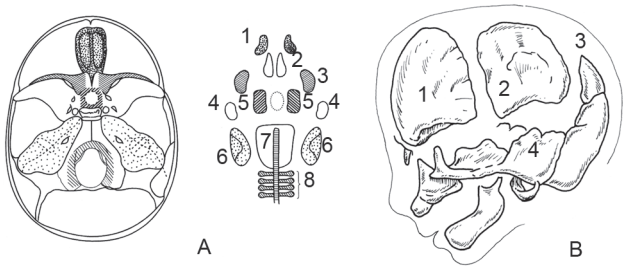

Figure 1. (A) Chondrocranium that will become skull base: 1) nasal capsules, 2) trabecular cartilages, 3) orbitosphenoid cartilage, 4) alisphenoid cartilage, 5) hypophyseal cartilages, 6) otic capsule, 7) parachordal cartilage, 8) occipital sclerotomes. (B) Neurocranium or membranous cranium that will become cranial vault: 1) frontal, 2) parietal, 3) interparietal bone of occipital scale, 4) temporal scale.

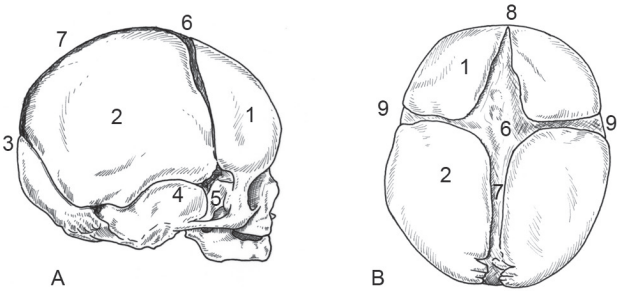

Figure 2. (A) Lateral view of newborn skull. (B) Upper view of newborn skull: 1) frontal, 2) parietal, 3) interparietal occipital bone, 4) temporal scale, 5) pterion, 6) anterior fontanel, 7) sagittal suture, 8) metopic suture, 9) coronal suture.

EPIDEMIOLOGY, INCIDENCE, AND FREQUENCY OF THE CONDITION

It has recently been reported that nonsyndromic, primary craniosynostoses from one or more sutures appear in 1/2100 children. It has been estimated that this represents 10-16 cases/10,000 newborns. This pathological suture closure presents in 1/2000 children in France.[25]

Secondary craniosynostoses include a number of syndromes ranging from 90 to 139 according to some authors. Metabolic, hematologic, storage dysfunctions and problems associated with medications can be associated with craniosynostosis.[50] Thompson and Hayward present a simple classification that summarizes these concepts (Table 1).[51]

Synostotic scaphocephaly is the most frequent craniosynostosis reported for most series (40%-60%).[24,39,41,42,52,53] Next is coronal suture craniosynostosis (13.1% -30%),[24,39,42,54] which may be either unilateral, (plagiocephaly) or bilateral (brachycephaly). Metopic stenosis (trigonocephaly) presents in 6.6%-20% of cases[24,39,42,55,56] although series from *Centre Hospitalier Universitaire des Enfants Malades Necker de Paris* (CHUNP) places it as the second most frequent craniosynostosis with 21.6%.[24] Cases where more than one suture is affected represent 4%-8% of cases. Esparza et al. report figures similar to the above for the Madrid population in 244 nonsyndromic cases and 120 patients for Porto Alegre series.[24,39,42,50]

Table 1. Thompson's craniosynostoses classification[51]

Primary	*One suture*	*Nonsyndromic*	*Scaphocephaly*
		Nonsyndromic	Plagiocephaly Trigonocephaly Brachycephaly Oxycephaly
	Multiple sutures	Syndromic	Crouzon Apert Pfeiffer Saethre-Chotzen
Secondary	Storage disorders Mucopolysaccharides		Hurler Morquio
	Metabolic disorders		Rickets Hyperthyroidism
	Hematologic disorders		Polycythemia vera Thalassemia
	Medical effects		Retinoic acid Diphenylhydantoin

At the HIMFG, coronal plagiocephaly is the most frequent nonsyndromic craniosynostosis (47%). It is possible that this frequency is associated with care provided by HIMFG because it is a tertiary-care hospital where complex cases are concentrated. Next we have scaphocephaly (30%) and nonsyndromic multiple craniosynostoses (4%). Syndromic craniosynostoses represent 17% of cases (Table 2).

Syndromic craniosynostoses represent 11.30%-27% of the total as observed from experiences at the HIMFG, CHUNP and Hospital October 12th in Madrid;[23,39] at the HIMFG the presentation rate is 17%. The most frequent syndromic craniosynostoses are associated with Crouzon's disease ranging from 29.8% to 67% (34.37% for October 12th Hospital and 67% for HIMFG). Apert syndrome varies between 20% (HIMFG) to 34% (October 12th Hospital), whereas Pfeiffer syndrome ranges between 4.4% (HIMFG) and 21.8% (October 12th Hospital). Finally, Saethre-Chotzen syndrome occurs in from 2.2% (HIMFG) to 18.1% (CHUNP) of cases. The largest international series was presented by CHUNP with 3199 cases, whereas the HIMFG series comprises 166 cases from 5 years' experience (Table 2).[24,57]

ETIOLOGY

Genetic Factors

Some syndromic craniosynostoses are associated with Msx2 haploinsufficiency and mutations in fibroblast

Table 2. Craniosynostoses at HIMFG and CHUNP

Nonsyndromic craniosynostoses	**HIMFG (*n* = 138)**	**CHUNP (*n* = 2710)**
Coronal plagiocephaly	47%	13.1%
Scaphocephaly	30%	48.6%
Trigonocephaly	12%	21.6%
Brachycephaly	7%	5.3%
Others	4%	11.4%
Syndromic craniosynostoses	**(*n* = 28)**	**(*n* = 489)**
Crouzon	67%	29%
Apert	20%	32%
Pfeiffer	4.4%	17%
Sastre-Chotzen	2.2%	18.1%
Others	6.4%	4.9%

HIMFG: Hospital Infantil de Mexico Federico Gomez (*n* = 166 cases). CHUNP: *Centre Hospitalier Universitaire des Enfants Malades Necker de Paris* (*n* =3199 cases).

growth factors (FGFs) as well as four of their receptors located in chromosomes 4p, 51, 8p and 10q.[58] There are alterations in transforming growth factor-β (TGF-β) with errors in biochemical or biomechanical signaling patterns. These factors are produced by the dura mater and cells from sutures. An appropriate function of these substances prevents suture closure. All these mechanisms can also be applied to nonsyndromic craniosynostoses.[25,48,59]

Hereditary forms are predominant in syndromatic craniosynostoses. The percentage of hereditary cases is 39.2% for Crouzon's disease, 50.6% for Saethre-Chotzen syndrome, 24.5%-30.2% for Pfeiffer syndrome and 33.3%-35.7% in frontonasal dysplasia. On the other hand, nonsyndromic craniosynostoses present a percentage ranging from 7.3% to 10.9%, except for brachycephaly where percentages increase to 29.6%-32.6%.[25]

Chromosomal alterations are frequent and have been detected in almost all genome chromosomes; however, there is a prevalence of alterations in chromosome 7p. Mutations of genes TWIST and GLI3 are responsible for certain craniosynostoses. Some examples are chromosome 10q, associated with Crouzon's disease, 8p with Pfeiffer syndrome and 7p with Saethre-Chotzen syndrome.[60] Syndromic craniosynostoses frequently represent an autosomal-dominant disorder.[25,61] Clinical onsets vary when there are mutations in several genes or if a single gene presents several mutations.[25,38]

Metabolic Factors

Rachitis in parents of children with oxycephaly has been associated as a risk factor for craniosynostoses. Hypophosphatemia, hypothyroidism, mucopolysaccharoidosis and smoking have been mentioned as possible risk factors for craniosynostoses. Epileptic pregnant women who are treated with valproate sodium may deliver a child with trigonocephaly.[25,62]

Epidemiological Factors

It has been suggested that a possible factor for developing Apert and Crouzon's disease is paternal age >34 years. Oxycephaly has been associated with a similar mechanism because in northern Africa where there are very young mothers paired with older fathers there is a high prevalence of this condition. Other authors mention that maternal age may also be associated with these syndromes.[25,61]

PATHOPHYSIOLOGY

Physiomechanical, chemical and genetic mechanisms have been associated with craniosynostosis.[49,63,64] These processes are found during the embryonic period in early stages such as formation of primary vesicles, specifically in prosencephalon.[63] Syndromic craniosynostoses are closely related with genetic alterations. Suture placement and its contact with dura mater in a specific area participate in the abnormal closure of sutures and ossification mechanism. It has been observed in laboratory animals that if sutures are placed at a different site, ossification will take place faster in those placed near the dura mater where sutures close rapidly and vice versa.[65] This finding has been associated with overexpression of TGF-β1, βFGF-mRNA, IGF-I and mRNA at the suture level.

Some mechanical factors have been suggested as responsible for trigonocephaly and scaphocephaly because a mechanical compression may increase TGF-β levels. Some authors report that breech births and twin pregnancies increase the frequency of craniosynostoses. Oligohydramnios may contribute to pathophysiological characteristics of these malformations.[52,55,66-69]

Impact over Cranial Cavity

According to CHUNP series, most craniosynostoses, both syndromic and nonsyndromic, present a decreased intracranial volume with the exception of most cases of Apert syndrome. A relationship between a smaller intracranial volume and intracranial hypertension (ICH) has been established. However, several authors have reported different ICH figures for nonsyndromic craniosynostoses. Renier reported figures >15 mmHg and found ICH in 66.6% of oxycephalies, 31.3% in brachycephalies, 15.2% in scaphocephalies, 12.7% in plagiocephalies and 7.9% in trigonocephalies. Lamboid craniosynostosis presented no ICH. A series with 41 cases with a high number of nonsyndromic craniosynostoses reported 92.6% of cases presented ICH but there was no relationship between intracranial volume and ICH.[20-23,27,70,71]

Intracranial hypertension is more constant in syndromic craniosynostoses having a relationship with 68.8% of Crouzon's cases, 45% of Apert cases and 29% for other syndromes. ICH has been found in 44.4% of complex craniosynostoses.[23,24,27,72] Recently, Tamburrini et al. found up to 24% of ICH cases associated with nonsyndromic

craniosynostoses and 52.8% associated with syndromic conditions.[2,3]

Cognitive capacities are also reduced.[27,72,73] Optic neuropathy produced by craniosynostosis with ICH and hydrocephaly with alteration of visual-evoked potentials (VEP) increases despite decompressing surgical treatment and only after correct cerebrospinal fluid diversion is it possible to revert alterations in VEP.[68] Other authors confirm this in 6%-15% of patients. These alterations are attributed to ICH multifactorial origin, which includes brain venous congestion, obstruction of upper airways and hydrocephaly.[3,74,75]

Ophthalmic Dysfunctions

Up to 67% of coronal plagiocephaly cases present vertical strabismus and possible development of amblyopia. All craniosynostoses can present a horizontal strabismus, which becomes more evident in upward gaze.[76-78]

Ophthalmic dysfunctions are relatively frequent in syndromic craniosynostoses. It has been observed that 40% of cases present photophobic astigmatism and, therefore, amblyopia.[65,76,78] Cases from Crouzon's, Apert and Pffeifer syndromes present "V" pattern exotropia in upward gaze.[76,78]

Papilledema (PE) and papillary atrophy (PA) are major complications associated with nontreated craniosynostoses but less frequent than ICH, which is present in all craniosynostoses.[79] Between 0.3% and 0.8% of cases of scaphocephaly, trigonocephaly and plagiocephaly present PE, whereas only 0.1% scaphocephaly cases have reported PA. There are no reports of brachycephaly combined with PE or PA. Oxycephaly cases present 9.8% and 12.7% PE and PA, respectively. These are the highest figures for optic atrophies associated with these conditions.

Complex craniosynostoses present PE in 4.3% of cases and PA in 0.9% of cases: Apert syndrome shows PE in 3.2% of cases without PA evidence. Crouzon's disease is the most common PE-affected condition with 16.6% of cases and PA in 3.4% of cases.[27]Sleep apnea and its associated hypoxia may worsen these conditions, producing a greater deficiency in visual sharpness.[1] Surgical correction of strabismus is suggested with special assessment depending on each case.

Impact over Intellectual Functions

CHUNP reported the largest series in the literature where craniosynostoses are associated with intellectual quotient (IQ). It has been confirmed that delaying brain decompression 1 year has negative consequences for intellectual development. Assessment using scales such as *Brunet-Lezine, Nouvelle echelle metrique de l'intelligence* and *Wechsler Intelligence Scale for Children* revealed an IQ >90 in 93.8% of scaphocephaly cases before the first year of age and this percentage decreased to 78.1% of cases after the first year of age. As for brachycephaly, 89.2% of cases presented an IQ >90 before the first year or age and this percentage decreased to 52.2% of cases after the first year of age.

Nonsyndromic craniosynostoses were associated with a higher deterioration of intellectual functions over time. Therefore, 86.4% of complex craniosynostoses presented an IQ >90 before the first year of age and this percentage dropped to 59.3% after the first year of age. Plagiocephaly cases presented a reduction from 90.4% before the first year of age to 80.7% after the first year of age. Oxycephalies are usually diagnosed after the first year of age and this is why it is difficult to find a comparative assessment, but only 40.8% of cases presented an IQ >90.

Apert syndrome was the most severe syndromic craniosynostosis where the proportion of cases with IQ >90 went from 45.5% before the first year of age to 7.4% after the first year of age. Crouzon's disease presented a proportion of 80% before the first year of age that dropped to 65.6% after the first year of age. During the same assessment, the remainder of the syndromic craniosynostoses dereased from 70% to 48.9% after the first year of age.[53] The French series, as well as most international literature reports, agrees that there is an intellectual impairment even in nonsyndromic craniosynostoses.[80-85]

CLINICAL AND IMAGING CHARACTERISTICS

Craniosynostosis is essentially diagnosed clinically. However, imaging plays an important role in the precise classification of malformations even before birth.[86]

Gender

There are reports in international literature where nonsyndromic craniosynostoses show a higher prevalence in males than in females: 3:1 for trigonocephaly, 4:1 for scaphocephaly and 1:2 for plagiocephaly.[24,53,70] At the HIMFG, we have observed a female prevalence both for nonsyndromic craniosynostoses (56%) as well as syndro-

mic events (62%). In our series with 166 individuals, 57% of cases were female.

Age

HIMFG patients were mostly newborns, infants and young children, representing 70% of cases, whereas 15% were older children and 15% were adolescents.

NONSYNDROIC CRANIOSYNOSTOSES

Next we present an analysis for each type of craniosynostosis, either syndromic or nonsyndromic with one or more sutures involved.

Scaphocephaly

Definition and epidemiology. This condition occurs after isolated closure of sagittal sutures. It occurs in 1/1700 to 1/2100 newborns in the U.S. It is predominant among males with a 4:1 presentation rate and represents between 40% and 60% of craniosynostoses. However, it represents 24% for all craniosynostoses treated at HIMFG after coronal plagiocephaly.[52,53,87]

Clinical characteristics. According to Virchow's law, malformations found in scaphocephaly include enlargement of fronto-occipital diameter and shortening of biparietal diameter (Figures 3-5). There are variants regarding frontal shape, which can be bilateral and rectangular, normal or semispheric. When the frontal diameter is larger, the suture has been predominantly closed on the anterior axis; however, when the occipital diameter is larger, this is a sign of posterior suture closing. Occipital diameter is generally conical with apex towards the middle of the occipital scale. When both poles have deformed, the entire suture has presented an aggressive closure. In severe malformations, bone curve is inverted at parietal and temporal levels, presenting convexity towards the brain surface. There is also recession to different degrees at the pterional level, which accents frontal deformation and is associated with stenosis level on the sphenofrontal suture. Stenosed bone is thickened just like pterion. There are no other sutures involved in the development of the malformation.[24,53]

Imaging. Along with clinical diagnosis, this entity can be identified with a single cranial x-ray (CXR) with lateral incidence (L) that supports diagnosis: we will generally find a lengthening of the anteroposterior (AP) diameter either with prevalence at frontal, occipital or both poles. This deformation resembles a zeppelin. It is frequent to find finger-like impressions at parietal levels and in a portion of the temporal and occipital bones. AP CXR shows absence of sagittal suture being replaced with dense bone in some cases. This entity shows a reduced biparietal diameter (Figure 4). Cranial computed tomography scan (CT) confirms clinical and CXR findings, clearly revealing biparietal and occipital brain compression. Brain inside this skull is compressed, especially at biparietal and occipital areas, which are the narrowest. At frontal level, skull deformation favors open subarachnoid spaces of the brain folds, particularly at the prefrontal level. It has been documented that these spaces will disappear as the patient

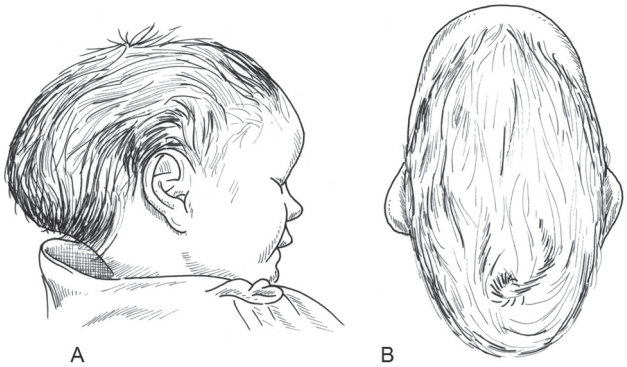

Figure 3. Scaphocephaly. (A) Lateral view with evident enlargement of anteroposterior diameter and forehead protrusion, same as occipital bone. (B) Upward view confirms lateral view and shortening of interparietal diameter.

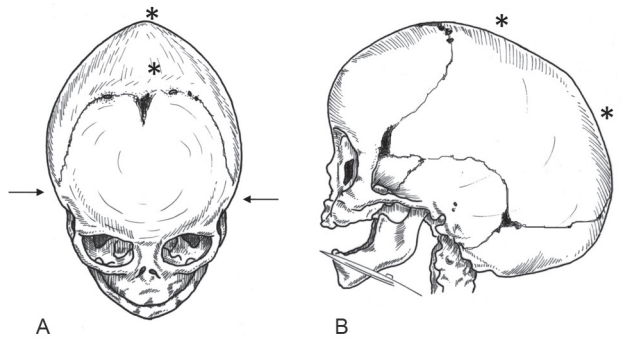

Figure 4. Scaphocephaly. 3DCT images: (A) Frontal cranium view and from above. Absence of sagittal suture is appreciated with elevation where (**) reduced interparietal diameter is shown. (B) Lateral projection where elongated cranial profile is observed with closed suture (**). Other sutures are distinguished clearly and correctly (arrowheads).

grows (Figure 5).[24] Sagittal suture closure can be identified through bone window x-ray and 3-dimensional computed tomography (3DCT). Coronal sections from bone window X-ray and 3DCT reveal a channel that contains the longitudinal sinus instead of the suture; this characteristic should be kept in mind at the time of surgery.[24,52,53] An electroencephalogram, developmental assessment and full ophthalmological examination are required with any type of craniosynostosis.

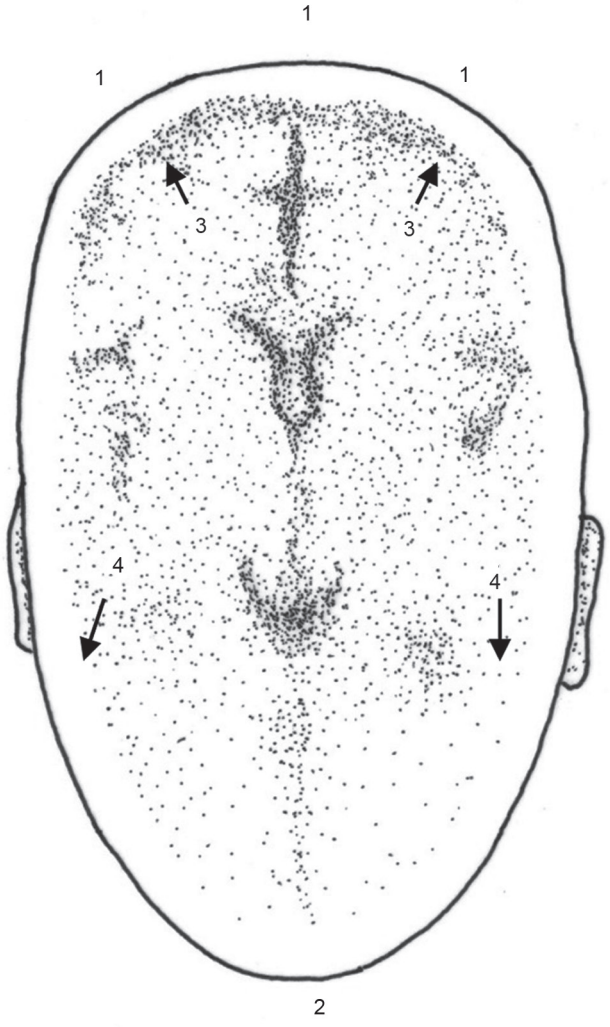

Figure 5. Scaphocephaly. CT scan axial sections: 1) forehead protrusion, flattened as a boat stern, 2) occipital protrusion, pointed as a boat bow, 3) wide subarachnoid spaces, ahead of frontal lobes, 4) parieto-occipital cortex compressed by narrowing of biparietal diameter.

Coronal Plagiocephaly or Unilateral Coronal Craniosynostosis

Definition and epidemiology. This entity is the second most frequent condition documented in literature. At HIMFG it represents the most frequent craniosynostosis with 40% of cases, higher than scaphocephaly. This condition ranks third on CHUNP series and represents 13% of nonsyndromic craniosynostoses. It presents a right side prevalence (61%) as well as a female prevalence (69%), which contrasts with scaphocephaly.[22,23,53,54,88] This malformation occurs after left or right coronal suture stenosis as well as involvement of sutures at the base level, especially frontosphenoidal and sphenotemporal through to the greater wing of the sphenoid (Figures 6-9). Unilateral coronal closure partially explains ocular orbital deformation backwards with an edge that lacks definition as well as nasal scoliosis. Base deformation with temporal bone towards stenosed coronal side presents affected sutures at the base that involve half of the cranial coronal ring with a sphenofrontal, sphenosquamous and sphenopetrosal stenosis on the affected side.[88,89] Strabismus favors amblyopia at the expense of the stenosed side.[65,77]

Clinical characteristics. As with other craniosynostoses, diagnosis is essentially clinical and accurate observation will allow a differential diagnosis regarding positional malformation, which is generally not subject to surgical treatment. At the frontal position, an orbitary dystopia will be observed on the affected site with orbit positioned upwards and backwards. Nasal scoliosis is common with scoliotic convexity located at the nose root towards the stenosed side. This sometimes conditions a divergent strabismus on affected side. On the sagittal plane there is lack of definition on the orbit edge, as well as flattening of the glabella on the affected site with protrusion of the contralateral glabella and pterional and temporal regions. When observing the patient's head from above, we find a clear exorbitism on the affected side with protruding eyelid and absence of orbit edge as well as flattening of the corresponding glabella. The external ear is closer to the orbit at the affected site. At the axial plane, there is recession of fronto-orbital region.[54,88,89] This particular cranial plicature with a torsion point at stenosed sutures both on vault and basal counterpart may produce a compensatory protrusion of the contralateral parietal bone.[40,89]

Some authors propose a complex cranial anthropometry with 59 indexes and distances to measure, which are

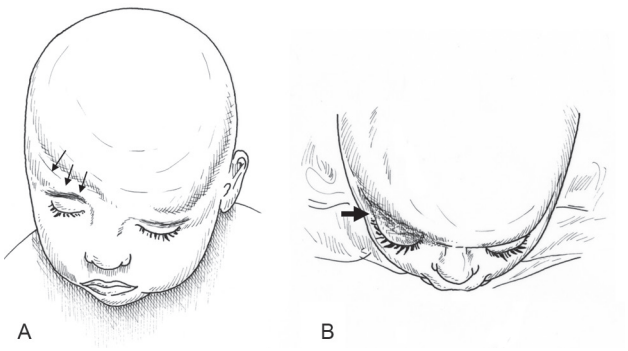

Figure 6. Right coronal plagiocephaly. (A) Patient viewed from the front with a slight upward angle where orbit is pulled backwards and inwards (arrowheads). Orbital edge, almost absent externally, has a posterior and downwards tilt. Forehead is flattened and with caudal traction. (B) View from above clearly reveals exorbitism of eye from affected side (arrowhead).

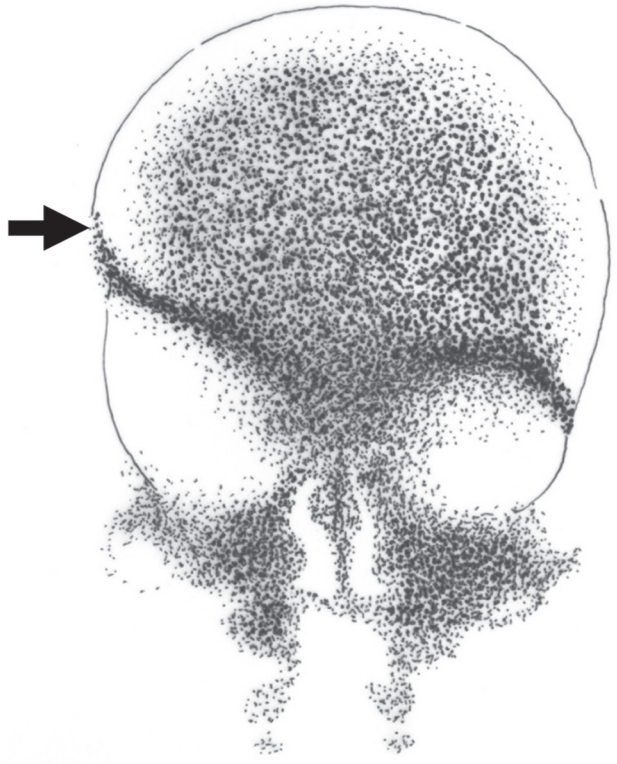

Figure 7. Left coronal plagiocephaly. Anteroposterior cranial x-ray reveals lesser wing of sphenoid pulled upwards on external side giving the impression of a "harlequin" orbit (arrowhead); this phenomenon is known as orbit "harlequinization" and confirms organic plagiocephaly diagnosis.

regarded as difficult to implement for an appropriate plagiocephaly diagnosis and treatment.[48] Oblique oval skulls, functional deviation and flattening are antagonists. The external ear moves away from the fronto-orbital region, which is in a rear position, whereas the contralateral auricle that is more protruding is closer to the fronto-orbital region without exorbitism on the affected side.[90]

Imaging. As with other craniosynostoses, imaging will confirm clinical diagnosis, which determined the type of presentation. Plagiocephaly shows typical images on CXR. PA reveals the lesser wing of the sphenoid raised on its external edge, which is a typical "harlequin" sign. In addition, it is asymmetric because the affected orbit is pulled outwards and upwards. Pterional and temporal protrusion can be observed on the affected side as well as nasal scoliosis. The lateral plate of the affected side reveals ossified stenosed suture without characteristic radiolucent lines (Figure 7). CT scan allows confirmation of the CXR images. We can observe the stenosed suture either in full or partially blurred. Three-dimensional reconstruction shows malformation as described and allows for careful surgical planning (Figure 8). Three-dimensional reconstructions of the skull base reveal that plagiocephaly from coronal stenosis presents specific characteristics. It is possible to distinguish deviation from temporal petrosa towards the stenosed side with an opening up to 71° of the petrosagittal angle where 50° is the normal opening angle. At the same time, ethmoid processes represented by the cribriform plate are deviated towards the stenosed side. Compression of the front pole at the craniosynostosis side is evident (Figure 9).[24,26,54,88,89]

Deformational Posterior Plagiocephaly

Definition and epidemiology. This condition presents no pathological closure of any suture. Deformation of the entire skull including cranial base at times is harmonic and balanced. Angles at the base are not altered as in plagiocephaly associated with coronal suture closure and sclerosis.[89]

Clinical characteristics. This malformation has been attributed to breech presentation during most of the pregnancy. In fact, during clinical examination we can observe that part of the face is set backwards. This position does not share characteristics with organic plagiocephaly. The external ear is set far from the orbit in functional plagiocephaly in contrast with organic plagiocephaly where,

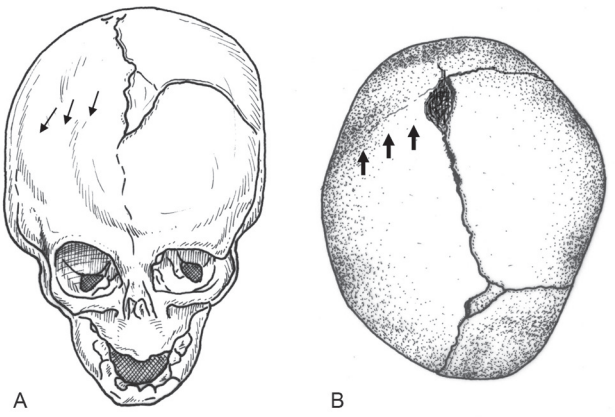

Figure 8. Coronal left plagiocephaly. CT scan images and 3DCT. (A) Reconstruction shows skull from front and slightly above where malformation is easily seen with absence of left coronal suture. Other sutures remain permeable. Malformations at forehead and orbit are as described on patient's facial images. (B) Skull seen from above where we can appreciate stenosed suture, deformation described at forehead, fontanel and other permeable sutures.

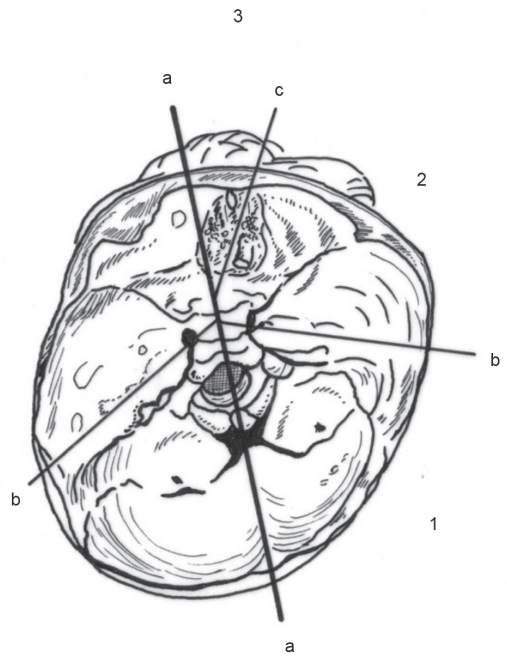

Figure 9. 3DCT reconstruction of skull base. Sagittal a-a line, petrosal b-b lines, ethmoid c line. Organic plagiocephaly shows an increased sagittopetrosal angle on affected side (1) as well as a reduced ethmoid-petrosal angle on the affected side (2). An ethmoid-sagittal angle opens that should normally not exist (3). The structure is drawn towards the base coronal ring, which is stenosed towards sphenofrontal and sphenotemporal sutures.

because of sphenopetrosal angle closure, the external ear is closer to the backward orbit. There is evidence that patients sleep on the occipital flattened side and support their head when awake. Deformation usually improves when the child is able to sit up and stay in an erect position during most of the day.[39]

Imaging. In this condition, both CRX and CT scan show all sutures open. There is no "harlequin" appearance and cranial base angles are normal.

Posterior Plagiocephaly (lamboid)

Definition and epidemiology. This entity presents closure and sclerosis of one or both lamboid sutures. This is not a common condition and ranks last among nonsyndromic craniosynostoses in CHUNP series (0.77%). This figure is even lower when associated with syndromatic craniosynostoses. Posterior plagiocephaly may be associated with scaphocephaly.[24,26,75]

Clinical characteristics. This condtion is generally identified by flattening of the back of the skull on the stenosed suture side. This deformation is not very evident because of its position where it is generally covered by hair. When it is present in a female with long hair, it is even more difficult to identify. This may produce certain generally mild and discreet cranial obliqueness. Closure of both lamboid sutures is very rare and produces a particular deformation with severe flattening of the back of the skull. This is the only craniosynostosis, both syndromic and nonsyndromic, that presents no ICH even though the number of cases is very small: six patients were reported by the CHUMP series.[27]

Imaging. Diagnostic imaging is carried out using CXR and confirmed using 3DCT. Electroencephalogram is required because surgical intervention will be defined according to a possible cortical irritation on the stenosed side. There have been few surgeries of this craniosynostosis at HIMFG. According to some authors, surgery is always recommended.[69,91,92]

Trigonocephaly

Definition and epidemiology. This entity ranks third according to the HIMFG series (10%) for nonsyndromic craniosynostoses and second according to the CHUNP series (21.6%) after scaphocephaly.[25,52,56]

Clinical characteristics. This malformation is associated with closure and sclerosis of the metopic suture.

In the axial plane, we observe a characteristic triangular forehead with apex pointing forward. The angle may present different closure degrees from acute to open. The frontal view reveals that orbits, both at sides and at the edge, show a backward position with medialization. At the same time, intercanthal internal and external distances decrease, reducing capacity of the anterior cranial fossa. We find hypotelorism with the vertical internal pillar and the external pillar is inclined inside with typical "raccoon eyes" presentation (Figures 10-12).[24,32] The best angle to verify the aforementioned characteristics of this malformation is to view the patient's head from above.

Imaging. CXR are always useful to verify thickening and increased bone density at the metopic level as well as hypotelorism and typical "raccoon eyes" presentation. Cranial CT scan shows, in frontal axial cuts, the characteristic deformation that names this craniosynostosis. It is possible to verify hypotelorism, thickening of the metopic suture and "pointy" forehead with several closure levels. We generally find a protrusion of the temporal fossa, which can be verified on plain x-rays and CT bone windows. Prefrontal regions are compressed by malformation (Figure 11). Reconstruction using 3DCT confirm clinical and CXR observations and allow the development of a surgical plan. 3DCT reconstruction of the base shows a narrow frontal fossa and narrowing at the pterional level (Figure 12).[24,26,55]

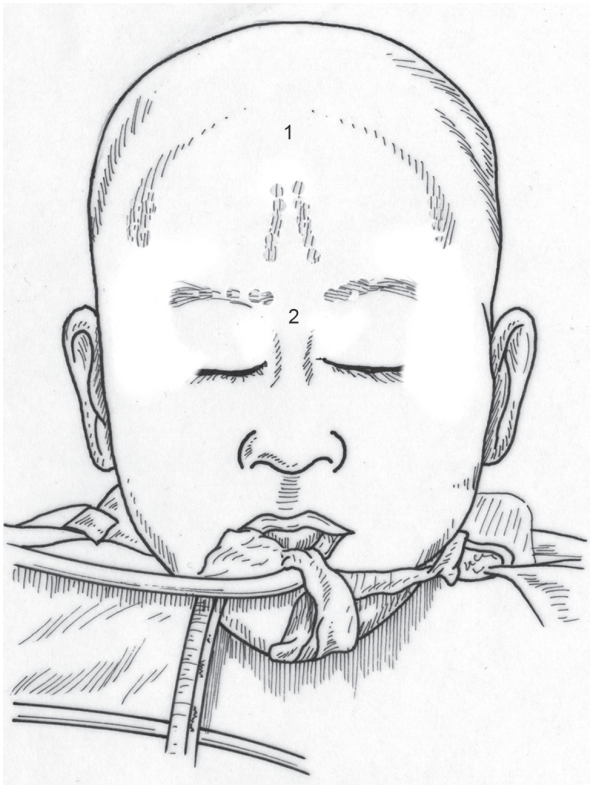

Figure 10. Trigonocephaly, frontal view. 1) Notice central-frontal prominence in triangular shape. 2) Outstanding hypotelorism in most cases.

Brachycephaly or Bilateral Coronal Craniosynostosis

Definition and epidemiology. Coronal sutures are stenosed in this malformation. This condition represents 7% of the HIMFG series for nonsyndromic craniosynostosis and 6% of total cases. In the CHUNP series, it represents 5.3% of total nonsyndromic events. There is a female prevalence (66%), which is similar to figures found in coronal plagiocephaly. Esparza and Ferreira reported figures similar to the above.[24,39,54,56,93] This craniosynostosis is associated with the highest rate of chronic ICH (31.3%), although without papilla edema, possibly because of an early surgery.

Clinical characteristics. In accordance with Virchow's law, frontal view reveals biparietal protrusion with a clear increase of temporoparietal diameter and orbitary edges with diverse blurring levels and frank hypertelorism as well as flattened forehead. External ears are separated and concavity faces downwards giving the impression of being lower than normal (Figures 13-15).[25,27,52,88] Lateral

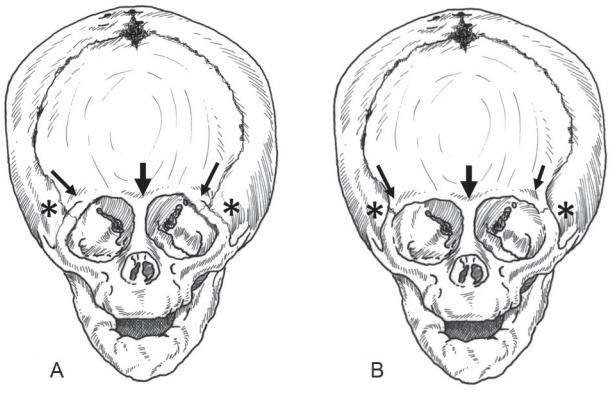

Figure 11. Trigonocephaly. 3DCT reconstruction. (A) Hypotelorism with typical "raccoon eyes" orbits; frontal pointy deformation is noticeable. (B) Hypotelorism with orbits near normal; it is possible but less frequent to find "raccoon eyes" orbits. For all cases we find a backwards position for external orbit edges, with upward and backward tilt of orbital edge (thin arrows); edges converge towards nasal bones following malformation path (thick arrow). There is a pterional, bilateral depression characteristic of this malformation (*).

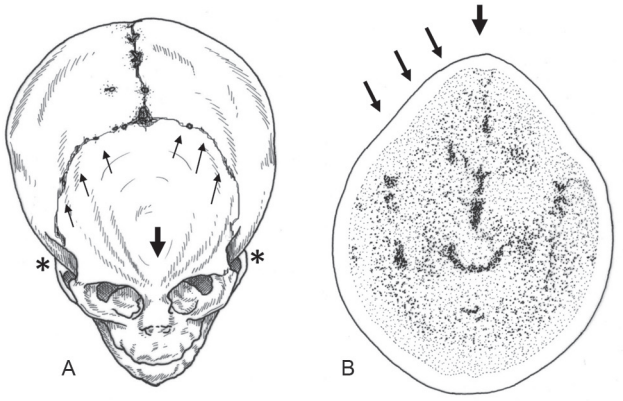

Figure 12. Trigonocephaly. (A) 3DCT reconstruction: thin arrows mark coronal suture that limits the size of the frontal shell, which is small and has a pointed medial section. Constant hypotelorism; nasal bones advance with backward movement of bilateral orbit edge (thick arrow). Pterional regions are recessed, characteristic of this malformation (*). (B) CT scan with axial cuts: pointed forehead is shown with external extreme points towards inside (thick arrow). Thin arrows mark frontal bones pressing bilateral prefrontal regions.

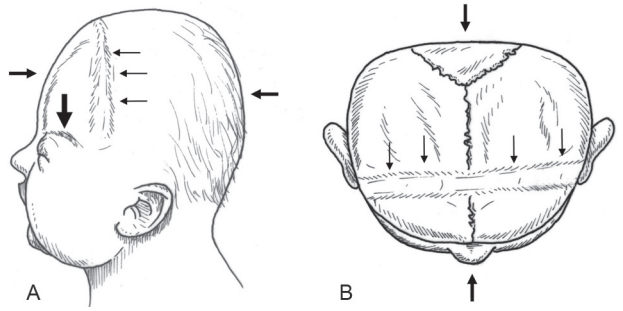

Figure 13. Brachycephaly. (A) There is a reduced anteroposterior diameter producing a profile similar to a tower (→ ←). Orbitary edge presents different blurring and exorbitism levels (↓). Stenosed suture can be frequently seen below the skin (thin arrows). (B) 3DCT reconstruction. Reduced anteroposterior diameter (↓↑). Stenosed suture is closed; other sutures including metopic are open and functional (↓↓↓).

view reveals a decrease in AP cranial diameter. Forehead flattening is confirmed by a reduced orbitary edge and, in most cases, it is possible to observe exorbitism because the upper facial third is displaced backwards. In some cases, the skull is displaced upwards, giving a tower appearance, which justifies this entity to be also known as "turricephaly." Looking at the patient's head from above allows us to confirm the forehead backwards setting, orbitary edge blurring and exorbitism.

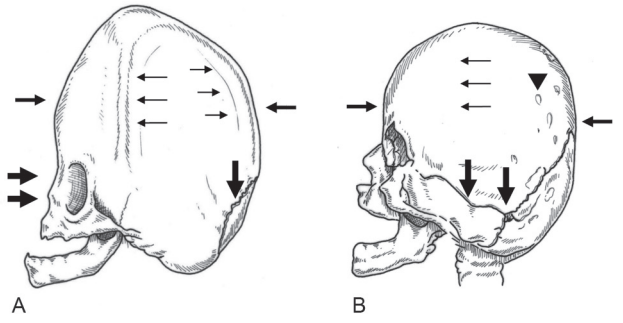

Figure 14. Brachycephaly. 3DCT reconstruction. (A) Syndromic craniosynostosis with brachycephaly (lateral projection). (A) + (B) Note a reduced anteroposterior diameter (→ ←). Stenosed suture is occasionally visible as a ridge (horizontal arrows). Other sutures are permeable (↓). (B) Nonsyndromic simple brachycephaly. Finger-like impressions are occasionally visible (▼).

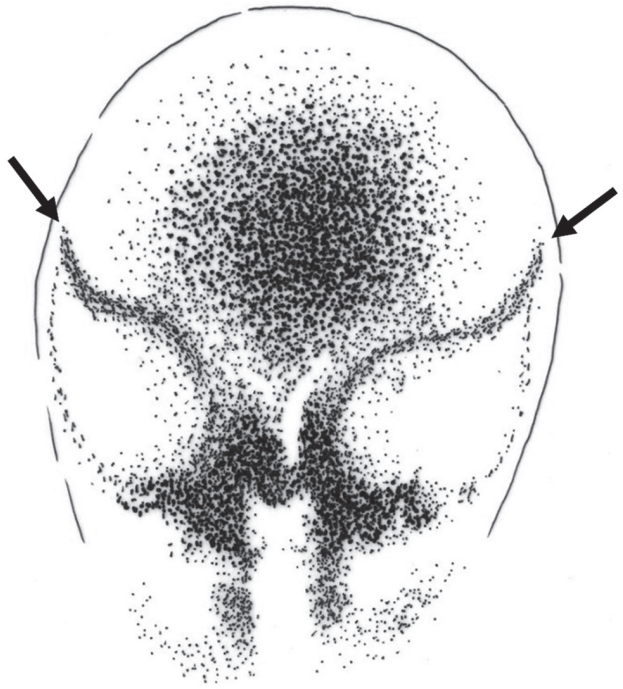

Figure 15. Brachycephaly. Anteroposterior cranial x-ray: "harlequinization" of both orbits (arrowheads) characteristic of this craniosynostosis.

Imaging. PA CXR shows "harlequinization" of both orbits and, sometimes, finger-like impressions associated with chronic ICH. There is an increase of bi-temporoparietal diameter and bone structure moves upwards resembling a tower. Lateral incidences lack coronal suture evidence and there are certain frontal flattening levels and orbitary edge blurring. Cranial CT and 3DCT reconstruction will confirm coronal suture closure and deformation that increase lateral diameter and shorten AP diameter. CT Bone windows will reveal coronal suture ossification and finger-like impression on internal table or even cranial perforations because of ICH (Figures 14-15).[26,93]

Oxycephaly

Definition and epidemiology. This is a noncongenital and nonsyndromic craniosynostosis that will occur between the second and third year of life even when children are born with all sutures permeable. This is a condition that prevails in northern Africa and is reported with relative frequency in French series because of the high immigration rate from those regions. Oxycephaly is a harmonious closure of all sutures in the cranial vault, resulting in a small and round skull with a special deformation that frequently presents severe ICH in most cases (61.6%), papillary edema (10%) and papillary atrophy (13%). Patients >1 year-old may present several blindness levels and >50% of cases report an IQ <90. The aggressiveness of this condition calls for surgical treatment at diagnosis.[24]

Clinical characteristics. When oxycephaly is mild, we observe only a small harmonious head. Severe oxycephaly reveals a spheric skull with forehead, temporoparietal and occipital regions towards the inside of the skull, producing a backwards position of forehead and retraction of supraorbitary edge, moderate exorbitism because of orbitary edge backward setting that follows a generalized narrowing of the skull. Face and facial skeleton are usually normal. Mild cases do not report a faciocranial disproportion, which is observed in severe cases where the patient has a very small skull producing a facial skeleton that looks larger.[24,26]

Imaging. CXR reveals a typical well-rounded skull, sometimes with a discreet bregma protrusion and mainly with severe finger-like impressions. Severe cases reveal forehead retraction with blurring or orbitary edge.

This study will be continued in the next issue of BMHIM.

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