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The metopic suture: natural history

Histoire naturelle de la suture métopique

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Abstract

The metopic suture (MS) is one of the main sutures of the calvaria; premature closure is responsible for trigonocephaly, while persistence (metopism) is considered a normal variant. The ages of onset and completion of MS closure and prevalence of metopism in normal children are poorly documented.

We studied the pattern of MS closure on 3D-CT scans of 477 children admitted for head trauma since 2012. We also studied the prevalence of trigonocephaly and the sex ratio in our clinical series of patients with all types of synostosis diagnosed during the last 4 decades. In the majority of children, MS closure started at 4 months and was complete at 9 months. The prevalence of metopism was stable after 1 year of age, at 5.1%; it was more than twice as frequent in girls (F/M ratio 2.1, non-significant). Our trigonocephaly series and the literature show a steady increase in prevalence over recent decades. During the same period, the prevalence of metopism decreased steadily.

Data from comparative anatomy and paleoanthropology suggest that postnatal MS persistence in our species results from the risk of dystocia caused by the closed pelvis associated with bipedalism.

The increasing incidence of trigonocephaly appears to parallel the fall in prevalence of metopism. The increasing use of cesarean section may have eliminated a potent selection factor in favor of postnatal persistence of the MS.

Key-words

Metopic suture – metopic synostosis – metopism – comparative anatomy – birth trauma

Résumé

La suture métopique (SM) est une des principales sutures de la voûte ; sa fermeture prématurée est à l'origine de la trigonocéphalie, tandis que sa persistance, nommée métopisme, est considérée comme une variante du normal. L'âge de début et de fin de la fermeture de la SM dans la population normale, ainsi que la prévalence actuelle du métopisme sont mal connus.

Pour étudier la fermeture de la SM, nous avons étudié le scanner 3D de 477 enfants normaux victimes de traumatisme crânien depuis 2012. Nous avons également étudié la prévalence de la trigonocéphalie parmi les patients porteurs de tous types de craniosténose suivis au cours des quatre dernières décennies.

La fermeture de la SM débute vers 4 mois et est complète vers 9 mois dans la majorité des cas ; la prévalence du métopisme devient stable après un an, établie à 5,1% ; celle-ci montre une nette prédominance féminine (F/M ratio 2.1 NS). Notre série de trigonocéphalie, ainsi que les données de la littérature, montrent une croissance régulière de l'incidence de la trigonocéphalie, et une décroissance du métopisme durant les dernières décennies.

Les données provenant de l'anatomie comparée et de la paléoanthropologie suggèrent que la persistance postnatale de la SM dans notre espèce est une adaptation au risque de dystocie due à un bassin fermé lié à la bipédie.

L'augmentation l'incidence de la trigonocéphalie apparaît parallèle à la décroissance du métopisme ; le recours croissant à la césarienne a possiblement neutralisé un important facteur de sélection en faveur de la persistance de la SM.

Mots-clés

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Suture métopique – trigonocéphalie – métopisme – anatomie comparée – traumatisme obstétrical

Introduction

The metopic suture (MS) is one of the main sutures of the calvaria, and its premature closure is responsible for trigonocephaly, one of the most common of all craniosynostoses. The natural history of the MS is different from that of other sutures, since it fuses and totally disappears early in life. Total disappearance of the MS in early childhood is a peculiarity it shares with other calvarial sutures (the mendosal and innominate), as well as facial sutures (such as the mandibular and premaxillary). The systematic presence of the MS at birth then early disappearance suggest its usefulness for cranial molding during delivery; this is corroborated by the high incidence of delivery complications, up to 30%, related to MS synostosis (1). The unusually late closure of the MS in our species has been attributed to bipedalism and the delivery risk associated with a closed pelvis (2).

There is much uncertainty regarding the normal age of closure of the MS. This has a bearing in pediatric studies, since premature MS closure is often wrongly attributed to children without trigonocephaly. For some authors, fusion starts after 1 year and is complete by 7 years of age (3); for others, it occurs at the end of the first year (4); according to most authors, however, closure takes place before 9 months (5, 6). Persistence of the MS in later life, named metopism, is found in a minority of the population. Although it can be part of major malformative syndromes such as craniofacial Tessier 14 cleft (7) or cleidocranial dysostosis (8), metopism is generally considered a normal variant and has not been much studied. Estimation of prevalence varies greatly between studies (9, 10), but the definition of metopism is imprecise; in particular, the age after which MS persistence can be considered as metopism is not known, since the age of anatomical specimens is often not specified.

Computed imaging now provides us with large databanks for normal individuals, such as victims of head trauma, which can be used for the purposes of anatomical studies (5). Because of the uncertainty regarding the age of normal MS closure and the prevalence of metopism in the general population, we decided to study three-dimensional computed tomography (3D-CT) scans of normal child victims of head trauma.

Physiological closure of the metopic suture

The main aim of the study was to determine the age of MS closure onset, and the age at which fusion is complete. The secondary aim was to determine the prevalence of metopism, defined as persistence of a totally unfused MS at an unusual age; this requires first determining the age at which presence of metopism can be asserted.

To study the pattern of MS closure, we retrieved data for up to 20 children for each month of age up to 12 months, and a large number of unselected older children. Patients with underlying constitutional disease, or with secondary traumatic lesions (such as subdural effusion) liable to interfere with skull growth, were not included. The MS was classified as totally unfused, partially fused, or totally fused. The age at which metopism can be asserted was defined as the age after which prevalence is stable.

We collected 3D CT scans of 477 pediatric skulls, aged 0 to 18 years, studied for recent head trauma since 2012. 262 children aged 12 months or under were available, 100 aged 13-24 months, and 115 older than 24 months. Since only 18 children aged 11 months were available, we decided to express the results as percentages of the total rather than as

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absolute numbers (figure 1). MS closure started in the majority of children at 4 months, and was complete at 10 months. Three of the 100 children aged 13 to 24 months (3.0%) had a totally unfused MS, compared with 8 of the 115 children (7.0%) aged 25 months or more. We conclude that metopism can be asserted as early as 1 year, and the prevalence of metopism over the whole series was established at 5.1%. Metopism was more prevalent in females (7.1%) than in males (3.4%), with an F/M ratio of 2.07, although the difference was not significant (Chi square 0.22).

Early closure of the metopic suture: trigonocephaly

When the MS fuses abnormally early, before birth as a rule, the child presents trigonocephaly; unlike other synostoses, MS synostosis is a question of when, not if. MS synostosis is rarely associated with abnormal closure of the sagittal suture, constituting leptocephaly (figure 2), a variant of scaphocephaly (11). MS synostosis can also be part of a pansutural craniosynostosis constituting cloverleaf skull, a malformation most commonly found in a genetic context. Apart from these rare associations, MS synostosis is distinct from other craniosynostoses.

MS synostosis is rarely related to genetic causes such as Twist mutation or chromosomal disorder (12). It is more often assumed to result from environmental causes such as Valproate (13), fetal alcohol (unpublished data) or intrauterine pressure in multiple pregnancy (14,15). In our experience (unpublished data), MS synostosis was found in association with identified syndromes or other malformative ailments in more than one-third of cases. Association with chromosomal or genetic syndromes, or with severe diseases such as cardiac malformation are likely to impact developmental outcome, so syndromic cases should be segregated from non-syndromic cases when evaluating the developmental impact of the MS synostosis.

For unknown reasons, the gender distribution of MS synostosis shows a large male preponderance, the M/F ratio being 3 to 1 (16). In our series too, the overall male/female ratio was 3.0; however, this ratio decreased over the years or, in other words, females accounted for much of the increase in absolute numbers (figure 3).

The male predominance in MS synostosis reflects the 4:1 male preponderance found in sagittal synostosis. Since these malformations occur early in life and even prenatally, hormonal influence is unlikely. Why males should be more susceptible to excessive midline closure, while females are more susceptible than males to defective midline closure in the form of dysraphic states, may be compared to the different fates of the urogenital sinus in the two sexes.

Secular trend

The incidence of MS synostosis has been relentlessly on the rise over recent decades (12, 14, 16, 17). We reviewed our craniofacial database starting at the end of the 1970s, with 1,318 patients followed for craniosynostosis born since 1977. MS synostosis accounted for 30% of children with synostosis born during the decade 1977-86, compared with 47% in the decade 2007-2016, making it now the most common form of craniosynostosis (figure 3). Although the trend in our series was highly significant ($p = 0.002$), many confounding factors interfere: increased awareness in pediatricians and the public (16), and the impact of prenatal diagnosis in lowering the prevalence of the more severe and often syndromic bicoronal synostoses. At all events, these figures point to environmental rather than genetic factors.

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Consequences

The most obvious consequence of MS synostosis is morphological deformity. Whether MS synostosis causes brain compression or not is elusive, and its neurological consequences are far from obvious. Rare imaging studies have shown cerebral hypoperfusion in unisutural craniosynostoses, which could be reversed after surgery (18); however, the question remains controversial. Fundoscopic evidence of intracranial hypertension is found in fewer than 2% of patients (19); however, this does not exclude focal compression by excessive flattening of the frontal bone. As stated above, developmental problems in MS synostosis are found mostly in syndromic cases, and relate more to genetic or chromosomal abnormalities, or feto-toxicity (fetal valproate syndrome) than to brain compression. However, long-term follow-up data are scarce. In a retrospective study, Renier et al. found that children operated after 1 year of age had poorer developmental outcome than those operated earlier (20); this could indicate that prolonged compression is detrimental to outcome, but also that children operated later had other problems, as in syndromic cases. The involvement of MS synostosis in dystocia has become increasingly recognized (1, 21, 22). This is likely because the synostotic skull lacks the deformability required for efficient labor (figure 4). These birth complications should be seen as a consequence of MS synostosis, and not be mistaken for its cause, unlike prenatal compression in case of multiple pregnancy.

Persistence of the MS: metopism, secular trends, and connection with trigonocephaly

Metopism, defined as persistence of the MS beyond the usual age of normal closure, is considered a normal variant, and could be considered the opposite of MS synostosis. The prevalence of metopism appears to have much decreased over time. In a study published in 1937, metopism was identified in 16% of skulls (9); subsequently, the percentage fell to 10% in a study published in 2000 (10), then to 2.6% in a recent study published in 2017 (23). Our study, conducted in a geographically homogeneous population of children born after 2000, with an inclusive definition (persistent MS after the age of 1 year) found a prevalence of 5.1%. The decreasing prevalence of metopism is to be compared with the increasing incidence of MS synostosis.

As a normal variant, metopism does not have any medical or morphological impact, and consequently has not been much studied. Figure 5 shows frontal 3D CT scans of children with metopism of increasing age; although no striking dysmorphism is obvious, the group shows a "family look", with broadened upper frontal region and temporal hollowing (figure 5). In other contexts, metopism is also commonly associated with malformations involving the frontal region; in our experience, we found it associated with cranium bifidum, dorsonasal dermal fistula, suprasellar teratoma, dermoid cyst of the glabella, cleidocranial dysostosis, hypertelorism and facial cleft (figure 6). Metopism is thus a common feature associated with a wide array of midline closure defects.

Interestingly, metopism appears to be more common in females (3.8%) than in males (1.8%) (23). We found the same female predominance, although the difference was not statistically significant. This predominantly female predominance mirrors the male predominance in patients with MS synostosis. The secular trends as well as the skewed sex ratio suggest that a continuum exists between metopism, normal MS closure, and MS synostosis.

Comparative anatomy

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As confirmed in our study, MS closure occurs a few months after birth in our species: roughly, between the time when the child begins to hold their head and when they acquire the seated posture. MS closure is thus a feature embedded in the overall development of the anatomy and functions of the brain and its covering, and associated with the huge postnatal growth of the cerebrum in our species.

The MS is part of the anterior neurocranium, which derives from the neural crest; it is a minute structure in lower mammals, much shorter than the prominent internasal suture. The MS enlarged hugely in our species as a result of the hypertrophy of the frontal regions of the brain (3). In great apes, the MS fuses at birth or shortly after, whereas in humans it remains patent until well into the age of eruption of deciduous teeth (24); the prevalence of metopism is also lower in apes than in humans (2). The persistence of the MS after birth is thus related to the huge postnatal growth of the brain in humans and in pre-human hominins. The Taung child, an *Australopithecus africanus* estimated to be 3-4 years old at the time of his death, showed incomplete closure of the MS, as did adult specimens of *Homo habilis* and *Homo ergaster* (2). In Neanderthal children, persistence of the MS was common (2, 24), with the MS and greater fontanel open in association with full deciduous dentition (figure 7). It should be remembered that the adult Neanderthal cerebrum was larger than ours, at 1,161 cubic centimeters compared to 1,097 cc (25), which may account for the need for prolonged postnatal growth and for a patent MS. Interestingly, recent sequencing of the Neanderthal genome showed a higher prevalence of isoform CBFA1 of the *RUNX2* gene (26). This gene, coding for a transcription factor, is implicated in cleidocranial dysplasia, a condition in which the greater fontanel is retained in adulthood, along with anomalies of other membranous bones such as the clavicles and ribs (figure 8), features which are reminiscent of the habitus of Neanderthal humans (26). The different isoforms of *RUNX2* in different hominid genera may reflect different regulation pathways, resulting in distinct morphology and MS closure timing (24).

Overall, data from paleo-anthropology show wide variability in MS fusion timing in the *Homo* genus. Falk et al. consider that the persistence of the MS after birth is part of a set of adaptations to solve the "obstetric dilemma" (the constraints posed by the closed pelvis resulting from bipedalism on the biomechanics of delivery of a baby with a large brain), and the need for fast postnatal brain growth and overdeveloped frontal neocortex (2). This hypothesis is corroborated by the high rate of dystocia in case of MS synostosis.

In this regard, it is tempting to link the secular trends in MS closure in modern times with the increasing practice of cesarean section, which has now reached a prevalence of 18.6% worldwide (27). Certainly, prior to C-section, a number of children with MS synostosis would have died during delivery, along with the mother. The widespread availability of C-section and the general improvement in perinatal care have certainly had an impact on the prevalence of live births with MS synostosis, and removed a powerful selection factor against patent MS at birth.

Conclusions

The metopic suture, unlike other calvarial sutures, is programmed to close early in infancy. Its pattern of closure is a continuous rather than binary variable: there appears to exist a continuum between delayed closure of the MS and its definitive persistence known as metopism. It is thus logical to associate the rising prevalence of MS synostosis and the decreasing prevalence of metopism.

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The pattern of MS closure is variable in evolution and in the present day population, closing earlier in great apes, later in early humans, and even now changing over recent decades. Such variability is a hallmark of mammalian species such as dogs, allowing man-made selection of highly diverse breeds, although in our species variations are inescapably constrained by the "obstetrical dilemma".

Better knowledge of the determinants of MS closure could help understand why other sutures in other craniosynostoses behave like the MS.

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Figure legends

Figure 1

Percentage of children by month of age with fully open, partially fused and totally fused metopic suture. Each group numbers 20 children, except the 11-months age group (19 cases).

Proportion d'enfants par classe d'âge (mois) avec suture métopique totalement ouverte, partiellement soudée, et totalement soudée. Chaque groupe comprend 20 enfants, sauf le groupe des 11 mois, les résultats sont donc exprimés en pourcentages.

Figure 2

Male child with leptocephaly (combined synostosis of the metopic and sagittal sutures)

A, B: the child seen aged 3 months; C, D: CT scan at 3 months

Garçon porteur d'une leptocéphalie (combinant fermeture de la suture sagittale avec fermeture précoce de la métopique) : A et B : l'enfant vu à 3 mois ; C et D : scanner 3D à 3 mois.

Figure 3

Secular trends regarding children diagnosed with metopic suture synostosis during the last 4 decades, by decade of birth. Dates relate to the patient's birth date. Blue line: Male/female ratio for patients diagnosed with MS synostosis; red line: proportion of children with metopic suture synostosis among the total number of children with craniosynostoses seen in our department.

Tendances sur le long terme concernant la prévalence et le sex-ratio : on note une augmentation de la proportion des craniosténoses métopiques par rapport aux autres craniosténoses, et dans le même temps une réduction partielle de la prévalence masculine.

Figure 4:

Child with MS synostosis, dystocic birth with forceps resulting in parietal fracture (A) and subdural bleeding (B); note the scar on the frontal scalp (C).

Enfant porteur d'une craniosténose métopique, naissance dystocique avec utilisation de forceps, fracture pariétale (A) et saignement sous-dural (B) ; noter la cicatrice du scalp frontal (C).

figure 5

Children with metopism at different ages; lateral frontal bulging above hollow temples give them a "family look".

Enfants présentant un métopisme à différents âges ; le bombement supra-temporal leur donne un "air de famille".

Figure 6

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Four examples of children having metopism associated with other midline anomalies: A: ethmoidal encephalocele; B: nasal dermal fistula; C: suprasellar teratoma; D: Stickler syndrome.

Quatre exemples d'enfants porteur d'un métopisme associé à diverses anomalies : A : encéphalocèle ethmoïdale ; B : fistule dermique nasale ; C : tératome supra-sellaire D : syndrome de Stickler.

Figure 7

Specimen displayed in the anthropology museum in Mexico City, showing persistent MS (along with the greater fontanel), in a Neanderthal child with all deciduous teeth erupted.

Spécimen de crâne d'enfant de Neanderthal exposé au musée d'anthropologie de Mexico, montrant la persistance de la métopique et de la fontanelle bregmatique, alors que la dentition lactéale est complète.

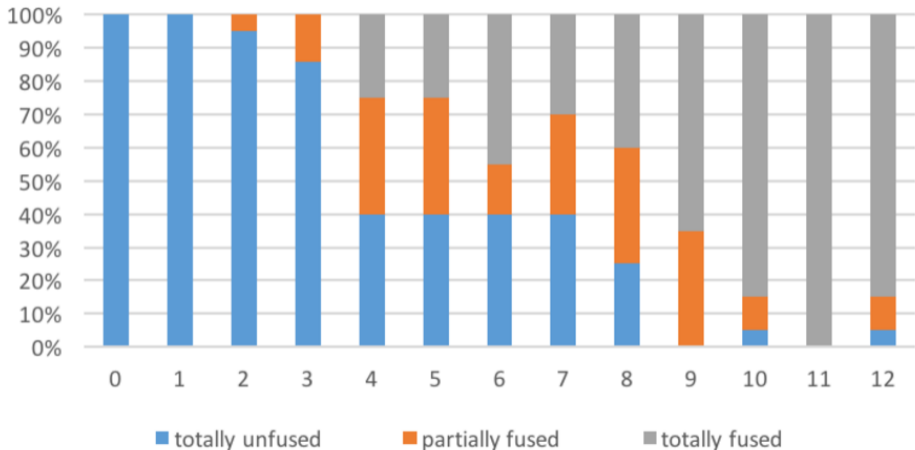
Figure 8:

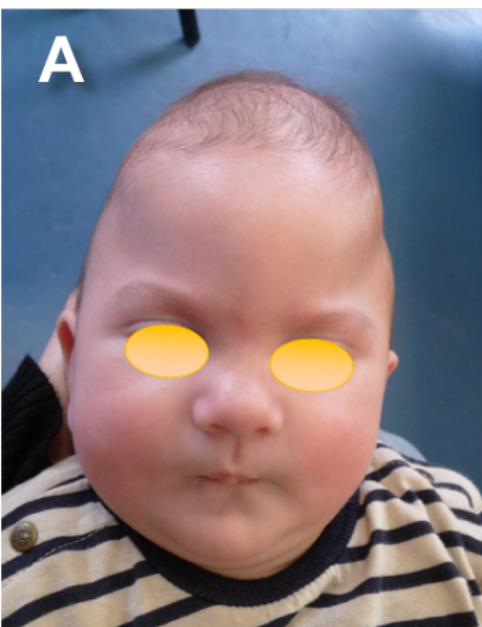
Child affected with cleidocranial dysostosis, with very large anterior fontanel extending from the nasion, and "kissing" shoulders" on account of severely hypoplastic clavicles.

A: CT scan, aged 6 months; B: skull X-ray, aged 26 months; C: the child aged 26 months; D: Thorax X-ray, aged 28 months.

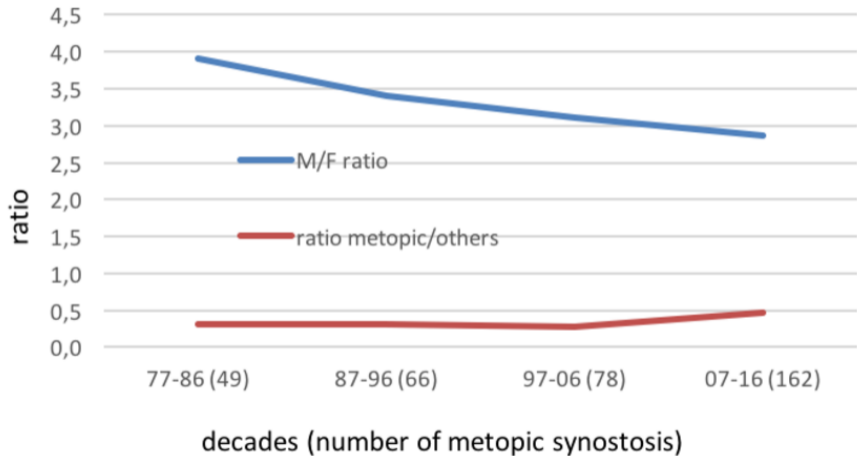
Enfant porteur d'une dysostose cléïdo-crânienne, avec une très grande fontanelle bregmatique étendue jusqu'au nasion, et des épaules jointives en raison de l'hypoplasie des clavicules. A : scanner à 6 mois ; B : radios de crâne à 26 mois ; C : l'enfant âgé de 26 mois ; D : radio de thorax à l'âge de 28 mois.

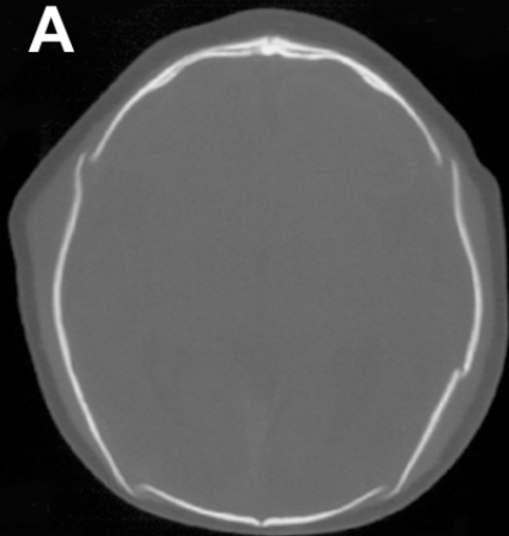
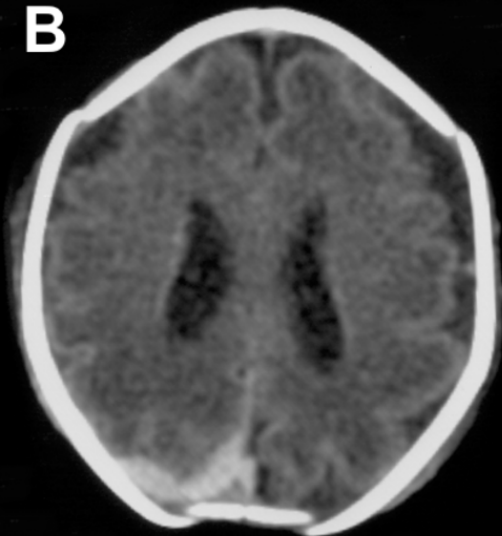
pattern of metopic fusion





secular trends



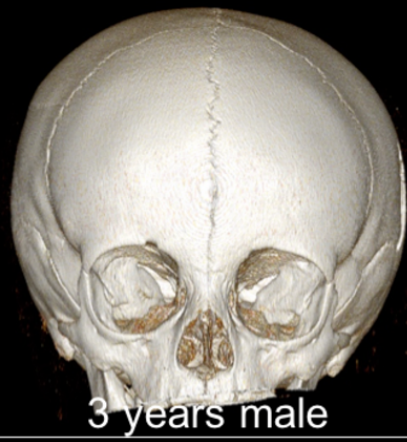
A**B****C****D**



21 months male



3 years female



3 years male



3 years male



4 years female



9 years male



9 years male



9 years male



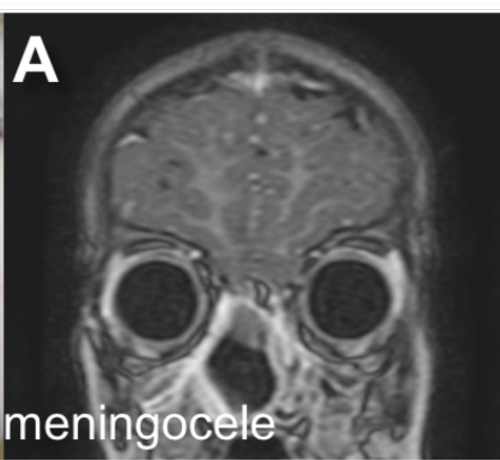
13 years female



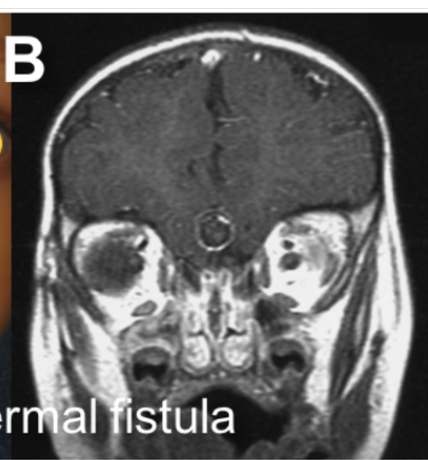
16 years female



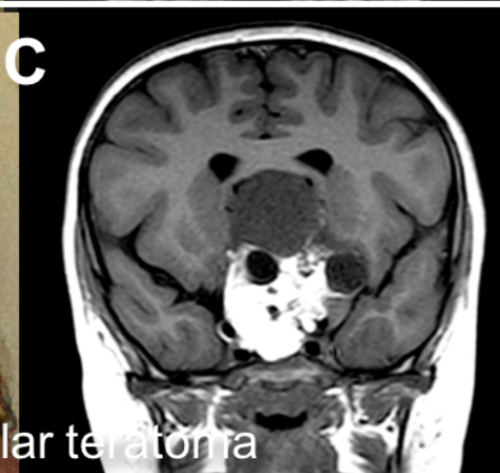
ethmoidal meningocele



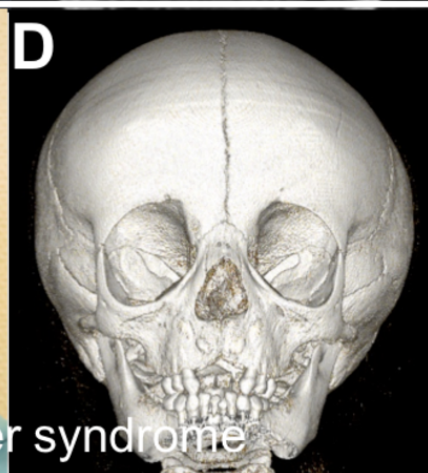
nasal dermal fistula



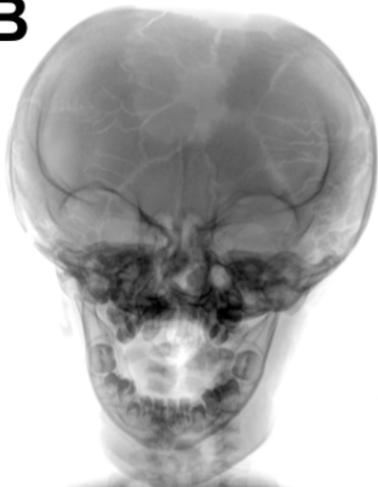
suprasellar teratoma



Stickler syndrome





A**B****C****D**