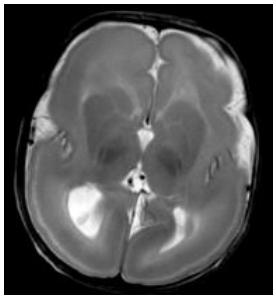
SPR 2015 Neuroradiology Session

May 1, 2015

SAM Questionnaire

Supratentorial Brain Malformations

Edward Yang, MD PhD



1. **Lissencephaly is characterized as a failure in neuronal migration. Which of the following genes has NOT been implicated as causal for lissencephaly?**

   A. LIS1
   B. TUBA1A
   C. DCX (doublecortin)
   D. ARX
   E. TSC2 (tuberin)

   Correct Answer: E

References

1. R. Guerrini and W.B. Dobyns. Malformations of cortical development: clinical features and genetic causes. *Lancet Neurology* 13: 710-726 (2014).
2. P.D. Griffiths, S-A Gardner, M. Smith, C. Rittey, and T. Powell. Hemimegalencephaly and Focal Megalencephaly in Tuberous Sclerosis Complex. AJNR 19: 1935-1938 (1998)

Rationale

The image depicts lissencephaly, in this instance due to the Miller-Dieker syndrome. Lissencephaly results from abnormal migration of neurons to the cortex such that a normal six layer cortex fails to form and a thick zone of arrested gray matter widens the cortex.

Option A is <u>not</u> correct. As the name suggests, Lis1 was the earliest characterized lissencephaly gene.

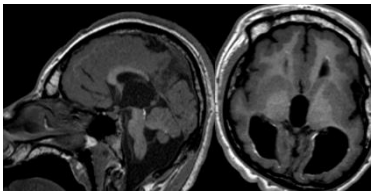
Option B is <u>not</u> correct. Tubulin mutations represent a small proportion of lissencephaly cases but are well accepted genetic etiology for this disorder

Option C is <u>not</u> correct. DCX mutations are the most common reason for X-linked lissencephaly.

Option D is <u>not</u> correct. ARX mutations are a rare but well accepted cause of lissencephaly, usually presenting as ambiguous genitalia and callosal dysgenesis in males.

Option E is correct. TSC1 and TSC2 cause tuberous sclerosis. The tubers in tuberous sclerosis represent a form of cortical dysplasia, and while other malformations (namely hemimegalencephaly) have been linked to TSC1/2, lissencephaly is not one of them.

2. **A 13 year old female with spastic quadraparesis is imaged with the MRI shown below. Which of the following is the MOST likely explanation for the brain malformation?**



   A. Megalencephaly Capillary Malformation Polymicrogyria (MCAP) syndrome
   B. Somatic mutation in AKT1
   C. Congenital cytomegalovirus (CMV) exposure.
   D. Filamin A mutation (FLNA)
   E. Trisomy 13

   Correct Answer: C

References

1. R. Guerrini and W.B. Dobyns. Malformations of cortical development: clinical features and genetic causes. *Lancet Neurology* 13: 710-726 (2014).
2. G.M. Mirzaa and A. Poduri. Megalencephaly and Hemimegalencephaly. *Am. Journal. Medical Genetics Part C* 166C:156-172 (2014).
3. G. Hedlund, J.F. Bale, and A.J. Barkovich. "Chapter 11: Infections of the Developing and Mature Nervous System" *in Pediatric Neuroimaging 5th edition* (eds. A.J. Barkovich and C. Raybaud), Philadelphia: Lippincott, Williams, & Wilkins (2012), pp 955-962.

Rationale

This case features marked microcephaly with diffuse polymicrogyria , callosal dysgenesis, cerebellar hypoplasia, and parenchymal calcifications. These findings are typical of congenital CMV exposure.

Option A is <u>not</u> correct. MCAP syndrome is associated with polymicrogyria but as the name suggests, there is enlarged head size unlike the shown image.

Option B is <u>not</u> correct. In the brain, somatic mutations of AKT1 result in hemimegalencephaly. In the shown case, the abnormality is diffuse and results in small head size.

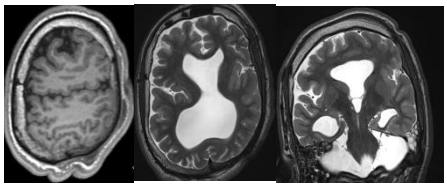
Option C is correct. CMV exposure in utero results in small head size, polymicrogyria, parenchymal calcifications, and cerebellar hypoplasia. All these features are present in the shown case.

Option D is <u>not</u> correct. In the brain, FLNA mutations are associated with periventricular nodular heterotopia rather than polymicrogyria. The microcephaly and parenchymal calcifications are also discordant features.

Option E is <u>not</u> correct. Trisomy 13 is most associated with holoprosencephaly rather than polymicrogyria.

3. This case was shown earlier. What embryologic process has failed to occur normally?

A. Hemispheric cleavage
B. Neuronal precursor proliferation
C. Neuronal migration
D. Commissuration
E. Fenestration of the posterior membranous area



Correct Answer: A

References

1. T.C. Winter, A.M. Kennedy, and P.J. Woodward. Holoprosencephaly: A Survey of the Entity, with Embryology abd Fetal Imaging. *Radiographics* 35:275-290 (2015).
2. R. Guerrini and W.B. Dobyns. Malformations of cortical development: clinical features and genetic causes. *Lancet Neurology* 13: 710-726 (2014).
3. T. Bosemani, G. Orman, E. Bolthauser, A. Tekes, T.A.G.M Huisman, and A. Poretti. Congenital Abnormalities of the Posterior Fossa. *Radiographics* 35:200-220 (2015).

Rationale

The panel of images demonstrate continuity of the cerebral hemispheres across the midline with vertically oriented sylvian fissures and an absent septum pellucidum. The genu and splenium of the corpus callosum are present but the midportion of the callosum is unidentifiable. This case was shown earlier and represents the middle interhemispheric variant of holoprosencephaly.

Option A is correct. Holoprosencephaly represents failure of the brain to cleave into two separated hemispheres.

Option B is <u>not</u> correct. Neuronal precursor proliferation occurs after hemispheric cleavage has already occurred. Failures in this step result in smaller overall size of the brain.

Option C is <u>not</u> correct. This step also occurs after hemispheric cleavage and leads to malformations such as gray matter heterotopia, pachygyria, polymicrogyria, and focal cortical dysplasia.

Option D is <u>not</u> correct. While the corpus callosum is not normal in this case, the reason for the abnormal configuration is failure of the hemispheres to separate, not failure of the commissures to form in the first place.

Option E is <u>not</u> correct. Fenestration of the posterior membranous area is an early step in formation of the brain, but it is tied to formation of the outlet foramina of the fourth ventricle. Failures in this process result in Dandy Walker spectrum abnormalities not holoprosencephaly.

Hindbrain Malformations
Gisele E. Ishak, MD

4. **Tubulinopathies are a known cause of malformation of cortical development. Recently, these disorders have been recognized with a distinct hindbrain malformation characterized by:**
   A. Brainstem hypoplasia
   B. Brainstem asymmetry and dysplasia
   C. Cerebellar hypoplasia
   D. Superior vermian dysplasia (diagonal folia)
   E. All of the above

   Correct Answer: E

References

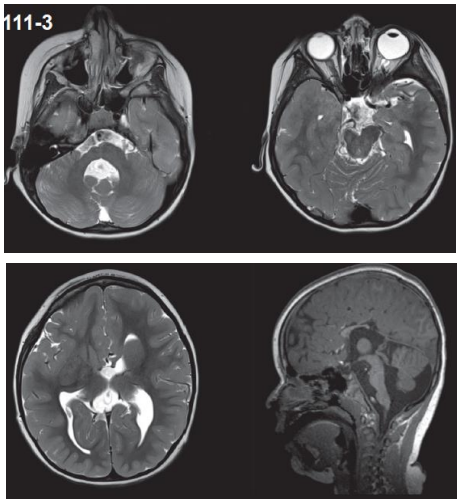
1. Poirier K, Saillour Y, Bahi-Buisson N, Jaglin XH, Fallet-Bianco C, Nabbout R, Castelnau-Ptakhine L, Roubertie A, Attie-Bitach T, Desguerre I, Genevieve D, Barnerias C, Keren B, Lebrun N, Boddaert N, Encha-Razavi F, Chelly J. Mutations in the neuronal ß-tubulin subunit TUBB3 result in malformation of cortical development and neuronal migration defects. Hum Mol Genet. 2010 Nov 15;19(22):4462-73.
2. Guerrini R, Mei D, Cordelli DM, Pucatti D, Franzoni E, Parrini E. Symmetric polymicrogyria and pachygyria associated with TUBB2B gene mutations. Eur J Hum Genet. 2012 Sep;20(9):995-8.

5. **Additional MRI features of tubulinopathies may include:**
   A. Basal ganglia dysplasia with wavy contour of the lateral ventricles
   B. Malformations of cortical development
   C. Corpus callosum hypoplasia or partial agenesis
   D. Globular thalami
   E. All of the above

   Correct Answer: E

References

1. Poirier K, Saillour Y, Bahi-Buisson N, Jaglin XH, Fallet-Bianco C, Nabbout R, Castelnau-Ptakhine L, Roubertie A, Attie-Bitach T, Desguerre I, Genevieve D, Barnerias C, Keren B, Lebrun N, Boddaert N, Encha-Razavi F, Chelly J. Mutations in the neuronal ß-tubulin subunit TUBB3 result in malformation of cortical development and neuronal migration defects. Hum Mol Genet. 2010 Nov 15;19(22):4462-73.
2. Guerrini R, Mei D, Cordelli DM, Pucatti D, Franzoni E, Parrini E. Symmetric polymicrogyria and pachygyria associated with TUBB2B gene mutations. Eur J Hum Genet. 2012 Sep;20(9):995-8.



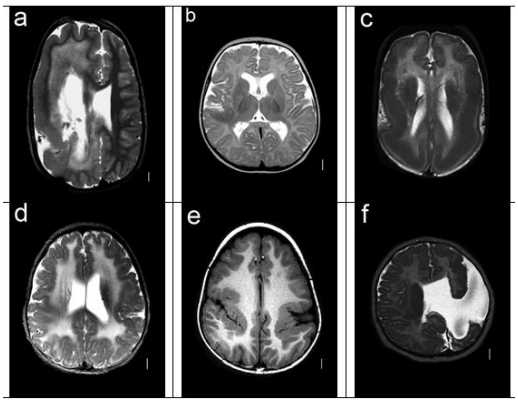
6. **You are shown 4 representative MRI images. What is the malformation?**
   A. PTCD (Pontine tegmental cap dysplasia)
   B. PCH (Pontocerebellar hypoplasia)
   C. Joubert and related disorders
   D. Dandy Walker malformation
   E. Tubulinopathy

   Correct Answer: E

References

1. Poirier K, Saillour Y, Bahi-Buisson N, Jaglin XH, Fallet-Bianco C, Nabbout R, Castelnau-Ptakhine L, Roubertie A, Attie-Bitach T, Desguerre I, Genevieve D, Barnerias C, Keren B, Lebrun N, Boddaert N, Encha-Razavi F, Chelly J. Mutations in the neuronal ß-tubulin subunit TUBB3 result in malformation of cortical development and neuronal migration defects. Hum Mol Genet. 2010 Nov 15;19(22):4462-73.
2. Guerrini R, Mei D, Cordelli DM, Pucatti D, Franzoni E, Parrini E. Symmetric polymicrogyria and pachygyria associated with TUBB2B gene mutations. Eur J Hum Genet. 2012 Sep;20(9):995-8.

Inside Out: The Nature and Genetic Basis of Cortical and Subcortical Malformations
William B. Dobyns, MD



7. **Which of the following images are most likely to be associated with autosomal recessive inheritance?**
   A. a
   B. b
   C. c
   D. d
   E. e
   F. f

   Correct Answer: D

Rationale

The correct answer is D, which shows cobblestone malformation in muscle-eye-brain disease.

8. **Which of the following is the most common cause of classic polymicrogyria?**
   A. Autosomal dominant inheritance
   B. Autosomal recessive inheritance
   C. X-linked inheritance
   D. Chromosome copy number variants (deletion 1p36, 22q11.2)
   E. Cytomegalovirus

Correct Answer: E

Rationale

The correct answer is E (cytomegalovirus). CMV may account for more than 10% of all PMG, making it far more common than any other recognized cause.

9. Mutations of core PI3K-AKT-MTOR pathway genes have been associated with all <u>except</u>?

A. Cobblestone lissencephaly
B. Polymicrogyria
C. Hemimegalencephaly
D. Focal cortical dysplasia type II

Correct Answer: A

Rationale

The correct answer is A. Mutations of several genes in the PI3K-AKT-MTOR pathway including PIK3CA, PIK3R2, PTEN, AKT3, MTOR, DEPDC5 and CCND2 have been found in patients with Polymicrogyria, hemimegalencephaly and focal cortical dysplasia type II. The group of cobblestone malformations are associated with mutations of genes that modify alpha-dystroglycan.

Biology of Craniosynostosis
Michael L. Cunningham MD, PhD

10. What is the most commonly fused suture in hereditary craniosynostosis?

A. Metopic
B. Coronal
C. Sagittal
D. Lambdoid
E. Squamosal

Correct Answer: B

References:

1. Robin NH, Falk MJ, Haldeman-Englert CR. FGFR-Related Craniosynostosis Syndromes. 1998 Oct 20 [Updated 2011 Jun 7]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1455/
2. Gallagher ER, Ratisoontorn C, Cunningham ML. Saethre-Chotzen Syndrome. 2003 May 16 [Updated 2012 Jun 14]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1189/
3. Cunningham ML, Seto ML, Ratisoontorn C, Heike CL, Hing AV. Syndromic craniosynostosis: from history to hydrogen bonds. Orthod Craniofac Res. 2007 May;10(2):67-81. Review. PubMed PMID: 17552943.

4. Muenke M, Gripp KW, McDonald-McGinn DM, Gaudenz K, Whitaker LA, Bartlett SP, Markowitz RI, Robin NH, Nwokoro N, Mulvihill JJ, Losken HW, Mulliken JB, Guttmacher AE, Wilroy RS, Clarke LA, Hollway G, Adès LC, Haan EA, Mulley JC, Cohen MM Jr, Bellus GA, Francomano CA, Moloney DM, Wall SA, Wilkie AO, et al. A unique point mutation in the fibroblast growth factor receptor 3 gene (FGFR3) defines a new craniosynostosis syndrome. Am J Hum Genet. 1997 Mar;60(3):555-64. PubMed PMID: 9042914; PubMed Central PMCID: PMC1712518.
5. Gripp KW, McDonald-McGinn DM, Gaudenz K, Whitaker LA, Bartlett SP, Glat PM, Cassileth LB, Mayro R, Zackai EH, Muenke M. Identification of a genetic cause for isolated unilateral coronal synostosis: a unique mutation in the fibroblast growth factor receptor 3. J Pediatr. 1998 Apr;132(4):714-6. PubMed PMID: 9580776.

Rationale

Option A. is not correct. While premature fusion of the metopic suture can be seen in many forms of hereditary craniosynostosis it much more frequently presents as an isolated finding. It is however seen in infants with abnormal frontal lobe development, primary microcephaly, and in the context of cytogenetic abnormalities.

Option B. is correct. Coronal synostosis is common to all the major forms of hereditary (syndromic) craniosynostosis including Apert, Pfeiffer, Crouzon, Saethre-Chotzen, and Muenke syndromes. Due to this fact craniosynostosis syndromes are not usually distinguished on the basis of their calvarial phenotype but rather their extracranial features.

Option C. is not correct. The sagittal suture is the most commonly fused suture in non-syndromic craniosynostosis. Although it can be fused in syndromic forms of synostosis, it is much less common than coronal synostosis in this population.

Option D. is not correct. Lambdoid synostosis is the rarest form of isolated synostosis and is infrequently affected in syndromic forms. One condition, the so-called "Mercedes" synostosis (or bilateral lambdoid and sagittal synostosis), occurs at higher frequency in individuals of Spanish descent. Although this suggests a genetic component, no causative mutations have been identified.

Option E. is not correct. Although squamosal synostosis can be seen in isolation and as part of Crouzon syndrome, it is not a common feature of hereditary synostosis.

11. What are the most commonly identified mutations in single suture craniosynostosis?

F. FGFR1, FGFR2 and FGFR3 (fibroblast growth factor receptor 1, 2, 3)
G. FGFR2 and TWIST1 (TWIST 1)
H. TWIST1 and TCF12 (Transcription factor 12)
I. FGFR3, TWIST1 and TCF12 (Transcription factor 12)
J. Mutations have not been identified in single suture craniosynostosis

Correct Answer: D

References:

1. Sharma VP, Fenwick AL, Brockop MS, McGowan SJ, Goos JA, Hoogeboom AJ, Brady AF, Jeelani NO, Lynch SA, Mulliken JB, Murray DJ, Phipps JM, Sweeney E, Tomkins SE, Wilson LC, Bennett S, Cornall RJ, Broxholme J, Kanapin A; 500 Whole-Genome Sequences (WGS500) Consortium, Johnson D, Wall SA, van der Spek PJ, Mathijssen IM, Maxson RE, Twigg SR, Wilkie AO. Mutations in TCF12, encoding a basic helix-loop-helix partner of TWIST1, are a frequent cause of coronal craniosynostosis. Nat Genet. 2013 Mar;45(3):304-7. doi: 10.1038/ng.2531. Epub 2013 Jan 27. Erratum in: Nat Genet. 2013 Oct;45(10):1261. PubMed PMID: 23354436; PubMed Central PMCID: PMC3647333.

2. Seto ML, Hing AV, Chang J, Hu M, Kapp-Simon KA, Patel PK, Burton BK, Kane AA, Smyth MD, Hopper R, Ellenbogen RG, Stevenson K, Speltz ML, Cunningham ML. Isolated sagittal and coronal craniosynostosis associated with TWIST box mutations. Am J Med Genet A. 2007 Apr 1;143A(7):678-86. PubMed PMID: 17343269.

Rationale

Although there are case reports and case series that have identified causative mutations in each of these genes, mutations in FGFR1 and FGFR2 are rare among cases of isolated craniosynostosis. The phenotypic features of the Apert, Crouzon and Pfeiffer syndromes are well characterized and distinguished primarily on their extracranial features. Although there are distinct phenotypic features in individuals with mutations in FGFR3, TWIST1, and TCF12, there are many well documented cases with isolated coronal craniosynostosis. Based on current literature it appears that mutations in FGFR3, TWIST1, and TCF12 account for more than 20% of isolated unilateral coronal craniosynostosis.

12. What biologic process has been found to be associated with the development of craniosynostosis?

K. Osteoblast proliferation
L. Osteoblast differentiation
M. Osteoblast migration
N. Enhanced extracellular matrix secretion
O. All of the above

Correct Answer: E

References

1. Miraoui H, Oudina K, Petite H, Tanimoto Y, Moriyama K, Marie PJ. Fibroblast growth factor receptor 2 promotes osteogenic differentiation in mesenchymal cells via ERK1/2 and protein kinase C signaling. J Biol Chem. 2009 Feb 20;284(8):4897-904. doi: 10.1074/jbc.M805432200. Epub 2008 Dec 30. PubMed PMID: 19117954.

2. Ratisoontorn C, Seto ML, Broughton KM, Cunningham ML. In vitro differentiation profile of osteoblasts derived from patients with Saethre-Chotzen syndrome. Bone. 2005 Apr;36(4):627-34. PubMed PMID: 15781003.
3. Stamper BD, Park SS, Beyer RP, Bammler TK, Farin FM, Mecham B, Cunningham ML. Differential expression of extracellular matrix-mediated pathways in single-suture craniosynostosis. PLoS One. 2011;6(10):e26557. doi: 10.1371/journal.pone.0026557. Epub 2011 Oct 19. PubMed PMID: 22028906; PubMed Central PMCID: PMC3197523.

Rationale

There is substantial scientific interest in understanding the biologic cause of syndromic and isolated craniosynostosis in hopes that we can translate this knowledge into clinical applications to improve the outcomes for patients. Although much work needs to be done, there is strong evidence that dysregulation of osteoblast differentiation occurs in both hereditary and sporadic forms. Conflicting data exists for the role of proliferation however enhanced osteoblast differentiation (as defined by increased expression of osteogenic markers, decreased migration, increased matrix production, and mineralization) appears to be a common feature of all forms.

Imaging of Craniosynostosis

Susan Blaser, MD, FRCPC

13. Regarding bilateral coronal synostosis, which of the following statements is false?

P. Rarely has pre- or post-operative complications
Q. Is frequently associated with limb anomalies
R. Is often syndromic
S. Frequently involves other sutures, particularly the coronal hemi-ring (contiguous frontoparietal, frontosphenoidal and frontoethmoidal sutures)

Correct Answer: A

References

1. Boyadjiev SA, International Craniosynostosis Consortium (2007) Genetic analysis of non-syndromic craniosynostosis. Orthod Craniofac Res 10:129–137
2. Sandberg DI, Navarro R, Blanch J et al (2007) Anomalous venous drainage preventing safe posterior fossa decompression in patients with Chiari malformation type 1 and multisutural craniosynostosis. Report of two cases and review of the literature. J Neurosurg 106:490–494

Rationale

A is false: Complications are relatively frequent in patients with bilateral coronal synostosis. Complications which can occur in pre- or post-operative period include acquired Chiari 1, hydrocephalus, foramen magnum stenosis, and sinovenous occlusion, amongst others. Bilateral coronal synostosis is frequently associated with limb anomalies. Involvement of contiguous sutures in the coronal hemi-ring is typical.

14. Involvement of which of the following causes progressive skull base shortening in the bicoronal synostoses?

A. Coronal suture
B. Posterior intraoccipital synchondrosis
C. Sphenooccipital synchondrosis
D. Frontoethmoidal

Correct Answer: C

References

1. Okamoto K, Ito J, Tokiguchi S, Furusawa T (1996);High-resolution CT findings in the development of the sphenooccipital synchondrosis. AJNR 17(1):117-20
2. Goldstein JA, Paliga JT, Wink JD et al (2014). Earlier evidence of sphenooccipital synchondrosis fusion correlates with severity of midface hypoplasia in patients with syndromic craniosynostosis. Plast Reconstr Surg 134(3):504-10
3. McGrath J, Gerety PA, Derderian CA et al (2012) Differential closure of the sphenooccipital synchondrosis in syndromic craniosynostosis. Plast Reconstr Surg 130(5):681e
4. Paliga JT, Goldstein JA, Vossough A et al (2014) Premature closure of the sphenooccipital synchondrosis in Pfeiffer syndrome: A link to midface hypoplasia. J Craniofac Surg 25(1):202-5

Rationale

C - Sphenooccipital synchondrosis - Growth of the skull base, particularly at the sphenooccipital synchondrosis, continues until the teen years (Okamoto 1996). Early fusion in the bicoronal synostoses leads to skull base shortening and resultant midface hypoplasia or retrusion (Goldstein 2014). Children with Apert and Pfeiffer syndrome are more severely affected than patients with Crouzon or Muenke syndrome (McGrath 2012, Paliga 2014). Early closure of the anterior and posterior intraoccipital synchondroses, on the other hand, leads to foramen magnum coarctation, rather than significant skull base shortening.

15. Regarding lambdoid synostosis, which of the following statements is true?

A. Is the most common of the craniosynostoses
B. It is always unilateral
C. It is usually associated with brain anomalies
D. Has the radiographic features of ‘mastoid bump’ and posterior plagiocephaly

Correct Answer: D

References

1. Menard RM1, David DJ (1998).Unilateral lambdoid synostosis: morphological characteristics. J Craniofac Surg. 9(3):240-6.
2. Rhodes JL, Tye GW, Fearon JA (2014) Craniosynostosis of the lambdoid suture. Semin Plast Surg 28(3):138-43. doi: 10.1055/s-0034-1384809

Rationale

D is true. Lambdoid synostosis is the least common, < 5%, of craniosynostosis cases. It is much less common than posterior positional (non-synostotic) plagiocephaly. Lambdoid synostosis may be bilateral in the syndromic and genetic synostoses, such as Pfeiffer, Apert and Crouzon and in other cases of progressive pansynostosis and kleeblatschädel. Brain anomalies and hydrocephalus are reported in the syndromic cases. Brain imaging is, therefore, useful in bilateral lambdoid synostosis. The 'mastoid bump' is typical and may be identified on radiographs and 3d CT.

Surgical Considerations in Synostosis

Richard Hopper, MD

16. Which finding is most predictive in distinguishing metopic synostosis from a metopic ridge?

A. vertical thickening of central frontal bone that is clinically palpable and visible on CT scan
B. closed metopic suture on CT scan
C. triad of narrow forehead, biparietal widening, and hypotelorism
D. abnormal relationship between lateral frontal bone and lateral orbit
E. posterior plagiocephaly

Correct Answer: D

Rationale

The metopic suture is the only calvarial suture that normally closes during infancy. Upon closure, a palpable and visible ridge often forms which can be confused with metopic craniosynostosis. Metopic ridging (MR) is treated non-surgically while metopic craniosynostosis (MCS) is treated surgically. Differentiating between the two is paramount; however, consensus is lacking about where a clear diagnostic threshold lies. Upon physical examination, the relationship between the lateral frontal bone and the lateral orbit is important in distinguishing between the two diagnoses. A CT scan can be helpful in making the diagnosis not to confirm a closed suture but to identify 3 or more MCS characteristics.

Option A. is <u>not</u> correct. Both metopic synostosis and metopic ridge are characterized by thickening of bone in the region of the metopic suture. This is typically palpable clinically and visible on CT scan.

Option B. is <u>not</u> correct Patients with abnormal forehead ridging typically present after six months of age. Since the physiologic closure of the metopic suture is between 2-8 months of age, the finding of fusion on CT scan is not diagnostic of either condition.

Option C. is <u>not</u> correct. Although the triad of narrow forehead, bi-parietal widening, and hypotelorism is known as the "classic triad" of metopic synostosis, on review of a

large series of patients, it was only found to be present in 12% of cases of metopic synostosis, demonstrating the variable phenotype of this condition.

Option D. is correct. The most consistent clinical finding in distinguishing metopic synostosis from metopic ridge was an abnormal relationship between the lateral frontal bone and lateral orbit. This has been clinically described as "pterion constriction" and relates to the abnormal position of the sphenoid relative to the middle cranial vault.

Option E. is not correct. Although patients with metopic synostosis and metopic ridge can have posterior plagiocephaly from post-natal deformation, it is not a characteristic finding of either condition.

References

1. Birgfeld CB, Salzman BS, Hing AV, Heike CL, Khanna PC, Gruss JS, Hopper RA. Making the diagnosis: metopic ridge versus metopic craniosynostosis. J Craniofac Surg. 2013 Jan:24(1):178-85.
2. Vu HL, Panchal J, Parker EE, Levine NS, Francel P. The timing of physiologic closure of the metopic suture: a review of 159 patients using reconstructed 3D CT scans of the craniofacial region. J Craniofac Surg. 2001 Nov; 12(6):527-32

17. What abnormal venous relationship can limit a surgical plan for cranial expansion for the treatment of complex (syndromic) craniosynososis?

A. invagination of the sagittal sinus in the inferior frontal bone; the "omega sign"
B. superior migration of the torcula with elevated transverse sinuses
C. transosseous venous channel from transverse sinus
D. asymmetric external jugular vein diameters
E. Enlarged jugular foramen diameter

Correct Answer: C

References

1. Abnormal venous drainage in syndromic craniosynostosis and the role of CT venography. Jeevan DS, Anlsow P, Jayamohan J. Childs Nerv Syst. 2008 Dec; 24(12):1413-20. Epub 2008 Jun 25
2. Enigma of raised intracranial pressure in patients with complex craniosynostosis: the role of abnormal intracranial venous drainage. Taylor WJ, Hayward RD, Lasjaunias P, Britto JA, Thompson DN, Jones BM, Evans RD. J Neurosurg. 2001 Mar; 94(3):377-85
3. Anomalous venous drainage preventing safe posterior fossa decompression in patients with chiari malformation type I and multisutural craniosynostosis. Report of two cases and review of the literature. Sandberg DI, Navarro R, Blanch J, Ragheb J. J Neurosurg. 2007 Jun; 106(6 Suppl):490-4
4. Venous hypertension in syndromic and complex craniosynostosis: The abnormal anatomy of the jugular foramen and collaterals. Florisson JM, Barmpalios G, Lequin M, van Veelen ML, Bannink N, Hayward RD, Mathijssen IM. J Craniomaxillofac Surg. 2015 Apr;43(3):312-8.

Rationale

Option A. is not correct. The sagittal sinus can often be invaginated in the inferior frontal bone in metopic synostosis and is known as the "omega sign". It is not common in complex synostosis. Although this finding needs to be recognized by the surgical team to plan their dissection, it does not alter the surgical plan or placement of osteotomies.

Option B. is not correct. The torcula and transverse sinuses can be inferiorly placed close to the skullbase in syndromic conditions such as Pfeiffer syndrome or Apert syndrome relative to non-syndromic synostosis. This can alter the placement of inferior transverse osteotomy placement to avoid iatrogenic venous injury. Superior placement of the sinus however would increase the options available for the posterior osteotomies and would not limit the surgical plan.

Option C. is correct. Transosseous venous communication between the venous sinus and the scalp has been well described in complex synostosis. It is suggested by a substantial circular opening in the occipital bone over the transverse or sagittal sinuses, and can be further delineated by contrast venous imaging. Surgical transection of this abnormal venous drainage can result in rapid increased intracranial venous pressure and death. Osteotomies and dissection must be limited to minimize the risk to these communications.

Option D. is not correct. Asymmetry between the external jugular veins has not been described as a finding that alters osteotomy placement in the treatment of craniosynostosis.

Option E. is not correct. Constricted or smaller jugular foramina have been described in a series of patients with complex syndromic synostosis, and have been hypothesized as being an indicator of increased intracranial pressure. This finding could alter surgical planning if increased intracranial pressure was suspected. Enlarged jugular foramina have not been associated with any finding that would change a surgical plan for cranial expansion.

18. Which statement is true regarding patients with sagittal synostosis?

A. Previously open surrounding sutures can become fused after strip craniectomy
B. Increased intracranial pressure is less than 3% in untreated mild cases
C. Compensatory frontal bossing is a fixed deformity and requires frontal cranioplasty
D. A vertex cranial bone bulge a year after cranial expansion is an incidental finding
E. Cranial vault volume is increased following both open and endoscopic strip craniectomy

Correct Answer: A

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Rationale

Option A. is correct. Radiographic closure of the lambdoid and coronal sutures has been observed in approximately 40% of coronal sutures and 75% of lambdoid sutures after total cranial vault remodeling for sagittal synostosis. These findings of secondary fusion have not been correlated with any change in head shape.

Option B. is <u>not</u> correct. In a series of 39 patients who elected to not have surgical treatment of sagittal synostosis due to a mild deformity or family choice, intraparencymal pressure monitoring demonstrated increased pressure in 44%. The pressure findings were not correlated with the degree of cranial deformity severity.

Option C. is <u>not</u> correct. The compensatory frontal bossing that occurs secondary to premature fusion of the sagittal suture approaches dimensions of normal controls within two years after isolated middle and posterior vault surgery. The normalization of the frontal bossing that occurs without frontal bone surgery appears to be secondary to the remainder of the skull "catching up" rather than a regression of the bossing measures.

Option D. is <u>not</u> correct. In a series of patients surgically treated for sagittal synostosis, seven were observed to develop a bone bulge on the vertex of the cranium within a year after surgery. All of these patients required repeat cranial remodeling for either deteriorating head shape, increased intracranial pressure or both. Although all vertex bulges after sagittal synostosis surgery have not been shown to require treatment, they are not incidental and indicate close observation or further diagnostic tests.

Option E. is <u>not</u> correct. Although cranial index (CI) or cranial ratios do change after cranial surgery for sagittal synostosis, the cranial vault volume (CVV) is not different between normal matched controls and patients with sagittal synostosis before and after surgery. The CI and CVV outcomes have not been shown to be different between open or endoscopic approaches.