Iceberg hemangioma: A segmental cutaneous lesion marking extensive extracutanous involvement

Ashaki Patel, BS,[a] Melinda B. Chu, MD,[a] Alan Wild, MD,[b] Martin Reis, MD,[c] Ilona J. Frieden, MD,[d] Beth Drolet, MD,[e] and Elaine C. Siegfried, MD[a,f]
St Louis, Missouri; San Francisco, California; and Milwaukee, Wisconsin

Key words: connective tissue; extracutaneous involvement; infantile hemangioma.

CASE 1

A 3-month-old white girl presented with a soft, bluish scalp mass extending from the posterior hairline to the occipital scalp, just right of midline (Fig 1, *A* and *B*). She also had stridor, plagiocephaly and decreased neck range of motion. After failure to respond to treatment for suspected croup, plagiocephaly and decreased neck range of motion prompted a workup for an invasive infantile hemangioma. Direct laryngotracheoscopy and computed tomography angiography (CTA) identified subglottic narrowing (Fig 2, *A*). Magnetic resonance imaging (MRI) of the head, neck, and upper thorax found additional multifocal extracutaneous lesions (Table I and Fig 1, *C*). Skin biopsy from a neck site found histologic findings typical of infantile hemangioma. The baby had a mixed, segmental hemangioma diagnosed. PHACE syndrome (Posterior fossa, Hemangioma, Arterial abnormalities, Cardiac abnormalities, Eye abnormalities, Sternal Cleft) was considered, but a thorough workup, including echocardiogram, ophthalmology evaluation, and CTA ruled out any intracranial, arterial, cardiac, or ophthalmic abnormalities. Abdominal ultrasound scan helped rule out any other visceral involvement. The patient was started on oral propranolol at 0.3 mg/kg every 8 hours, increased over 3 days to 1.0 mg/kg every 8 hours. Stridor resolved within 1 week, and repeat laryngotracheoscopy confirmed a significantly increased airway diameter (Fig 2, *B*). At 1 month follow-up, the cutaneous component of her hemangioma was less bulky, and neck range of motion and plagiocephaly were dramatically improved.

Abbreviations used:

CTA:	computed tomography angiography
IH:	infantile hemangiomas
LUMBAR:	lower body hemangioma and other cutaneous defects, urogenital anomalies, ulceration, myelopathy, bony deformities, anorectal malformations, arterial anomalies, and renal anomalies ()
MRA:	magnetic resonance angiogram
MRI:	magnetic resonance imaging
PELVIS:	perineal hemangioma, external genitalia malformations, lipomyelomeningocele, vesicorenal abnormalities, imperforate anus, skin tag
PHACE:	posterior fossa, hemangioma, arterial abnormalities, cardiac abnormalities, eye abnormalities, sternal cleft

CASE 2

An 18-week-old white girl presented for evaluation of a small bump on the scalp, which was first noted shortly after birth but rapidly enlarged interfering with head position when supine. The soft, 11- × 15-cm bluish mass had a central area of pallor with

From the Departments of Dermatology,[a] Otolaryngology,[b] Radiology,[c] and Pediatrics,[f] Saint Louis University; the Department of Dermatology, University of California San Francisco[d]; and the Department of Dermatology, Medical College of Wisconsin.[e]

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Correspondence to: Ashaki Patel, BS, Saint Louis University, Department of Dermatology, Cardinal Glennon Children's Hospital, 1465 S. Grand Ave, St. Louis, MO 63104. E-mail: ashaki.patel@health.slu.edu.

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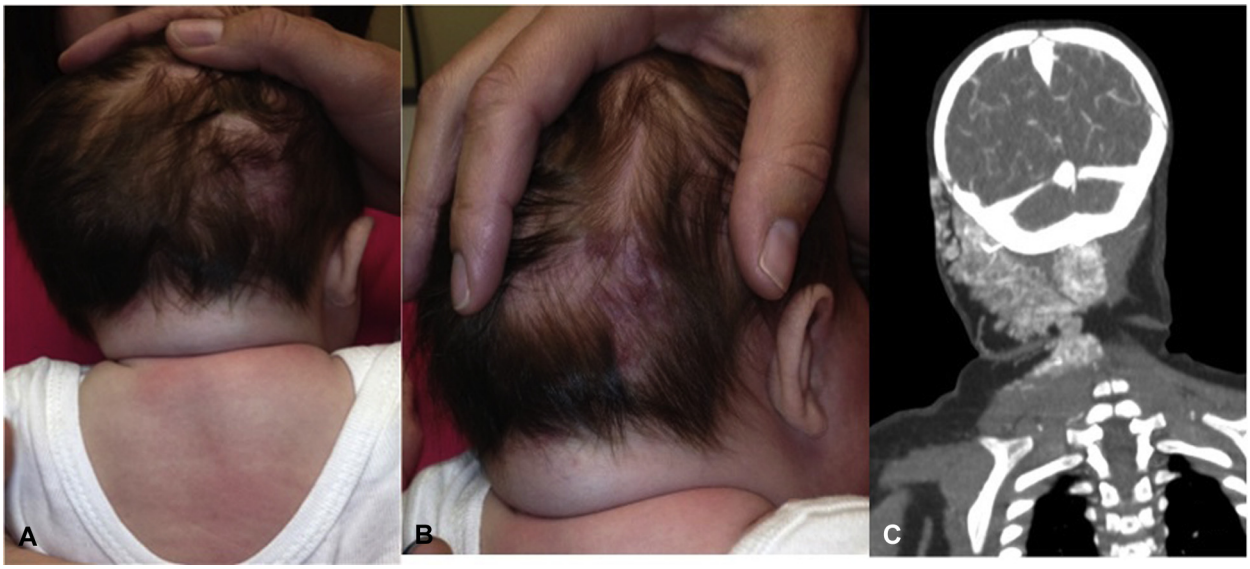

Fig 1. **A**, Soft bluish hemangioma of posterior scalp and nuchal area on physical examination. **B**, Oblique view of soft bluish hemangioma on the scalp and posterior neck. **C**, Entire posterior view with MRI showing diffuse multifocal subglottic and mediastinal involvement.

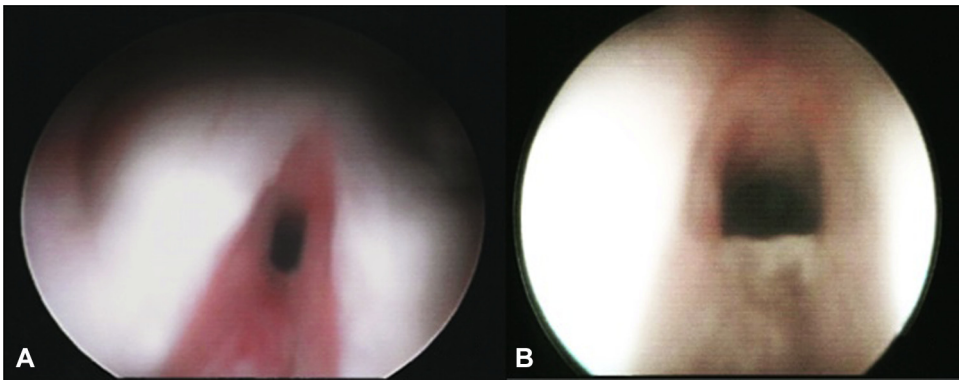

Fig 2. **A**, Bronchoscopy shows life-threatening airway compromise caused by paratracheal hemangioma. **B**, Significant increase in size of airway after 7 days of propranolol.

fine telangiectasia and extended from the nape to the occiput with associated hair thinning. There was no palpable thrill. A similar 3-cm soft bluish mass was noted on the midback. MRI found extensive hemangiomas involving the paratracheal space and the paraspinal area with involvement of the neural foramina and epidural space causing spinal cord deviation (Table I). Oral prednisone yielded 50% reduction of the cutaneous component. Repeat MRI at 15 months found similar partial involution of the extracutaneous lesions. Prednisone was gradually tapered and discontinued at age 17 months. At age 9 years, her cutaneous examination was still notable for a 9- × 7-cm soft, mobile mass at the nape and inferior scalp without overlying skin changes. MRI found evidence of fat with some increased vessels. Surgical debulking was planned, as propranolol was not standard therapy when this child presented.

CASE 3

An 8-week-old white girl presented to the emergency room 3 times within 1 week for evaluation of progressive stridor and respiratory distress that did not respond to oral corticosteroids, racemic epinephrine, and inhaled albuterol. Her skin examination featured a soft, blue 1- × 0.6-cm papule on the right upper eyelid and a 1.0- × 2.5-cm pink patch with central bright red 2-mm papules on her occipital scalp, left of midline. Airway symptoms prompted bronchoscopy, which found a subglottic mass occupying 25% of the airway with extension down to the posterior wall of the trachea and carina. MRI and magnetic resonance angiogram (MRA)

Table I. Age, distribution, complications, and response to treatment for cases 1 through 4

	Case 1	Case 2	Case 3	Case 4
Age when lesion first noticed	1 mo	Birth	2 mos	Birth
Age at imaging	3 mos	3 mos	2 mos	5 mos
Cutaneous distribution	Base of neck to occipital scalp, right of midline (segmental)	Nape of neck to the occipital scalp, and mid back (segmental)	Left upper eyelid and left occipital scalp (segmental)	Right temple and posterior occiput (segmental)
Extracutaneous distribution	• Right juxta-zygomatic area • Posterior orbit • Posterior paravertebral space • Carotid space • Retropharyngeal space • Subglottic space • Paratracheal space	• Posterior neck to left posterior triangle • Paratracheal area • Paraspinal space • Neural foramina • Epidural space	• Soft tissues and perivascular space of left neck • Left thoracic inlet and left thoracic apex	• Right juxta-zygomatic area, • Right parapharyngeal space extending into the carotid space • Right supraclavicular region • Right middle and posterior mediastinum • Right spinal canal through C6-C7 and T3-T4
Extracutaneous complications	Plagiocephaly Stridor	Plagiocephaly	Stridor and respiratory distress	Plagiocephaly
Response to beta-blocker	• Reduction in size of cutaneous distribution • Resolved plagiocephaly	• Reduction in size of cutaneous distribution although surgical debulking needed • Resolved plagiocephaly	• Resolution of respiratory distress	• Reduction in size of cutaneous distribution • Resolved plagiocephaly

found an asymmetric enhancing mass in the neck and chest (Table I). MRI of the head was unremarkable except for a slightly tortuous and narrowed left internal carotid artery. An echocardiogram and ophthalmic evaluation also helped rule out PHACE syndrome. Abdominal ultrasound scan helped rule out any other visceral involvement. The patient had a mixed, segmental hemangioma diagnosed and started on a 10-month course of oral propranolol, 1.5 mg/kg/d, with rapid resolution of stridor and diminution in size of her hemangiomas. A posttreatment coronal MRI at 1 year of age is seen in Fig 3.

CASE 4

A 5-month old white girl was evaluated for multiple bright red, superficial and deep, soft papules grouped on the right temple. There was also a cluster of red macules over the posterior aspect of the neck with underlying subcutaneous fullness (Fig 4, *A* and *B*). She had mild plagiocephaly and was noted to favor turning to her left side. Neck fullness along with plagiocephaly and skin examination prompted an MRI/MRA. MRI/MRA imaging was remarkable for similarly enhancing cutaneous and extracutaneous lesions (Fig 4, *C* through *F*). She had a mixed, segmental hemangioma diagnosed, and an echocardiogram and ophthalmic evaluation helped rule out PHACE syndrome. Abdominal ultrasound scan helped rule out any other visceral involvement. The extracutaneous lesions were associated with spinal cord displacement and mild central canal stenosis, with mass effect on the proximal trachea and mediastinal structures with right upper lobe atelectasis, encasing the proximal right vertebral artery immediately distal to its origin and displacing the proximal common carotid artery (Fig 4, *E* and *F* and Table I). The cutaneous component of her hemangioma, neck range of motion, and plagiocephaly all improved within 2 weeks after starting propranolol at 1 mg/kg/d.

DISCUSSION

Infantile hemangiomas (IH) most often occur as isolated cutaneous lesions, although they can be associated with extracutaneous lesions or congenital morphologic anomalies.[1] Several unique IH

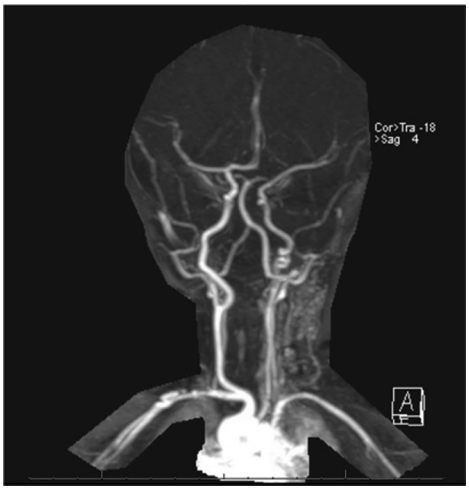

Fig 3. Coronal MRA shows the extracutaneous lesion in the left neck, extending into the left thoracic area.

patterns have been described with dramatic and distinctly distributed cutaneous lesions. PHACE and LUMBAR (Lower body hemangioma and other cutaneous defects, Urogenital anomalies, Ulceration, Myelopathy, Bony deformities, Anorectal malformations, Arterial anomalies, and Renal anomalies)/PELVIS (Perineal hemangioma, External genitalia malformations, Lipomyelomeningocele, Vesicorenal abnormalities, Imperforate anus, Skin tag) syndromes feature large segmental, superficial, and deep plaques on the face and lumbosacral areas, respectively, with associated central nervous system dysraphism and arterial anomalies.[1] Large superficial or deep segmental hemangiomas in a mandibular "beard" distribution can mark a subglottic hemangioma. Multiple hemangiomas of the skin serve as a clue to potential visceral hemangiomas.[1,2] A retrospective study of IH showed the liver, gastrointestinal tract, brain, mediastinum, and lung to be the most commonly involved organ sites.[2] Another study specifically looked at central nervous system involvement of IH. Although central nervous system involvement by IH is an unusual occurrence, early recognition on MRI can change treatment.[3]

We describe 4 patients with similarly distributed mixed, segmental hemangiomas unilaterally involving the posterior aspect of the scalp and neck and associated extensive extracutaneous hemangiomas of paratracheal and mediastinal spaces, without any visceral involvement. We have dubbed this configuration, *iceberg hemangioma* because the cutaneous component only hints at the extensive underlying hemangiomas.

IH can have both superficial and deep components. Similarly, extracutaneous hemangiomas are characteristically visceral or parenchymal, although reasons for involvement in these cellular tissue planes have never been explored. The cutaneous and extracutaneous hemangiomas in all 4 iceberg cases were all segmental IH of the face/neck with associated multifocal extracutaneous hemangiomas exclusively localized to deep connective tissue. This finding suggests a possible propensity for connective tissue rather than visceral tissue, as is seen in other hemangioma syndromes like PHACE, LUMBAR and PELVIS.

IH in an iceberg distribution is rare, but recognition is important for correct diagnosis and treatment of extracutaneous symptoms that mimic other conditions. Limited neck range of motion was a feature of cases 1, 2, and 4 and was associated with plagiocephaly, initially interpreted as a benign consequence of positioning. However, rapid and dramatic improvement on propranolol supported a pathologic association in cases 1 and 4. The paraspinal, neural foramen, and epidural involvement with spinal cord deviation seen in case 4 shows a hemangioma-associated neural risk.

The most significant risk for an infant with an iceberg hemangioma is airway compromise. Early recognition and initiation of medical management can prevent life-threatening complications. The patients in cases 1 and 3 presented to the emergency room with stridor, initially misdiagnosed as croup. Although neck radiograph is often ordered as a screening study for suspected croup, it may not be helpful in distinguishing between the symmetrical airway narrowing (steeple sign) characteristic of croup and the circumferential paratracheal involvement with airway narrowing seen with an iceberg hemangioma.[2] The patients in cases 1 and 3 required bronchoscopy to confirm the diagnosis, delaying definitive treatment. Careful evaluation for other clinical features can help distinguish iceberg IH from croup. Biphasic stridor without accompanying constitutional symptoms in infants under 3 months of age is more characteristic of airway hemangioma, whereas viral croup typically presents with low-grade fever, rhinitis, barking cough, and inspiratory stridor in slightly older patients (6 to 36 months).[4,5]

Overall, there are many different clinical scenarios that require further workup. For one, segmental and multifocal hemangiomas should be followed very closely.[6] Any segmental or multifocal hemangioma, especially ones that present with other severe symptoms such as stridor, limited neck range of motion, plagiocephaly, trouble swallowing, or gastrointestinal bleeding should be further worked up with an abdominal ultrasound scan or MRI to check for extracutaneous involvement. Additionally, clinicians should

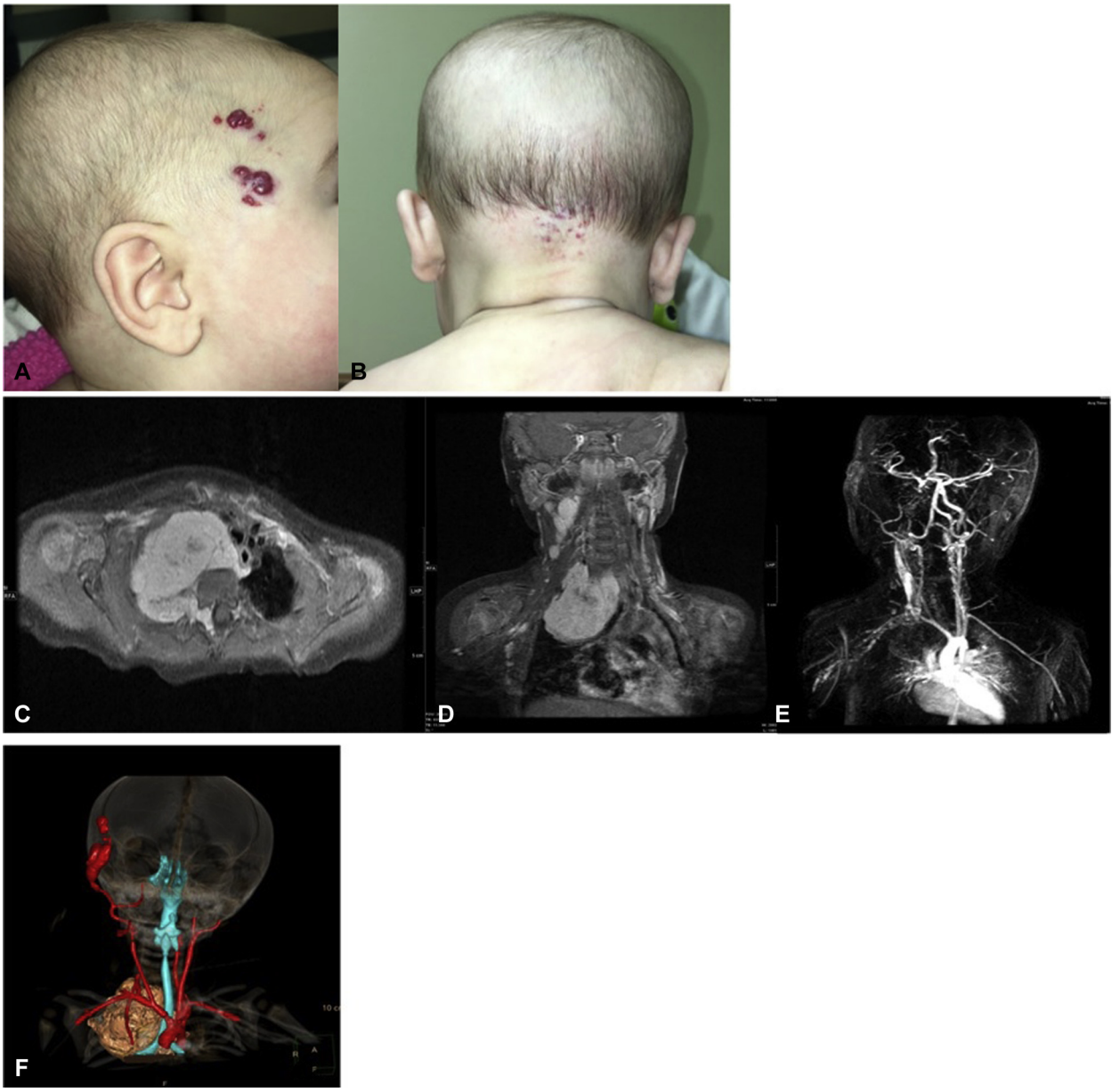

Fig 4. **A**, Multiple cherry red papules clustered on the right temple. **B**, Numerous red macules on occipital scalp scattered over an underlying fullness in posterior neck. **C**, T1 postcontrast axial image shows the lesion in the right supraclavicular region extending into the superior mediastinum displacing the thoracic content and entering into the extradural space of the spinal canal. **D**, T1 postcontrast coronal image shows similar involvement as that in **C**. **E**, MRA image of the neck shows marked narrowing of the cervical and intracranial right internal carotid artery with distal reconstitution in the supraclinoid portion. **F**, Three-dimensional image from neck CTA shows the airway narrowing, vessels, and right upper chest mass.

know that size, location, and morphologic subtype are major factors that predict complications or need for further treatment.[6] Hemangiomas that are 30.36 to 44.2 cm^2, located on face or perineal areas, and/or are of the segmental morphologic subtype have been recognized as predictors of complications and therefore require further workup.[6] Although there is no set guideline on workups for these types of hemangiomas, we suggest that imaging studies, to recognize extracutaneous involvement, such as abdominal ultrasound scan, MRI, MRA, or CTA should be used. Additionally, if there is heightened suspicion for PHACE, LUMBAR, PELVIS, or beard syndromes,

a workup for associated signs should be done. This workup could include an echocardiogram, ophthalmology evaluation, renal evaluation, physical examination, and/or ultrasound scan to look for urogenital malformations or ulcerations.

Although MRI/MRA are preferred imaging modalities to define the extent of extracutaneous involvement, radiologists vary in their expertise distinguishing IH from other lesions. The pattern of growth, clinical appearance, and imaging characteristics need to be considered as a whole. If diagnosis based on imaging is uncertain, tissue biopsy can be performed. Several case reports have documented rhabdomyosarcoma or neuroblastoma misdiagnosed as hemangioma of infancy by MRI.[7,8]

We report on 4 infants with a similar distribution IH on the occipital scalp and posterior aspect of the neck. We designated this rare subtype, *iceberg hemangioma*, to highlight the possibility of multifocal hemangiomas of the deep connective tissue associated with segmental cutaneous IH. Additionally, these cases highlight the associated risks of such iceberg hemangiomas, including life-threatening laryngotracheal involvement. Presenting clinical signs and imaging may mimic other conditions, obscuring the correct diagnosis and delaying effective systemic treatment.[9] Optimal evaluation requires a coordinated multidisciplinary effort, including pediatrics, otolaryngology, dermatology, and radiology departments.

REFERENCES

1. Chen TS, Eichenfield LF, Friedlander SF. Infantile hemangiomas: an update on pathogenesis and therapy. *Pediatrics*. 2013;131(1):99-108.
2. Metry DW, Hawrot A, Altman C, Frieden IJ. Association of solitary, segmental hemangiomas of the skin with visceral hemangiomatosis. *Arch Dermatol*. 2004;140(5):591-596.
3. Viswanathan V, Smith ER, Mulliken JB, et al. Infantile hemangiomas involving the neuraxis: clinical and imaging findings. *AJNR Am J Neuroradiol*. 2009;30(5):1005-1013.
4. Yates PD. Chapter 33. Stridor in Children. In: Lalwani AK, ed. *CURRENT Diagnosis & Treatment in Otolaryngology—Head & Neck Surgery*. 3rd ed. New York: McGraw-Hill; 2012. Available at: http://www.accessmedicine.com/content.aspx?aID=55768949. Accessed December 2, 2016.
5. Spinks J. A clue on the face. *BMJ case Rep*. 2010;2010.
6. Haggstrom AN, Drolet BA, Baselga E, et al. Prospective study of infantile hemangiomas: clinical characteristics predicting complications and treatment. *Pediatrics*. 2006; 118(3):882-887.
7. Megarbane H, Doz F, Manach Y, et al. Neonatal rhabdomyosarcoma misdiagnosed as a congenital hemangioma. *Pediatr Dermatol*. 2011;28(3):299-301.
8. Frieden IJ, Rogers M, Garzon MC. Conditions masquerading as infantile haemangioma: Part 2. *Australas J Dermatol*. 2009; 50(3):153-168; quiz 69-70.
9. Broeks IJ, Hermans DJ, Dassel AC, van der Vleuten CJ, van Beynum IM. Propranolol treatment in life-threatening airway hemangiomas: a case series and review of literature. *Int J Pediatr Otorhinolaryngol*. 2013;77(11):1791-1800.