

**CASE REPORT****OPEN ACCESS**

DOI: 10.5281/zenodo.4118744

**INFANTILE HEMANGIOMAS: A UNIQUE PRESENTATION OF PHACE(S) AND LUMBAR SYNDROME**

Ayesha Javaid, Fayeza Javaid \*, Muhammad Javaid Iqbal\*\*

Department of Ophthalmology, Khyber Teaching Hospital Peshawar-Pakistan, \*Department of Surgery, Hayatabad Medical Complex Peshawar-Pakistan, \*\*Consultant Ophthalmologist Peshawar-Pakistan

**Review Began 05/01/2021****Review Ended 10/02/2021****Published 20/02/2021**

Infantile hemangiomas are mostly benign tumors of the pediatric age group. We present the case of a 14-year-old female who consulted the Medicine out patients' department (OPD) of Hayatabad Medical Complex with the chief complaint of severe headache and blurry vision for the last 4 months. The patient had large irregular segmental hemangiomas with bony deformities. Past medical and surgical history was insignificant. Magnetic resonance imaging (MRI) showed finding consistent with cerebellar tonsillar ectopia. The presence of such symptoms helped us in diagnosing her as a case of PHACE(S) syndrome [posterior fossa anomalies (P), hemangiomas (H), arterial anomalies (A), cardiac abnormalities and coarctation of aorta (C), eye abnormalities (E), and the sternal defects (S)] with an unusual presentation of LUMBAR syndrome [Lower body hemangioma and other cutaneous defects, Urogenital anomalies, Ulceration, Myelopathy, Bony deformities, Anorectal malformations, Arterial anomalies, and Renal anomalies]. Diagnosis of such rare cases is important. Proper surgical techniques and use of better medical technology are required to make an early diagnosis. Further studies/case reports around the world would assert our findings that PHACE and LUMBAR can present together in a patient as well.

Keywords: PHACE(S) syndrome; Infantile hemangiomas; Mittendorf Dots

**Citation:** Javaid A, Javaid F, Iqbal MJ. INFANTILE HEMANGIOMAS: A UNIQUE PRESENTATION OF PHACE(S) AND LUMBAR SYNDROME. THE STETHO 2021;2(2):1-3

## INTRODUCTION

About 5-10% of the tumors among the pediatric group are benign infantile hemangiomas (IH) (1). Large and segmental IH that occupy the head and neck region when further evaluated under imaging and clinical workup often detects multiple correlated changes that are often defined in PHACE syndrome (2). The multi-organ birth defects along with the genetic mechanisms underlying the formation of IH in case of these two syndromes, i.e. PHACE (an acronym for Posterior fossa brain malformations, segmental facial Hemangiomas, Arterial anomalies, Cardiac defects, Eye anomalies, and sternal defects or supraumbilical raphe) and LUMBAR (an acronym for Lower body hemangiomas, Urogenital anomalies, Myelopathy, Bone deformities, Anorectal malformations/ Arterial anomalies, Renal anomalies) are still unclear (3). PHACE(S) syndrome is a nerve and skin disorder of unknown cause. The abbreviation highlights the common features of PHACE syndrome with cerebrovascular malformations dominating the rest of the features. The true incidence of PHACE is yet not known however females are more commonly affected as compared to males (4). LUMBAR syndrome is a rare syndrome of segmental lower-body IH with underlying structural abnormalities. The precise cause is unknown but thought to be due to field defect early in a child's development. PELVIS and SACRAL are alternative acronyms for the same associations (5). LUMBAR and PHACE syndromes have large segmental hemangiomas and cerebrovascular defects in common. (6)

## CASE REPORT

14-year-old girl, from a poor socioeconomic background presented to our department of medicine as an outpatient with complaints of headache and blurry vision for the last 4 years. These symptoms were mild in the beginning but had increased over the last two months. The headache was dull in character and was not relieved with sleep. Her vision wasn't assessed previously but she complained of blurring of vision increasing over time. Patient had no other complaints apart from this. On general physical examination, the patient had large segmental flat hemangiomas spreading irregularly over the left side of her body including the forehead on left side and the jaw which blanched on pressure. The hemangiomas were more like a reddish rash spread. Her entire upper

and lower trunk on the right side had a similar irregular spreading of the IH. There was a surgical scar on the forehead and the right upper arm which were due to surgical removal of raised bulky infantile hemangiomas in her childhood. The patient had a typical syndromic baby face with wide medial epicanthus. The redness was spread in a similar pattern over her left buttock, sacral region and her left lower limb. Gynecological examination revealed absence of clitoris with exposed urethral opening and an intact vagina and anus.



**Figure 1: L-R (ABOVE) Showing large segmental IH on back and abdomen. (BELOW) left leg large segmental IH.**

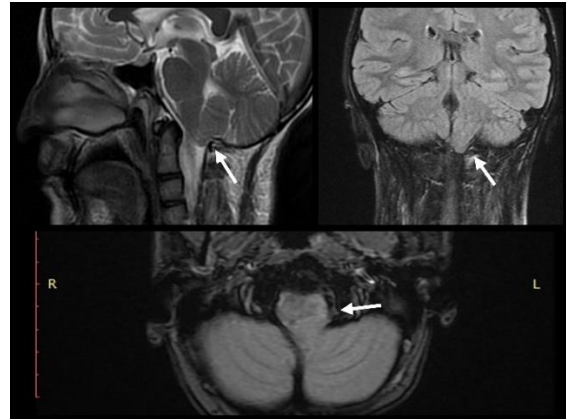


**Figure 2: (ABOVE) L-R shows left hand showing asymmetric enlargement of the middle phalange. (BELOW) L-R shows bony deformities of distal phalanges and syndactyly and hypertrophy of the soft tissues**

Hand and foot deformities were also noticed. Physical examination of upper and lower limbs displayed asymmetric enlargement of the digits and soft tissue of the middle finger of the left hand but no syndactyly. Right hand and rest of the fingers of the left hand appeared normal. Lower limb showed soft tissue hypertrophy involving the second toe in left, while 2<sup>nd</sup> and 3<sup>rd</sup> toe in right foot along with syndactyly and hypertrophy of the soft tissues more marked on the left side.

A complete ophthalmological examination was also performed. Her visual acuity was reported to be 6/6 in her right eye and 6/60 in left eye. Slit lamp examination revealed bilateral inferior fornix vascular malformation and bilateral lamellar cataracts. Fundal examination showed bilateral tilted discs with hyperemia, multiple arterial and venous tortuous dilatations and left hypoplastic optic nerve. Rest of the general, respiratory, abdominal and neurological examinations were unremarkable. After discussing it with a multidisciplinary team (MDT) meeting, a diagnostic and treatment plan was formulated. Complete baseline blood investigations as well as inflammatory markers CRP and ESR were planned, x-ray chest, spine upper and lower limbs were ordered to look for bony deformities, ultrasound of abdomen to look for any intra-abdominal hemangiomas, MRI with MRA brain to look for AV malformations, CT abdomen and echocardiography of the heart were ordered.

X-ray hands displayed irregular restricted growth of the third distal phalanx of right hand while overgrowth of the third distal phalanx of the left hand with fusion of the fifth proximal middle and distal phalanx. X-ray feet also showed multiple irregular shaped growth of all the phalanges of lower limbs bilaterally. MRA brain was normal with no aneurysm or stenosis, whereas MRI scan of the brain revealed slight caudal descent of left cerebellar tonsil through the foramen magnum (about 5mm) suggesting cerebellar tonsillar ectopia. There was evidence of few dilated tortuous vessels in the left orbit in retroorbital region and also in scalp near the vertex extending into the adjacent diploic space likely to be angiomatic malformations. Rest of the investigations were normal.



**Figure 3: MRI Brain shows left cerebellar ectopia**

Treatment was planned involving physicians, ophthalmologists and pediatricians and a unanimous decision of providing the patient with paracetamol for headache relief was the best decision as no cerebrovascular abnormalities were detected. For the defective vision the ophthalmology department explained the prognosis to the patient and decided to make no surgical intervention as the chances of visual improvement were negligible. After discharge the patient was asked to come for her follow-up after two months.

## **DISCUSSION**

The IH's presenting in PHACE syndrome tend to be segmental and large (>5cm in dimensions). Segmental haemangiomas are those that affect one or more regions and do not rise from the base level focal point. telangiectasias, solitary lesions, confluent plaques, small papules are different ways these IHs can present, as in our case, the patient presented with large (10-15cm in diameter) irregular segmental flat patches. (7) The facial IH presentation was classified into 4 parts that are not based on dermatomal distribution or Blaschko lines but on the basis of development of the face such as frontonasal, frontotemporal, maxillary, and mandibular. The frontotemporal and frontonasal IH segments bear a higher risk of ocular and brain involvement, as in our case, whereas those on the mandibular region are at a greater risk of developing midline complications and cardiovascular abnormalities (8). Our patient had a large segmental frontotemporal haemangioma on her left side of the face with left mild cerebellar ectopia. Ocular involvement showed left optic disc hypoplasia with bilateral cataracts and AV malformations in the

anterior chamber, few dilated tortuous vessels in the left orbit in retroorbital region and also in the scalp. The face is the most commonly affected site, but lesions can develop on the scalp and postauricular and cervical regions. Large and segmental IHs on the upper thoracic trunk, and proximal limb regions have also been described in PHACE syndrome (9). Our patient had large irregular flat haemangiomas in the upper thoracic trunk and lower back on the left side with left upper limb involved.

In 30% to 80% of patients with PHACE syndrome structural brain changes have been recorded. In unilateral IH, the cutaneous IH and vascular changes tend to be on the same side of the lesion, as in our case, all the lesions were on the left side with left sided cerebellar ectopia. In most cases, the cerebral lesions never progress or complicate and remain constant, but the associated signs and indications of seizures, neuropsychomotor developmental delay and headaches if existing, should be monitored. Our patient suffered no complications due to cerebellar ectopia apart from frequent headaches which were treated with a simple analgesic. In such patients where Pituitary structural abnormalities like vision problems or symptoms that are suggestive of endocrine diseases exist, they should be examined and a proper follow up should be planned (10). The posterior fossa abnormalities range from focal regions of cerebellar dysplasia or ectopia to various cystic malformations including the Dandy-Walker complex.

Headaches in such patients are more frequent and intense and begin at an unusually early age as in our case. Posterior fossa anomalies in patients with PHACE have an overall frequency by published report from 30.4% to 81% (11). The main presenting complaint of our patient was getting frequent headaches and upon further evaluation and assessment there was no evidence of cerebral ischemia or vasculopathy involving the brain. Neurological referral for different age groups should be considered for patients complaining of severe headaches, headaches that do not resolve with simple analgesics, headaches that can functionally disable them or headaches with suspected secondary causes. However, the involvement of arterial abnormalities in PHACE is a relative contraindication for vasoconstrictive headache medication including triptans, dihydroergotamine, and ergotamine tartrate (12). Our patient's headache responded very well to oral analgesics and so the medication was continued till follow up to see how she was doing.

Eye involvement is present in approximately one-third of the PHACE(S) syndrome patients. The reported ocular manifestations of this syndrome could be classified into posterior segment abnormalities (morning glory disk anomaly, persistent foetal vasculature, peripapillary staphyloma, retinal vascular anomalies, optic nerve hypoplasia and atrophy, choroidal haemangioma, retinal coloboma) and anterior segment abnormalities (cataract, conjunctival haemangioma, microphthalmia posterior embryotoxon, Mittendorf dots corneal opacity) (13). Our case had both posterior segment as well as anterior segment involvement (bilateral inferior fornix vascular malformation and bilateral lamellar cataracts with bilateral tilted discs, hyperaemia, multiple arterial and venous tortuous dilatations and left hypoplastic optic nerve).

There are many similarities between LUMBAR and PHACE, like presence of large and flat segmental IH (often of minimal-growth morphology), predominance of female, regional cutaneous IH and underlying anomalies of that region. LUMBAR might thus be considered similar to PHACE, but presenting in the lower half of the body. Like PHACE, it appears rare for patients with LUMBAR to manifest the complete spectrum of the syndrome. The incidence of LUMBAR is very low and the data available to understand the entire presentation is also deficient as most cases are not properly evaluated for each potential category of anomalies or sometimes the awareness related to PHACE syndrome makes LUMBAR syndrome reporting significantly low. we suspected our patient had PHACE(S) as well as LUMBAR syndrome. The findings that supported LUMBAR syndrome were large segmental haemangiomas of lower half of the body, bony deformities in limbs and urogenital abnormality. IHs associated with LUMBAR are also most commonly, segmental and in addition are often MG (minimal growth) in morphology. Studies suggest that MG IH showed a strong tendency localize to the lower half of the body compared with the upper half (14). But our case had both upper and lower left side of the body involved. In a study conducted on LUMBAR syndrome the Urogenital abnormalities like Bladder (exstrophy, elongated, problems), Ureters (reflux, pyelo-ureteral duplication) Clitoris (clitoromegaly, hemi clitoris or absent clitoris) were recorded in about 20- 40%. Ambiguous genitalia with Ulceration were present in about 71% cases. Our patient had no bladder or ureteric problems but she had absent labia minora on gynaecological examination.

The affected limbs of patients with LUMBAR syndrome were described as shorter and atrophic in comparison with the unaffected limb. Grossly abnormal limb development, with an unusual “pterygium-like” structure fusing the foot to hip were noted in some cases. Although previously it has been suggested that extremity IHS do not affect development of the limbs, the findings of LUMBAR suggests otherwise, that atrophy or hyperplasia that occur might be closely related to underlying arterial anomalies of the affected limb. This feature may also help distinguish LUMBAR from other vascular syndromes that affect the limbs. Similar to our case, Bony deformities such as Foot deformity with abnormal fusion of bones, Leg discrepancy in length or diameter, Hip bone hyperplasia or dysplasia and Sacral abnormalities are present in 8-17% of the cases having LUMBAR syndrome (15). Our patient had significant hypertrophy of the affected limb with bony deformities involving both lower limbs (syndactyly and atrophic phalanges).

## CONCLUSION

Since PHACE(S) and LUMBAR syndrome are rare disorders, it is difficult to come up with appropriate timely diagnosis when the patient presents. Although quality of life of such patients is significantly improved with symptomatic and specific treatment, both medical and surgical. Awareness amongst ophthalmologists, physicians, neurologists, paediatrician and cardiovascular surgeons should be raised regarding this syndrome in order to ensure prompt treatment and early management. Furthermore, patient education is also necessary regarding the disease and regular follow ups should be advised to see the pattern of the syndrome changing with age. Parents should be counselled regarding prognosis of the syndrome once diagnosed. Psychotherapy should be provided to such children because of the social embarrassment faced due to the haemangiomas. A multidisciplinary approach should be taken involving a team for the best care of such rare cases. More case reporting and studies would ensure the best management and good outcomes of such patients.

## REFERENCES

1. Kilcline C, Frieden IJ. Infantile hemangiomas: How common are they? A systematic review of the medical literature. *Vol.*

- 25, *Pediatric Dermatology. Pediatr Dermatol*; 2008. p. 168–73.
2. Hess CP, Fullerton HJ, Metry DW, Drolet BA, Siegel DH, Auguste KI, et al. Cervical and intracranial arterial anomalies in 70 patients with PHACE syndrome. *Am J Neuroradiol*. 2010 Nov;31(10):1980–6.
3. Siegel DH. PHACE syndrome: Infantile hemangiomas associated with multiple congenital anomalies: Clues to the cause. *Vol. 178, American Journal of Medical Genetics, Part C: Seminars in Medical Genetics. Blackwell Publishing Inc.*; 2018. p. 407–13.
4. Heyer GL. PHACE(S) syndrome. In: *Handbook of Clinical Neurology. Elsevier B.V.*; 2015. p. 169–83.
5. Drolet BA, Chamlin SL, Garzon MC, Adams D, Baselga E, Haggstrom AN, et al. Prospective study of spinal anomalies in children with infantile hemangiomas of the lumbosacral skin. *J Pediatr*. 2010 Nov 1;157(5):789–94.
6. Iacobas I, Burrows PE, Frieden IJ, Liang MG, Mulliken JB, Mancini AJ, et al. LUMBAR: Association between cutaneous infantile hemangiomas of the lower body and regional congenital anomalies. *J Pediatr*. 2010 Nov 1;157(5):795–801.e7.
7. Metry DW. Potential complications of segmental hemangiomas of infancy [Internet]. *Vol. 23, Seminars in Cutaneous Medicine and Surgery. Semin Cutan Med Surg*; 2004 [cited 2020 Jul 17]. p. 107–15. Available from: <https://pubmed.ncbi.nlm.nih.gov/15295920/>
8. Haggstrom AN, Lammer EJ, Schneider RA, Marcucio R, Frieden IJ. Patterns of infantile hemangiomas: New clues to hemangioma pathogenesis and embryonic facial development. *Pediatrics [Internet]*. 2006 Mar [cited 2020 Jul 17];117(3):698–703
9. Nabatian AS, Milgraum SS, Hess CP, Mancini AJ, Krol A, Frieden IJ. PHACE without Face? Infantile hemangiomas of the upper body region with minimal or absent facial hemangiomas and associated structural malformations. *Pediatr Dermatol [Internet]*. 2011 May [cited 2020 Jul 17];28(3):235–41.
10. Melnick LE, Yan AC, Licht DJ, Treat JR, Castelo-Soccio L. PHACE syndrome: A retrospective review of 23 patients. *Pediatr Dermatol [Internet]*. 2014 [cited 2020 Jul 17];31(3):390–2.
11. Garzon MC, Epstein LG, Heyer GL, Frommelt PC, Orbach DB, Baylis AL, et al. PHACE Syndrome: Consensus-Derived Diagnosis and Care Recommendations. *J Pediatr*. 2016 Nov 1;178:24–33.e2.
12. Yu J, Siegel DH, Drolet BA, Blei F, Epstein LG, Metry D, et al. Prevalence and Clinical Characteristics of Headaches in PHACE Syndrome. *J Child Neurol [Internet]*. 2016 Mar 1 [cited 2020 Jul 17];31(4):468–73.
13. Kronenberg A, Blei F, Ceisler E, Steele M, Furlan L, Kodsi S. Ocular and systemic manifestations of PHACES (Posterior fossa malformations, Hemangiomas, Arterial anomalies, Cardiac defects and coarctation of the aorta, Eye abnormalities, and Sternal abnormalities or ventral developmental defects) syndrome. *J AAPOS [Internet]*. 2005;9(2):169–73.
14. minimal or arrested growth: A retrospective case series. *Arch Dermatol [Internet]*. 2010 [cited 2020 Jul 17];146(9):971–6.
15. Martines F, Immordino V. Arteriovenous malformation of the base of tongue in pregnancy: case report. *Acta Otorhinolaryngol Ital*. 2009;29(5):274–8

## Address for Correspondence:

Ayesha Javaid, Department of Ophthalmology, Khyber Teaching Hospital Peshawar-Pakistan

Cell: +92-331-9303711

Email: ayesh.javaid@gmail.com