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Case Series

The effectiveness of oral propranolol for infantile hemangioma on the head and neck region: A case series

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ABSTRACT

Introduction: Infantile hemangioma is the most common tumor in infancy, with 60% occurring on the face and neck. A large tumor involving the facial region will cause significant aesthetic and functional impairment and isn't always easy to treat surgically. A non-invasive treatment is needed for this condition. Propranolol has recently been used as a choice of treatment in infantile hemangioma.

Presentation of case: We presented two cases of large problematic infantile hemangioma that were successfully managed with oral propranolol.

Discussion: Large problematic lesions that ulcerate and bleed often need surgery; however, a substantial defect resulting from surgery is tricky to reconstruct and can cause significant scar. Propranolol is used because of its efficacy and low risk characteristics.

Conclusion: Propranolol is an effective treatment to reduce the need of surgical intervention in problematic hemangioma.

1. Introduction

Hemangiomas are the most common tumor in infancy, presenting the majority of proliferating vascular tumors [1]. Infantile hemangioma (IH) is a benign endothelial tumor with unique characteristics, with 60% occurring on the head and neck region. It grows rapidly, slowly regresses, and never recurs. Infantile hemangioma (IH) is a benign endothelial tumor with unique characteristics, with 60% occurring on the head and neck region. It grows rapidly, slowly regresses, and never recurs. Infantile hemangiomas usually grow faster during the first 9 months of age (proliferating phase). After 12 months, the tumor begins to regress (involuting phase) and involution ceases in most children by 4 years (involuted phase) [2]. When the patients reach involuted phase, one-half of children will have residual telangiectasias, scarring, fibrofatty residuum, redundant skin, or destroyed anatomical structures [3]. This can cause significant aesthetic and functional impairment and low self-esteem when the infant grows older. Tumors located on the face will be challenging to solve because of the possibility of functional problems and poor cosmetic outcomes.

Propranolol has recently been proven to be another choice to treat infantile hemangioma [4]. Propranolol dose to treat hemangioma is 0.25 mg/kg/day as the initial dose, and increased gradually until the target dose of 2 mg/kg/day [5]. Infants receiving propranolol are monitored for potential drug toxicity. Although being the last resort, surgery is still indicated in problematic hemangioma located on the craniofacial region, those causing airway obstruction or functional problem, and ulcerative masses. This case series reports cases of large craniofacial infantile hemangioma treated with propranolol. Our cases include problematic hemangiomas, which often require surgery. Patients were recruited in one year period and treated in an academic teaching hospital. All parents gave consent to publish their children's medical information and images in writing this paper. This work has been reported in line with the SCARE criteria [6] and PROCESS Guidelines 2020 [7]. This work is registered in Research Registry with the unique identifying number: researchregistry6863 [8].

2. Presentation of cases

2.1. Case 1

A 3-month-old male came with the presence of mass on the right palpebral region that appeared 2 weeks after birth. At first, the mass was

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a small ecchymotic area, but enlarged rapidly, causing difficulty in opening his right eye. (Fig. 1) Initially, he went to the ophthalmologist and was given an ointment, however the mass still progressed. Patient then was referred to our center, which is a national referral hospital. The mass is located on the right palpebral region, 4×3×0,5 cm, well-defined, bluish in color, no color change upon palpation, absence of pain. He was given propranolol at 0.25 mg/kg/day and increased to 2 mg/kg/day. Frequent blood pressure, heart rate, and respiratory examinations were also performed to the check patient's tolerance. A dramatic effect was found with marked reduction after 2 months (Fig. 2) and even better after 6 months (Fig. 3). At 1 year of age, tumor size is stable and with no functional disturbance to open and close his eyes. (Fig. 4).

2.2. Case 2

A 4-month-old female presented with rapidly growing mass on the left cheek appearing 3 weeks after birth. Not only she had difficulties in opening her eyes. The mass also ulcerates and bleeds easily. Initially, she was brought to a dermatologist but was given no specific treatment for the mass. The mass reached 8×7×2 cm in size with multiple ulceration at the surface. (Fig. 5) She was started with oral propranolol until the target dose is reached at 2 mg/kg/day. We administered gentamycin eye ointment to protect her eyes. At 3 months after therapy, both the color and ulceration show improvements. (Fig. 6) We continued the treatment until the patient is 2 years old, which resulted in satisfactory result. (Fig. 7).

3. Discussion

The typical presentation of infantile hemangioma is a solid vascularized mass with cutaneous lesions that may present as red patches at any part of the body and usually appear after two weeks of age [9]. The diagnosis of IH is based on clinical presentation and rarely needs imaging. The tumor rapidly grows until the patient is 9–12 months old, termed the proliferating phase, and usually regresses after 3.5 years of age during the involuting phase [10]. Intervention on IH depends on the size, location, age of lesion or patient, and potential sequelae of the lesion [11]. Most IH doesn't require any treatment as it can regress on its own. However, high-risk lesions, such as those occurring on the face with >5 cm of diameter, located on the central face area, and bulky face lesion, can cause functional compromise, ulceration, and risk of permanent disfigurement [12]. Treatment of IH includes medication, interventional therapy, and, very rarely, surgical therapy. Corticosteroids were previously used as a first-line treatment since the 1960s, with prednisolone being the most common drug, given at 2-3 mg/kg/day [12]. It is used primarily during the proliferative phase of IH. However, some research found that prednisolone is less effective than propranolol and is associated with significantly more adverse events [13,14]. Other medications used include imiquimod, vincristine, bleomycin A5, and interferon-a; however, they are abandoned due to serious side effects [15].

Beta-blockers are emerging medications used to treat IH because of their efficacy and low-risk characteristics. It was first introduced by Labrèze et al [16] in 2008, and its therapeutic effect may be due to vasoconstriction, decreased expression of VEGF and bFGF genes from down regulation of the RAF-mitogen-activated protein kinase pathway [17], and from apoptosis of capillary endothelial cell [18].

One of the most commonly used beta-blockers is propranolol. Propranolol is given orally with starting dose of 0.25 mg/kg/day and can be increased up to 2 mg/kg/day with divided doses. Previously, beta-blocker's safety profile is unknown for the treatment of hemangioma, with known side effects of transient bradycardia, sleep disorders, somnolence, irritability, bronchiolitis, hypotension, bronchospasm, and hypoglycemia [5]. The occurrence of hypoglycemia can be prevented by feeding and giving the drug at the same time. In our center, patients are closely monitored in the outpatient setting when first administered with propranolol, started with the minimum dose, and titrated until 2 mg/kg/day.

Several articles in the literature report the use of propranolol in the management of IH [19–23]. Szychta et al [19] did a prospective cohort study, including patients with rapidly growing hemangioma, lesion with functional or significant cosmetic deformity, and lesion likely to affect physiological functions. The result shows promising outcomes: overall aesthetic improvement and decrease of tumor volume. The duration of propranolol treatment should be prolonged in cases of large or compound hemangiomas for an additional six months after the final desired effect to prevent rebound growth. Evaluation of IH after propranolol can be done with periodic photographs and ultrasound examinations [22]. Photographs can enable direct visualization of volume change, while ultrasound examinations can provide the quantitative data.

Most of the patients in our center usually come when the mass is already large in size. If left untreated, there is a risk of disfigurement. Lesions with ulceration and those that easily bleed are some of the indications of surgical therapy. Surgery is the last resort in IH; however, early surgery might be needed in the airway and visual obstruction. Surgery can cause morbidity because it will leave a large defect and is challenging to reconstruct. A flap or a graft might be needed to cover the large defect, posing a risk of a scar on the donor area. Surgery is only considered in life-threatening lesions, fibrofatty residue, deformed areas, and persistent scars after the involution phase and when the mass is unresponsive to medical therapy [24]. Meanwhile, an increase in dosage beyond the recommended dose doesn't reduce the need for surgery [25].

Beta-blocker as pharmacological therapy is recommended during the proliferative phase to limit the growth of the hemangioma, with optimism that surgery will not be needed. Both our patients in our center exhibit satisfactory results with oral propranolol. No side effects were recorded during the administration of the drug. Therapy should be continued minimally until the patient reaches the age of 7 to 8 months and until 12 months of age. The nature of the lesion of our second patient indicates the need for surgery. However, surgery poses a risk of significant deformity, bleeding, and iatrogenic injury, especially if done during the proliferating phase [26]. For a resection to be made, the plastic surgeon must be confident that the resulting scar will be better than the defect left after the tumor regress [2]. Administration of propranolol has helped to reduce the mass size significantly, although fibrofatty tissue remains. Surgery during the proliferative phase is only considered if there is a failure of pharmacotherapy or when surgery is indicated in the future with the same risk of a scar [26].

4. Conclusion

Propranolol provides satisfactory result to treat infantile hemangioma. Propranolol reduces the need of surgery in problematic hemangioma if given early in proliferating phase.

CRediT authorship contribution statement

PK: Conceptualization, data collection, writing-original draft
NTP: Conceptualization, data collection, writing-original draft
VJ: Visualization, writing-review and editing
CLS: Writing-original draft, funding acquisition

Declaration of competing interest

There is nothing to disclose. There is no conflict of interest among authors.

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Ethical approval

Not applicable.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

PK and NTP collected the data. PK, NTP, VJM and CLS wrote this paper. All authors read and approved the final manuscript.

Registration of research studies

This work is registered in Research Registry, with UIN: researchregistry6863 and URL: https://www.researchregistry.com/browse-the-registry#home/registrationdetails/60afbef80b117e001eedd365

Availability of data and material

Not applicable.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Appendix A

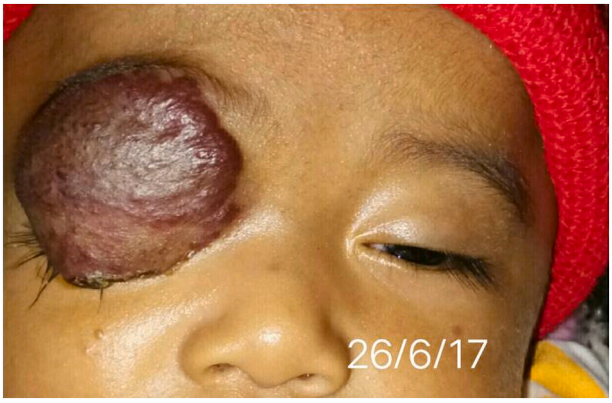

Fig. 1.

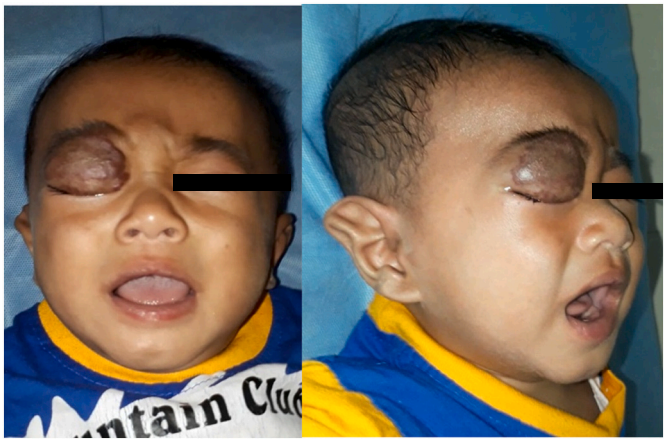

Fig. 2.

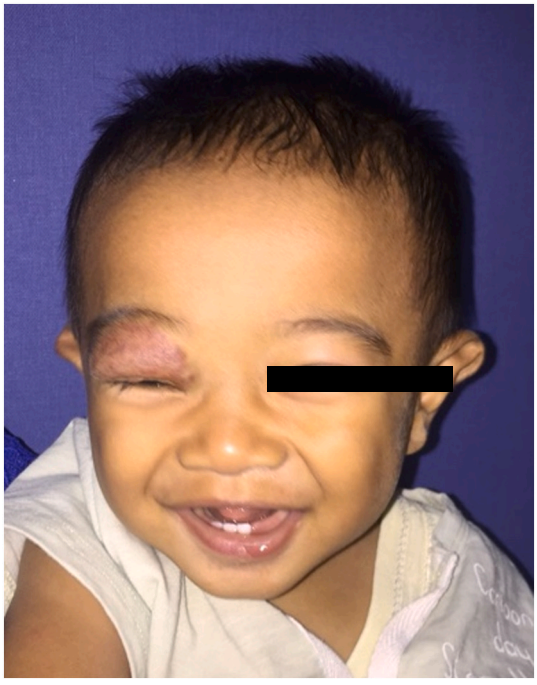

Fig. 3.

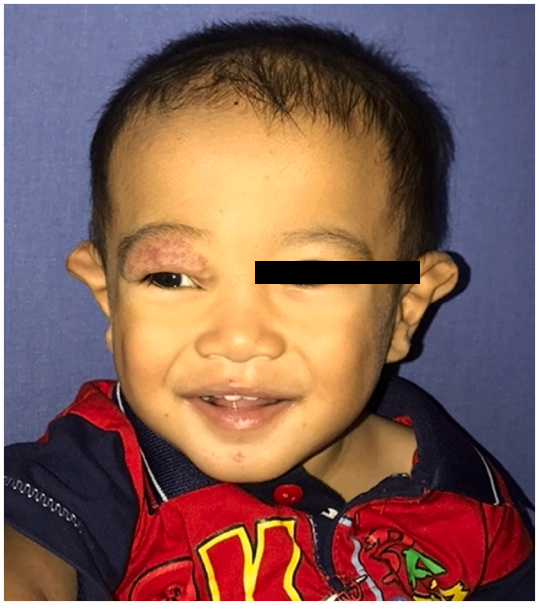

Fig. 4.

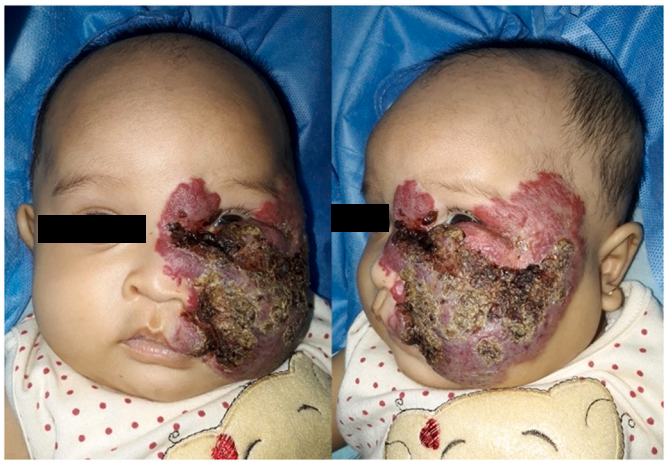

Fig. 5.

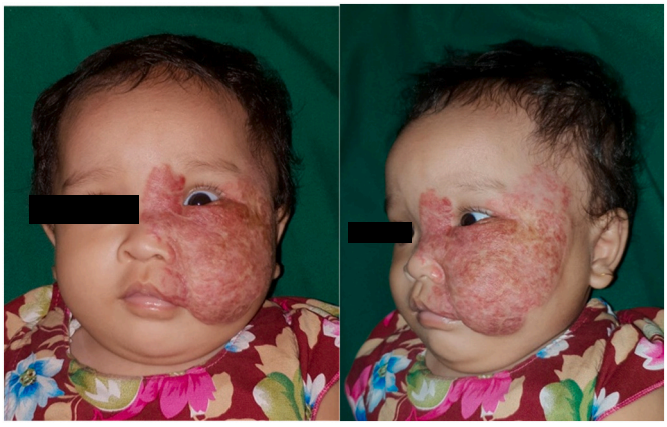

Fig. 6.

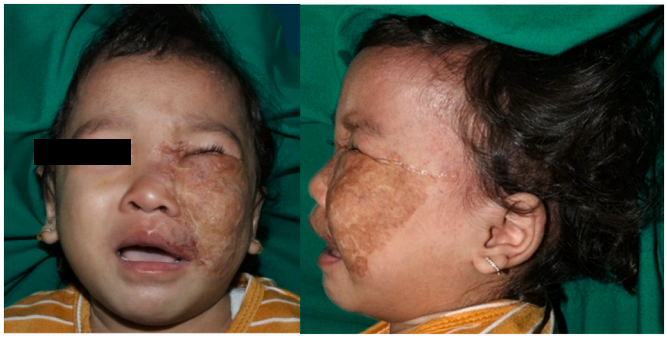

Fig. 7.

References

[1] C. Léauté-Labrèze, J.I. Harper, P.H. Hoeger, Infantile haemangioma, Lancet 390 (10089) (2017) 85–94, https://doi.org/10.1016/S0140-6736(16)00645-0.

[2] E.D. Rodriguez, J.E. Losee, P.C. Neligan, Plastic Surgery E-Book vol. 3, Head and Neck Surgery and Pediatric Plastic Surgery. Elsevier Health Sciences, Craniofacial, 2017. https://books.google.co.id/books?id=gR0xDwAAQBAJ.

[3] S. Yuzuriha, F. Nagai, M. Noguchi, How to manage disfiguring scars in involuted infantile hemangioma, Adv Wound Care 8 (6) (2019) 221–229, https://doi.org/10.1089/wound.2018.0847.

[4] B.A. Drolet, P.C. Frommelt, S.L. Chamlin, et al., Initiation and use of propranolol for infantile hemangioma: report of a consensus conference, Pediatrics 131 (1) (2013) 128–140, https://doi.org/10.1542/peds.2012-1691.

[5] S.T. Tan, T. Itinteang, P. Leadbitter, Low-dose propranolol for infantile haemangioma, J Plast Reconstr Aesthet Surg 64 (3) (2011) 292–299, https://doi.org/10.1016/j.bjps.2010.06.010.

[6] R.A. Agha, M.R. Borrelli, R. Farwana, et al., The SCARE 2018 statement: updating consensus surgical CAse REport (SCARE) guidelines, Int J Surg 60 (2018) 132–136, https://doi.org/10.1016/j.ijsu.2018.10.028.

[7] R.A. Agha, C. Sohrabi, G. Mathew, et al., The PROCESS 2020 guideline: updating consensus preferred reporting of CasE series in surgery (PROCESS) guidelines, Int J Surg 84 (2020) 231–235, https://doi.org/10.1016/j.ijsu.2020.11.005.

[8] Research Registry, Research registry, Published May (2021) 27. https://www.researchregistry.com/browse-the-registry#home/registrationdetails/60afbef80b117e001eedd365/.

[9] M. Wildgruber, M. Sadick, R. Müller-Wille, W.A. Wohlgemuth, Vascular tumors in infants and adolescents, Insights Imaging 10 (2019) 30, https://doi.org/10.1186/s13244-019-0718-6.

[10] R.A. Couto, R.A. Maclellan, D. Zurakowski, A.K. Greene, Infantile hemangioma: clinical assessment of the involuting phase and implications for management, Plast Reconstr Surg 130 (3) (2012). https://journals.lww.com/plasreconsurg/Fulltext/2012/09000/Infantile_Hemangioma__Clinical_Assessment_of_the.22.aspx.

[11] A.B. Callahan, M.K. Yoon, Infantile hemangiomas: a review, Saudi J Ophthalmol 26 (3) (2012) 283–291, https://doi.org/10.1016/j.sjopt.2012.05.004.
[12] M. Luu, I. Frieden, Haemangioma: clinical course, complications and management, Br J Dermatol 169 (1) (2013) 20–30.
[13] M.A. Malik, P. Menon, Rao KLN, R. Samujh, Effect of propranolol vs prednisolone vs propranolol with prednisolone in the management of infantile hemangioma: a randomized controlled study, J Pediatr Surg 48 (12) (2013) 2453–2459, https://doi.org/10.1016/j.jpedsurg.2013.08.020.
[14] K. Sawa, A. Yazdani, M.J. Rieder, G. Filler, Propranolol therapy for infantile hemangioma is less toxic but longer in duration than corticosteroid therapy, Plast Surg Oakv Ont 22 (4) (2014) 233–236, https://doi.org/10.4172/plastic-surgery.1000892.
[15] K.R. Satterfield, C.B. Chambers, Current treatment and management of infantile hemangiomas, Surv Ophthalmol 64 (5) (2019) 608–618, https://doi.org/10.1016/j.survophthal.2019.02.005.
[16] C. Léauté-Labrèze, E.D. de la Roque, T. Hubiche, F. Boralevi, J.-B. Thambo, A. Taïeb, Propranolol for severe hemangiomas of infancy, N Engl J Med 358 (24) (2008) 2649–2651, https://doi.org/10.1056/NEJMc0708819.
[17] G. d'Angelo, H. Lee, R.I. Weiner, cAMP-dependent protein kinase inhibits the mitogenic action of vascular endothelial growth factor and fibroblast growth factor in capillary endothelial cells by blocking Raf activation, J Cell Biochem 67 (3) (1997) 353–366.
[18] Smith SKS, D.M. Smith, Beta blockade induces apoptosis in cultured capillary endothelial cells, Vitro Cell Dev Biol-Anim 38 (5) (2002) 298–304.
[19] P. Szychta, K. Stewart, W. Anderson, Treatment of infantile hemangiomas with propranolol: clinical guidelines, Plast Reconstr Surg 133 (4) (2014) 852–862.
[20] Z.M. MacIsaac, H.S. Nayar, R. Gehris, D. Mehta, S. Geisler, L.J. Grunwaldt, Treatment for infantile hemangiomas: selection criteria, safety, and outcomes using oral propranolol during the early phase of propranolol use for hemangiomas, J Craniofac Surg 27 (1) (2016). https://journals.lww.com/jcraniofacialsurgery/Fulltext/2016/01000/Treatment_for_Infantile_Hemangiomas__Selection.40.aspx.
[21] W. Ren, S. Li, L. Gao, et al., Low-dose propranolol for infantile hemangioma of the head and neck: analysis of 23 consecutive patients, Pediatr Int 59 (2) (2017) 213–217, https://doi.org/10.1111/ped.13109.
[22] L. Zhang, W.-E. Yuan, J.-W. Zheng, Pharmacological therapies for infantile hemangiomas: a clinical study in 853 consecutive patients using a standard treatment algorithm, Sci Rep 6 (1) (2016), 21670, https://doi.org/10.1038/srep21670.
[23] J. Kim, J.W. Hong, T.S. Roh, W.J. Lee, Oral propranolol therapy in 23 infants with infantile hemangioma, Arch Plast Surg 45 (6) (2018) 517.
[24] N. Harter, A.J. Mancini, Diagnosis and Management of Infantile Hemangiomas in the neonate, Curr Adv Neonatal Care 66 (2) (2019) 437–459, https://doi.org/10.1016/j.pcl.2018.12.011.
[25] S.F. Polites, M. Watanabe, T. Crafton, et al., Surgical resection of infantile hemangiomas following medical treatment with propranolol versus corticosteroids, J Pediatr Surg 54 (4) (2019) 740–743, https://doi.org/10.1016/j.jpedsurg.2018.08.001.
[26] A.K. Greene, J.K. Mulliken, Vascular anomalies, in: Plastic Surgery, 4th ed., Elsevier, 2017, p. 832.