Drug Repurposing Beta-blocker: A Safe and Effective Treatment for High Risk Ulcerated Intergluteal Infantile Hemangioma – A Case Report*

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Abstract

Infantile hemangiomas are known to be the most common tumors of childhood. These vascular tumors have a distinctive clinical course characterized by a proliferation phase (early and late), followed by a plateau phase and lastly the involution phase. Despite the ability to involute, certain complications, ulcerations being the most common, indicate prompt treatment. Early intervention during the proliferative phase with oral propranolol has been emphasized to achieve an optimum outcome. In this case, a 7-month-old infant presented with a 4.4cm by 3.2cm infantile hemangioma (IH) with ulceration on the left intergluteal area during the late proliferative phase. Prior to propranolol treatment, routine laboratory work-up, 21-lead electrocardiogram and ultrasound of the kidneys, ureter and bladder were done, revealing unremarkable results. The patient was referred to a Pediatric Cardiologist and assessment deemed no contraindications for beta-blocker treatment. That patient was placed on a 12-hour day admission for the initiation of oral propranolol at a starting dose of 1.0mg/kg/dose and was later discharged, stable, at 1.5mg/kg/dose. Escalation of doses were done by 0.5 every 2 weeks under close supervision on subsequent follow-ups via telemedicine. Four months following the initiation of propranolol treatment regression of the size of the lesion with residual fibrosis were observed. Oral propranolol appears to be an effective and safe therapeutic approach for ulcerated infantile hemangiomas, even during the late proliferative phase. Results achieved significant contraction and resolution of the ulceration and rapid involution of the lesion.

Keywords: Hemangioma, Ulcerated, Propranolol

INTRODUCTION

Infantile hemangiomas are known to be the most common vascular tumors of childhood. A majority of these cases are not visible at birth but start to appear at 2-3 weeks of life. Infantile hemangiomas have a distinctive clinical course characterized by a proliferation phase, followed by a plateau phase and lastly the involution phase.[1] However, despite the ability of these vascular tumors to spontaneously involute, several infantile hemangiomas can develop complications, with ulceration being the most common. Ulcerations usually occur during the proliferative phase and are usually present in sites such as the perioral, perianal and intertriginous areas where there is moisture and friction. These complications may be associated with pain, bleeding, infection and

Disclosures: *The author has formally acknowledged and signed a disclosure affirming the absence of any financial or other relationships (including personal connections), intellectual biases, political or religious affiliations, and institutional ties that could potentially result in a conflict of interest.*

***2nd Place, 30th Philippine Medical Association Residents' Research Case Report Presentation, May 18, 2024**

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scarring, hence early diagnosis and prompt treatment are essential to achieve a good clinical outcome.[2,3]

Amongst various treatment modalities that could be given for infantile hemangiomas, oral propranolol has been considered as the current standard of care. Conventionally, literatures state that an early initiation of these non-selective beta blockers is paramount to obtain the best outcome, mainly before 3 months of age.[4,5]

We report a case of a 7-month-old infant from the Philippines diagnosed with Infantile Hemangioma during the late proliferation phase. The patient was treated with oral propranolol which provided marked improvement.

CASE REPORT

This is a case of a 7-month-old female infant, born at term, presenting with a superficial infantile hemangioma over the left intergluteal cleft during the global COVID-19 Pandemic. The lesion appeared 2 weeks after birth starting as a solitary erythematous patch that has slowly progressed in thickness and size which later developed a central ulceration. On physical examination there was a solitary, bright red plaque (4.4cm by 3.2cm) with a central ulceration (3.5cm by 3.1cm), with erythema and telangiectasias at the surrounding border at the left intergluteal cleft (Figure 1.). Patient appeared irritable and showed extreme discomfort that was aggravated upon urination and defecation. Prenatal history and family history were noncontributory.

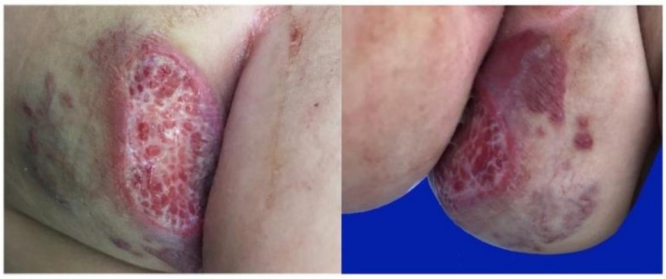

Figure 1. Solitary, bright red plaque (4.4cm by 3.2cm) with a central ulceration (3.5cm by 3.1cm), with erythema and telangiectasias at surrounding border at the left intergluteal cleft.

Prior to the commencement of oral propranolol treatment, routine laboratory work-up (complete blood count, blood chemistry, kidney and liver profile) were done, revealing no signs of bacterial infection and organ involvement. Infantile hemangiomas located in the perineal or lumbosacral regions can be at risk for LUMBAR syndrome, which includes an associated collection of disorders including bony deformities and renal anomalies, ergo, ancillary imagings (radiographic imaging of the sacrum and coccyx and ultrasound of the kidneys, ureter and bladder) were requested and proved to be unremarkable. Lastly, a 21-lead electrocardiogram was carried out showing sinus tachycardia and was referred to a Pediatric Cardiologist for further evaluation and clearance preceding therapy. Final assessment showed no contraindications for beta-blocker treatment hence the patient was scheduled for a 12-hour day admission at the outpatient department for close-supervision upon oral propranolol administration, with a starting dose of 1.0mg/kg/dose. Vital signs during the period of the admission were normal and was discharged at 1.5mg/kg/dose of Propranolol. Due to the current surge of the Covid-19 cases in the hospital, the mother was advised to continue the Propranolol treatment at home and have regular follow-up visits done via telemedicine using Facebook Messenger every 2 weeks. The parent was properly instructed on the clinical cues of adverse events, such as decrease in activity, wheezing or hypotension and was instructed to immediately contact us should any arise. This new protocol would allow a decrease in the number of OPD visits hence minimizing exposure to Covid-19. Escalation of oral propranolol dose was done by 0.5 every 2 weeks.

Four months following the initiation of propranolol treatment and through continued follow-up visits, regression of the size of the lesion with residual fibrosis were observed (Figure 2).

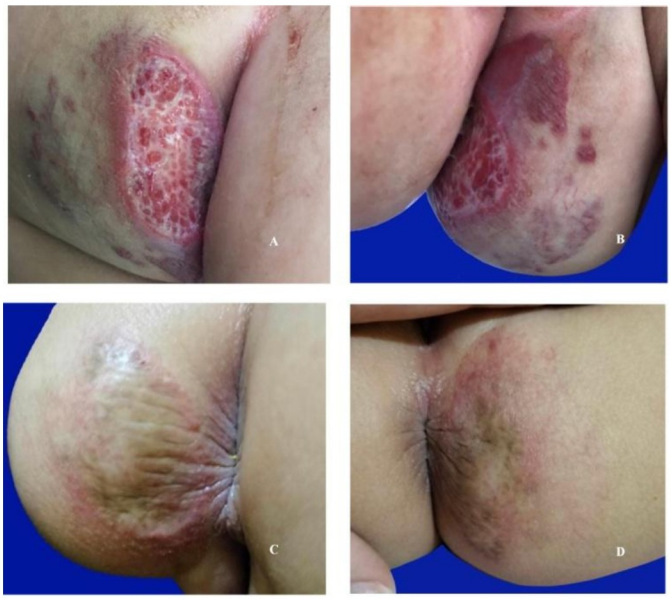

Figure 2. Comparison photos (A and B) on the day of consultation and (C and D) after initiation of oral propranolol for 4 months. There is notable complete resolution of ulceration and involution of the hemangioma leaving residual fibrosis.

DISCUSSION

Infantile Hemangiomas, in comparison to other vascular tumors, present with a unique evolution characterized by 3 phases: the proliferative phase (early and late), plateau phase and involution phase. The early proliferative phase is associated with rapid nonlinear growth and by 5 months of age, infantile hemangiomas would have completed all growth. The late proliferative stage is attributed to an ongoing slower growth that occurs after rapid growth and typically ends by 9 months of age.[7]

Infants with infantile hemangiomas located on the lower body (perineum or lumbosacral area) are at risk for LUMBAR syndrome which describes a constellation of features involving lower body hemangioma, urogenital abnormalities, myelopathy, bony deformities, anorectal malformations and renal anomalies. This syndrome should be considered on any infants with hemangiomas presenting in the perineal or lumbosacral areas. Thorough physical examination and further radiologic imagings are warranted to rule out any presence of anomalies.[4]

Ulceration is known to be the most common complication, occurring mainly in the proliferative phase, as seen in our patient. This complication can be followed by intense pain and discomfort along with secondary infection and functional compromise. Lesions found in the intergluteal areas are difficult to manage as these regions are continuously exposed to urine and feces during infancy.[2,3]

Early intervention during the rapid proliferative phase with oral propranolol has been emphasized in order to achieve an optimum aesthetic and functional improvement.[6]

In our clinical case, the infant came to us with a 4.4cm by 3.2cm lesion with an associated ulceration during the late proliferative phase. This warranted prompt treatment with oral propranolol, however, even with its high safety profile, literatures have reported untoward adverse events of non-selective beta-blockers, namely, hypotension, bronchospasm and hypoglycemia.[8]

This required our patient to be placed on a 12-hour day admission at the out-patient department, despite the decrease in access to public hospitals during the Covid-19 pandemic, in order to provide close supervision during the first day of administration and was monitored via telemedicine on subsequent follow-ups.

In conclusion, oral propranolol appears to be an effective and safe therapeutic approach for ulcerated infantile hemangiomas, even during the late proliferative phase. Results achieved significant contraction and resolution of the ulceration and rapid involution of the lesion. No adverse effects were observed during the first initiation and subsequent follow-up visits done via telemedicine.

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