Superficial Genital Infantile Hemangiomas

Aleksandra MATIĆ^{1,2}, Milan MATIĆ^{1,3}, Sonja PRČIĆ^{1,2}

¹University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia

²Pediatrics Clinic, Institute for Child and Youth Health Care of Vojvodina, Novi Sad, Serbia

³Clinic of Dermatovenereology, Clinical Center of Vojvodina, Novi Sad, Serbia

*Correspondence: Aleksandra Matić, E-mail: aleksandra.matic@mf.uns.ac.rs

UDC 616-006.3-053.3-085:611.6

Abstract

Introduction. Superficial infantile hemangiomas (IH) are rarely localized in the genital region. **Case Report.** We present 8 infants with IHs in the genital region (3 boys and 5 girls). Our patients had only superficial IHs, their internal organs were not affected and there were no associated anomalies. In the boys, IHs were localized on the scrotum and the foreskin in 2 cases and 1 case, respectively. In the girls, IHs were on the labia majora and near the vaginal introitus. None of the IHs showed any IH-related complications. No therapy for IHs was administered in any of the presented infants, either because IHs were small and non-aggressive, or because their parents rejected the proposed therapy. **Conclusion.** Genital IHs have increased tendency for ulceration, so thorough examination and follow-up are of outmost importance. If therapy is indicated, oral propranolol is the treatment of choice for genital IHs.

Key words: Hemangioma; Infant; Scrotum; Genital Neoplasms, Female, Propranolol; Drug-Related Side Effects and Adverse Reactions

Introduction

Infantile hemangiomas (IHs) are the most frequent vascular tumors of infancy. The estimated incidence reported in the literature ranges from 4% to 5% during the first year of life (1–3).

The vast majority of IHs are benign, with no need for intervention (1, 2). However, substantial subset of IHs can be the cause of a variety of medical, functional and/or aesthetic adverse effects, which depends on the size and clinical characteristics of IH as well as its localization. Superficial IH can emerge on any part of the skin or mucous membranes; the genital region being no exception, although it is a rare localization of IHs (4).

The aim of this paper is to present a series of patients with superficial IHs with rather distinctive localization in the genital region, and to point to the clinical characteristics and management of this type of IH.

Case Reports

We present 8 infants with IHs in the genital region – 3 boys and 5 girls.

All the presented infants had only superficial IHs. On ultrasound, no IHs were revealed on the internal organs. Furthermore, none of our patients had any dysmorphic features or congenital anomalies. Each of the presented boys had a single IH, which was in the genital area. IHs were slow in growth, reaching the full size at the age of 2-3 months. The first signs of involution of IHs were noted at the age of 9-11 months. One boy was prematurely born; he received the resuscitation at birth and mechanical ventilation during first 10 days of life, and developed posthemorrhagic hydrocephalus, which was treated with ventriculo-peritoneal shunt. His IH was on the bottom of his right scrotum and was the biggest in size of all the three presented IHs in our male patients (**Figures 1a and 1b**). The other two boys were born at term. One of them had inconspicuous neonatal period (the other boy with scrotal IH – **Figure 2**), and the other one had minor respiratory problems. The most important characteristics of genital IHs in the presented boys are shown in **Table 1**.

All genital IHs in the presented girls were on the labia majora and/or near vaginal introi-

Figure 1. Case of a boy No 1: a preterm boy with globular superficial infantile hemangioma at the bottom of his right hemiscrotum A) at the postnatal age of 2 months, B) at the postnatal age of 3.5 months

tus. Two girls were found to have two genital IHs, and three girls had one genital IH. Two girls had just two IHs in the genital regions, with no additional IHs (**Figure 3**). In addition to one genital IH, each of the other three girls had 1 to 4 extragenital IHs, localized on the forehead, abdomen, and/or extremities. Once they appeared, all genital IHs grew very slowly until the age of 3 postnatal months. Afterwards genital IHs showed very little changes in size and appearance until the first signs of their involution, which were noted at the age of 9-10 postnatal months. Extragenital IHs showed a slightly more advanced growth comparing to the genital IHs in the same infant. Three of the presented girls were born

preterm, while 2 were born at term. All the presented girls had some early morbidity after birth: respiratory distress, jaundice, urinary tract infection, early anaemia; hence their prolonged primary hospitalization after birth. The characteristics of genital and extragenital IHs in the presented girls are given in **Table 2**.

Neither ulceration nor any other IH-related complications were found in the presented cases, whether genital or extragenital ones. In addition, no therapy for IHs was administered in any of the presented infants, either because IHs were small and non-aggressive, or because their parents rejected the proposed therapy for IHs (boy No 1, with globular scrotal IH and girl No 3, who had 5 IHs in total).

Table 1. Common characteristics of genital IHs in the presented boys

	Preterm	Localization of genital IH	Description of genital IH	The largest diameter of IH	Extragenital IHs
Boy No 1	yes	scrotum	bright-red flattened globe with a smooth surface	9 mm	none
Boy No 2	no	scrotum	round bright-red, slightly elevated	5 mm	none
Boy No 3	no	prepuce	oval-elongated, bright-red, slightly elevated	5 mm	none

Table 2. Common characteristics of genital IHs in the presented girls

	Preterm	Number of genital IHs	Localization of genital IHs	Largest size of IHs	Appearance of genital IHs	Number of extragenital IHs	Localization of extragenital IHs
Girl No 1	yes	1	labia majora	3 mm	oval - elongated, bright-red, flat	1	knee
Girl No 2	yes	2	labia majora, near vaginal introitus	10 mm and 5 mm	irregular shape and oval-elongated; both bright-red, smooth and almost flat	none	/
Girl No 3	yes	1	labia majora	5 mm	oval-elongated, bright-red, smooth, flat	4	forehead, scalp, abdomen, lower leg
Girl No 4	yes	1	near vaginal introitus	5 mm	oval, smooth, flat	1	upper leg
Girl No 5	no	2	labia majora	5 mm and 3 mm	oval, smooth, flat	none	/

All parents of the infants were advised to pay special attention to the hygiene of their child's genital region, especially in case of elevated/pendulated IHs, like it was the case with boy No 1.

Discussion

IHs are more often localized in some regions of the skin and mucous membranes for the reasons not known so far, while some other regions are rarely affected. Literature data show that only 1% of all IHs are in the anogenital region (4).

According to the depth of the affected tissue, IHs are classified as superficial (localized primarily on the surface of the skin), deep (within the deep dermis and subcutaneous tissue) or mixed – superficial and deep, also known as combined IHs (1, 5). All the presented infants had the superficial type of IHs. IHs localized in the genital region with a deep component are much more aggressive and with more complications. They can interfere with the sperm production in case of scrotal deep IH, through the direct involvement in the physical growth of developing testis as well as by increasing local temperature in the testicle because of the nearby IH (6, 7). In a scrotal as

Figure 2. Case of a boy No 2: a term boy at the postnatal age of 3 months with round infantile hemangioma at the left hemiscrotum.

Figure 3: Case of a girl No 2: two superficial infantile hemangiomas at the labia majora and near vaginal introitus at the age of 3 months

well as penile deep IH, an important disfigurement and malfunction can occur (7). If an IH is purely superficial, these complications are rarely expected. In girls, genital IH can be the cause of recurrent vaginal bleeding (8) or redness, pruritus and pain (9). The thorough evaluation and follow-up of every genital IH is therefore very important. Furthermore, the detailed complete examination of the infant is necessary in order to look for the possible presence of dysmorphic features and associated anomalies. Particular attention should be paid to the anatomy of anogenital region in infants with large IHs in this area because of possible associated anomalies within PEL-VIS syndrome of varying degree (10).

Superficial IHs have a specific appearance, which is mainly sufficient for the correct diagnosis. In morphologically less obvious cases, imaging studies (ultrasound and MRI) and the typical clinical course are diagnostic clues for IH. (1, 2). Classical superficial IH is not visible at birth but appears at the age of several weeks or months. IHs are characterised by specific natural evolution, which implies proliferative phase and subsequent spontaneous involution. These features of IH are important elements of IH diagnosis. Typical appearance and clinical course were noted in all the presented cases of IHs.

As previously mentioned, the potential for adverse effects depends on morphology and growth rate, but also on localization of IH. Genital IHs are especially prone to ulceration, due to the irritating and macerating properties of stool and urine, frequent friction and occlusive effect of diapers (6, 11). The additional trigger for ulceration of IH in this anatomic area is decreased oxygenation of the surface of the hemangioma (6, 7). About 75% of total hemangioma ulcerations are found in the diaper area, out of which 26% in the gluteal region, 23% at the perineum, 18% around the anus, and 8% at the scrotum (12). Ulceration often develops at the height of the proliferative phase of IH evolution, especially in the cases of rapid growth. Generally, larger, more prominent and more granulated IHs are prone to ulceration (1, 2). Ulceration is among very important adverse effects of IHs because of accompanied pain and bleeding, as well as residual scarring with the potential for significant life-lasting disfigurement and functional impairment. For ulcerated IH oral propranolol is the treatment of choice.

In all the presented patients, genital IHs are superficial with very limited growth and relatively small final size – less than 10 mm. Therefore, we did not expect complications such as ulceration, bleeding or the harmful effect of the increased temperature of the hemangioma on the developing testicles in the presented boys with scrotal IHs. Furthermore, the majority of the presented infants were prematurely born with prolonged primary hospitalization and significant early morbidity, even with life-long serious consequences in our boy No 1. In such cases the parents are usually less willing to accept additional therapy. Complicated IHs – those which are life-threatening, function-threatening, ulcerated or with high risk thereof, or with acute and/or chronic disfigurement – must be treated. In complicated IHs the first line therapy is oral propranolol, and topical timolol only in special cases. The widely accepted indication for treatment with oral propranolol is also the presence of 5 or more IHs in the child (1), as it was the case with the presented girl No 3. The rationale for introducing the treatment for IH is much wider than the above-mentioned and includes aesthetics as well as parents' concerns and wishes in non-complicated IHs (2, 13). One should have in mind that the involution of IH might be complete or with some permanent residuals in the form of telangiectasias, scarring, atrophic skin, fibrofatty tissue or changes in pigmentation (5). Anyhow, before the introduction of any IH therapy, detailed explanations of all the options should be provided to infants' parents. The final decision, except in very few life-threatening cases, should be made jointly between the attending doctor and the parents. After all, every therapeutic option requires full-cooperation with the parents, because of the necessity for long-term and regular administration of medications as well as monitoring of treatment effects and potential adverse events. When it comes to genital IHs, the therapy of choice would be oral propranolol (14, 15). It should be considered in large IHs (over 10 mm in diameter), those with fast growth, significantly raised above the surrounding skin and/or with significantly granulated surface. Oral propranolol has shown good effects with no adverse events in a series of 9 genital IHs cases (15). The topical therapy with timolol-maleate is less applicable

in this type of IH due to the increased potential for adverse effects. Occlusion effect of diapers as well as the proximity of the mucous membrane in some genital IHs are responsible for the increased systemic absorption of timolol and subsequent higher potential for adverse events such as bradycardia, hypotension, apnoea, hypothermia and sleep disturbances (14). There were attempts at applying topical timolol for IH localized on the labia majora under occlusion on everyday basis in ambulance settings (16), but it was for study purposes; for everyday practice it is rather inconvenient for infant and parents.

Conclusion

Genital IHs have the increased tendency for ulceration, so thorough examination and follow-up are of outmost importance. Furthermore, looking for dysmorphic features and anomalies (particularly of anogenital region), as well as for additional IHs on other body parts, are mandatory in such infants. Parents should be advised to pay special attention to the hygiene as well as daily examination of the genital area. If therapy is indicated, oral propranolol is the treatment of choice for genital IHs.

References

1. Krowchuk DP, Frieden IJ, Mancini AJ, Darrow DH, Blei F, Greene AK, et al. Clinical Practice Guideline for the Management of Infantile Hemangiomas. *Pediatrics*. 2019;143(1):e20183475.
2. Darrow DH, Greene AK, Mancini AJ, Nopper AJ; Section on dermatology, Section on otolaryngology-head and neck surgery, and Section on plastic surgery. Diagnosis and management of infantile hemangioma. *Pediatrics*. 2015;136(4):e1060-104.
3. Munden A, Butschek R, Tom WL, Marshall JS, Poeltler DM, Krohne SE, et al. Prospective study of infantile hemangiomas: incidence, clinical characteristics, and association with placental anomalies. *Br J Dermatol*. 2014;170(4):907-13.
4. Grantzow R. Treatment of genital infantile hemangiomas. In: Mattassi R, Loose D, Vaghi M, editors. *Hemangiomas and vascular malformations*. Milano: Springer; 2015. p. 151-4.
5. Vivar KL, Mancini AJ. Infantile hemangiomas: an update on pathogenesis, associations, and management. *Indian Journal of Paediatric Dermatology*. 2018; 19(4):293-303.
6. Patoulis I, Farmakis K, Kaselas C, Patoulis D. Ulcerated scrotal hemangioma in an 18-month-old male patient: a case report and review of the literature. *Case Rep Urol*. 2016;2016:9236719.
7. Chavan D, Javalgi AP. Scrotal hemangioma: a case report. *J Clin Diagn Res*. 2014;8(12):ND03-4.
8. Ganti AK, Ray J, Mooney KL, Zambrano E, Hillard PJA, Fok W. Unusual cause of pediatric vaginal bleeding: infantile capillary hemangioma of the cervix. *J Pediatr Adolesc Gynecol*. 2019;32(1):80-2.
9. Silva JMD, Calife ER, Cabral JVS, Andrade HPF, Gonçalves AK. Vulvar hemangioma: case report. *Rev Bras Ginecol Obstet*. 2018;40(6):369-71.
10. Girard C, Bigorre M, Guillot B, Bessis D. PELVIS Syndrome. *Arch Dermatol*. 2006;142(7):884-8.
11. Chen TS, Eichenfield LF, Friedlander SF. Infantile hemangiomas: an update on pathogenesis and therapy. *Pediatrics*. 2013;131(1):99-108.
12. Morelli JG, Tan OT, Yohn JJ, Weston WL. Treatment of ulcerated hemangiomas infancy. *Arch Pediatr Adolesc Med*. 1994;148(10):1104-5.
13. Semkova K, Marina S, Kazandjieva J. Topical treatment of infantile hemangiomas – where are we now? *Serbian Journal of Dermatology and Venereology*. 2011;3(4):145-52.
14. Frommelt P, Juern A, Siegel D, Holland K, Seefeldt M, Yu J, et al. Adverse events in young and preterm infants receiving topical timolol for infantile hemangioma. *Pediatr Dermatol*. 2016;33(4):405-14.
15. Tran C, Tamburro J, Rhee A, Golden A. Propranolol for treatment of genital infantile hemangioma. *J Urol*. 2016;195(3):731-7.
16. Moehrl M, Leaute-Labreze C, Schmidt V, Röcken M, Poets CF, Goelz R. Topical timolol for small hemangiomas of infancy. *Pediatr Dermatol*. 2013;30(2):245-9.

Površinski genitalni infantilni hemangiomi

Sažetak

Uvod. Infantilni hemangiomi su retko lokalizovani u genitalnoj regiji. **Prikaz slučaja.** Prikazujemo osmoro odojčadi sa infantilnim hemangiomima u genitalnoj regiji (tri dečaka i pet devojčica). Svi prikazani pacijenti su imali samo površne infantilne hemangiome, bez infantilnih hemangioma na unutrašnjim organima i bez pridruženih anomalija. Kod dečaka, infantilni hemangiomi bili su lo-

kalizovani na skrotumu u dva slučaja i prepucijumu u jednom slučaju. Kod devojčica, infantilni hemangiomi bili su na velikim usnama i u blizini introitusa vagine. Nijedno prikazano odojče nije imalo komplikacije. Takođe, ni u jednom slučaju nije primenjena terapija za infantilne hemangiome, bilo zato što su bili mali i sporog rasta, ili zato što su roditelji odbili predloženu terapiju. **Zaključak.** Ge-

genitalni infantilni hemangiomi imaju povećanu tendenciju ka ulceraciji, te su detaljan pregled i redovno praćenje izuzetno važni kod ovakve dece. Ako postoji indikacija

za terapiju, oralni propranolol je lek izbora za genitalni infantilni hemangiom.

Ključne reči: Hemangiom; Odojče; Scrotum; Neoplazme ženskih genitalija; Propranolol; Neželjena dejstva i reakcije na lekove

Received 17.03.2019.

Accepted 7.04.2019.