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CASE REPORT

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Complicated Infantile Hemangiomas in the palate: case report of a newborn patient and review of the literature

Marco Pensabene[1*], Chiara Cambiaso[1], Maria Patti[1], Maria Sergio[1], Gregorio Serra[2], Francesco Grasso[1], Fabio Baldanza[1], Mario Giuffre'[2], Giovanni Corsello[2] and Maria Rita Di Pace[1]

Abstract

Background Infantile hemangiomas (IH) are the most common benign vascular tumors in neonates, with a prevalence of 5-10% in full-term infants. Its occurrence in the palate is rare. While typically self-limiting, complicated IHs can lead to significant morbidity, especially when involving critical structures.

Case presentation We report the case of a full-term newborn presenting with a 2×2 cm exophytic lesion on the hard palate, causing feeding difficulties, anemia, and recurrent bleeding. Early administration of oral propranolol, initiated on the 11th day of life, proved effective in managing this complicated IH. The treatment, started at a dose of 0.5 mg/kg/day and gradually increased to 3 mg/kg/day, resulted in rapid ulceration healing and lesion regression. Follow-up over eight months confirmed the therapy's efficacy and safety, with no adverse effects reported.

To contextualize this case, a systematic review of the literature was conducted following PRISMA guidelines, focusing on neonatal IHs of the head and neck treated with beta-blockers. Out of 1052 papers identified between 2015 and 2024, only four relevant studies were included. These cases highlighted propranolol's role as a first-line treatment for complicated IHs, even in neonates. However, the review also emphasized diagnostic challenges, particularly in atypical locations such as the hard palate, which may delay therapy.

Conclusions This case and literature review underscore the importance of early diagnosis and a multidisciplinary approach for managing high-risk IHs. While propranolol is generally avoided in neonates younger than 45 weeks of corrected gestational age due to potential adverse effects, our findings suggest that close monitoring in a hospital setting enables its safe administration. This report contributes to the growing evidence supporting propranolol as a safe and effective therapy for neonatal IHs and highlights the need for further research to refine treatment protocols for this vulnerable population.

Keywords Infantile Hemangiomas, Neonates, Oral hemangiomas, Propranolol treatment, Oral tumors

*Correspondence:
Marco Pensabene
marco.pensabene@policlinico.pa.it
[1] Pediatric Surgery Unit, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties "G. D'Alessandro", University of Palermo, Palermo, Italy
[2] Neonatal Intensive Care Unit, Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties "G. D'Alessandro", University of Palermo, Palermo, Italy

Background

Infantile hemangiomas (IH) are the most frequent soft tissue tumors in children, affecting 5–10% of full-term newborns [1]. However, their prevalence is higher among preterm and low birth weight infants, as well as in females [2, 3]. These lesions are developmental in nature, becoming noticeable 1–3 weeks after birth, and usually manifest during the first months of life. They undergo a rapid growth phase within the first few months, attaining

approximately 80% of their final size by 4–6 months of age [3]. After this growth phase, the lesions enter a plateau stage, followed by a regression phase, which typically achieves about 90% resolution by the age of 4 years. For deeper lesions, the involution process may extend until around 8 years of age. While IH are benign, oral propranolol is recommended for high-risk cases during the second month of life to prevent complications such as bleeding, deformities, or functional impairments. Treatment, usually lasting 6–12 months, helps to reduce the recurrence risk. However, guidelines advise against initiating therapy in infants younger than 45 weeks of post-conceptional age, especially preterm neonates, due to the potential higher incidence of propranolol adverse effects related to immaturity. Although about 60% to 80% of IHs are seen in the head and neck region, oral mucosa is involved in 10% of patients [3–5].

We report on a full-term newborn with complicated IH of palate, leading to feeding impairment and blood loss. The patient underwent early administration of oral propranolol from the 11th day of life, during the hospitalization within the neonatal intensive care unit (NICU). Driven by our personal experience and clinical contribution, we performed a review of the literature on the topic, highlighting strengths, precautions and potential pitfalls of early beta-blocker treatment. To our knowledge, this is the first reported case of complicated IH of palate treated with oral propranolol in neonatal age.

Case presentation

Our patient was delivered at 39 weeks of gestation at the birthing center of a small town of a neighboring province (with respect to our Mother and Child Department of the University Hospital of Palermo, Italy) of Western Sicily. He was born via emergency cesarean section due to maternal pre-eclampsia. At birth, a 2×2 cm opalescent lesion was noted on the palate, leading to feeding difficulties (Fig. 1A).

The neonate was soon referred postnatally to our Hospital for further evaluation. Physical examination disclosed good general conditions, and neither signs of cyanosis and respiratory distress nor dysmorphic features were noted. The lesion was round, protruding from the mucosa of the bone palate into the oral cavity. A small hematoma was present, suggesting prior bleeding. Once the patient started oral feeding, melena appeared due to persistent blood loss, and required the patient's admission to the NICU. A central umbilical line was placed, and total parenteral nutrition was initiated. Blood transfusion, owing to persistent and severe anemia, was needed on day 3 (hemoglobin levels reduced from 14.2 g/dL to 6 g/dL). To obtain precise anatomical details and to exclude bone damage, a Magnetic Resonance Imaging (MRI) was performed on the fifth day. Imaging revealed a hyperintense signal on T2-weighted images and an isointense signal on T1-weighted ones, involving the maxillary bone. The lesion was mostly exophytic in the oral cavity, measuring 15x18x11 mm.

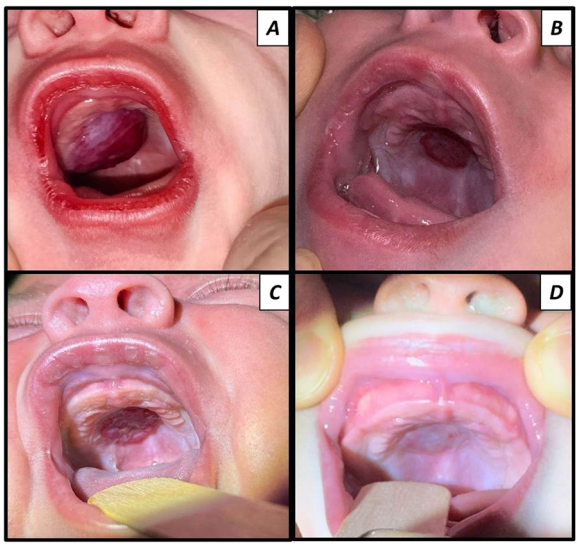

Fig. 1 **A**-**D** The picture shows the involution of the palatine lesion through 8 months of follow-up, respectively at birth (**A**), after one (**B**), four (**C**) and eight (**D**) months of oral propranolol administration

According to MRI findings, showed the absence of a "tangle-like" image which is typically observed in arteriovenous malformations (Fig. 2).

After evaluation of such instrumental findings, in addition to clinical ones, we considered more reliable the diagnosis of Infantile hemangioma, despite congenital Hemangioma or pediatric bone hemangioma could not have been excluded at all. Thereafter, a multidisciplinary assessment involving radiologists, neonatologists, pediatric surgeons, and dermatologists, agreed to recommend the prompt start of oral propranolol therapy. The latter, indeed, began on the 11 th day of life (corrected gestational age 40^{+4} weeks) due to transient hypothyroidism, which delayed initiation. Treatment started in the NICU at the initial dose of 0.5 mg/kg/day, administered twice per day, and was gradually (weekly) increased up to the final therapeutic regimen of 3 mg/kg/day. Throughout the hospital stay, vital parameters and blood glucose levels were strictly monitored, and resulted normal. The ulceration healed within the first two weeks, and oral feeding was successfully resumed on the 10th day of therapy.

The patient was discharged in stable condition on day 13, and a weekly outpatient clinical control was planned until the described therapeutic dose was reached; then, clinical controls were planned monthly. At one month evaluation, the lesion significantly regressed, with

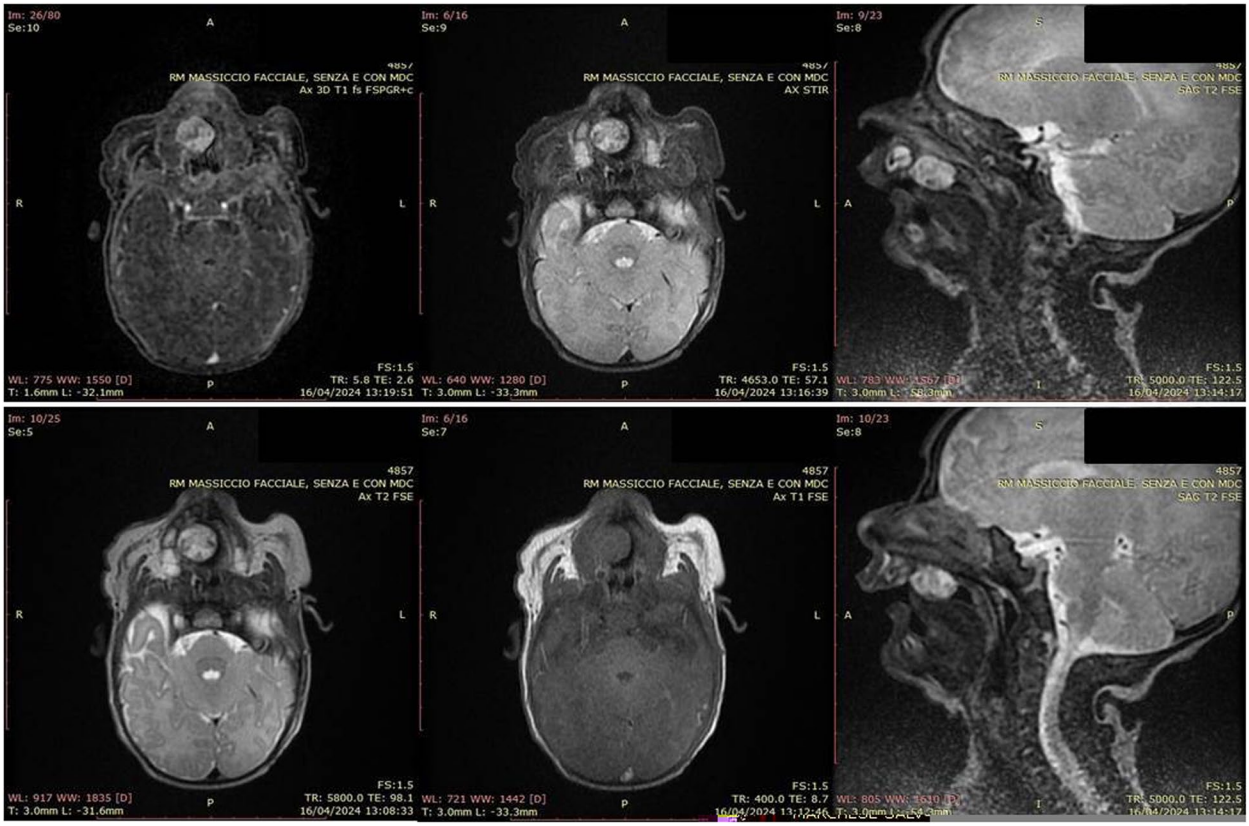

Fig. 2 MRI appearance of the palatine IH. The lesion appears as a huge mass involving the maxillary bone, but mainly growing within the oral cavity. A strict relation between the mass and the tongue should be highlighted, which could have been implied in the ulceration and bleeding of the mass

notable reduction in size and no signs of ulceration or bleeding. During follow-up, moreover, no propranolol-related adverse effects or recurrent bleeding were observed (Fig. 1b). After 4 months the patient remained in good condition: the lesion reduced in volume and the discolored (Fig. 1c), and neither signs of ulceration and bleeding, nor feeding or breathing impairment were noticed. To date, after 8 months of follow-up, the therapy is well tolerated, and no adverse effects or other abnormalities are currently reported(Fig. 1d).

Discussion and conclusions

Infantile hemangiomas (IHs) affect approximately 4.5% of term neonates, and should be distinguished from Congenital Hemangioma, which they clinically resemble, but differ from in immunohistochemical characteristics (CH are negative ti GLUT1, the hallmark of IH) and natural history. In fact, CH reach their maximum size at birth and follow different involution patterns: they may fully regress within 12 months (RICH), partially regress (PICH), or remain unchanged (NICH). RICH could be associated with thrombocytopenia, which was not observed in the presented case [3].

The highest prevalence of IH is observed among females, preterm and in Caucasian ethnicity. Recognized risk factors include placental anomalies, prematurity, and low birth weight. Ulceration is the most common complication, affecting about 16% of patients [1, 2]. IHs are a recognized cause of quality of life (QoL) impairment [6]. Actually, when complications occur, a significant worsening of psychosocial well-being and overall health status of the family is reported by parents of affected infants, who may exhibit irritability, feeding difficulties, and sleep disturbances. In this regard, it has been shown that treatment could improve QoL, even allowing no adverse effects or complications [6].

The head and neck district is frequently affected by IHs, and ulceration may occur in areas prone to maceration, decubitus or frictional stress, such as lip, postauricular sulcus, neck folds or occipital skin [7–9]. IHs may affect various mucosal sites, including lips, buccal and nasal mucosa, conjunctiva, tongue, and floor of the mouth. Occurrence of IH in the mouth or airway could

be associated with syndromes or midline defects [10–14], while isolated non-syndromic IHs of the hard palate are rare, with fewer cases documented. Then, starting from the current clinical report, we conducted a systematic review, using the PubMed database, on Infantile Hemangiomas of the head and neck arising in newborn infants. We included all papers published between January 2015 and December 2024. The research was conducted, according with PRISMA guidelines [15], inserting the following key-words: "Newborn Infantile Hemangiomas"; "Complicated Infantile Hemangiomas"; "Oral Infantile Hemangiomas"; "Propranolol in Newborn"; "Mouth Infantile Hemangioma". Filters used were: publication date from 2015/01/01 to 2024/31/12; age: children 0–23 months; language: English; species: humans. After entering such terms and adopting these inclusion criteria in the search engine, the analysis obtained 1052 papers. Those focusing on pharmacological or pathological aspects were excluded, and only clinical papers were considered for assessment. Among the latter, those not reporting beta-blockers-treatment were ruled out, as well as those focusing on specific syndromes or malformative associations like PHACE or LUMBAR. With regard to anatomical selection, since the IHs frequently occur in the head/neck district, we aimed to focus our attention only on the lesions specifically arising within the mouth and the hard palate. Therefore, reports on IH occurring in different locations were excluded. After such selections, 1028 papers were excluded and 24 were considered for further evaluation. Among them, 9 studies were removed due to a different localization of the described lesions; 6 papers reporting patients on wide and heterogeneous populations were also excluded since they provided insufficient clinical details; 2 papers were not included as they were reporting focusing on diagnostic tools; at last, 3 studies were rejected for further different reasons: one was written in Chinese language; another was the chapter of a book dealing with general dermatological conditions of the newborn; the last one did not include data on beta-blockers treatment.

The flow-chart of the review design is resumed in Fig. 3.

Finally, 4 papers were included in our survey for analysis [16–19]. In 2019, Țarcă et al. reported a case of a 3-month old twin preterm patient with a complicated IH of soft palate, pharynx, tongue and epiglottis [17]. The evolution was favorable after oral propranolol treatment, which allowed the reduction of the lesion without any concerns in drug tolerance. The Authors enhance some risk factors typically occurring in patients with IH, such as prematurity and low-birth weight; their paper highlights the difficulties encountered by clinicians in the diagnostic process, including the differential diagnosis (e.g. with rhabdomyosarcoma, congenital skin defects) [20, 21], from which HIs must be distinguished, especially in neonatal age, where both cutaneous and systemic manifestations may be hidden/shaded or not specific (respiratory distress, due to epiglottis involvement, and

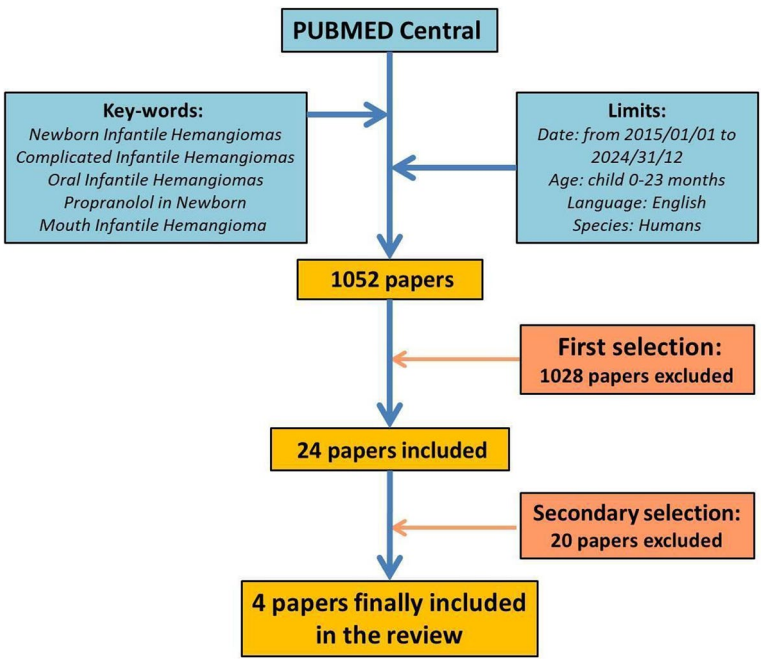

Fig. 3 Flow-chart of the review design

progressive feeding difficulties/dysphagia leading to dystrophia).

In 2020 Ishikawa et al. [16] reported a case of a 9-weeks-old patient referred for feeding difficulties and poor weight gain. On the physical examination no cutaneous IHs were observed, but an ulcerated mucosal 1 cm-wide lesion was detected on the hard palate. Thus, suspecting a complicated IH, the patient started oral propranolol, with a progressive healing of the ulceration and improvement in suckle, feeding and weight gain.

In 2023, Zuhir et al. reported a case of an IH of the left cheek, with involvement of the periorbital region and the palatine mucosa [18]. Despite facial distortion due to nasal involvement, the septum appeared normal at MRI evaluation, and neither signs of bleeding or ulcerations were clinically present, nor functional impairment of the eye. The patient significantly improved after oral propranolol administration, with a prompt reduction of the lesion volume, and a progressive resolution of facial distortion. Recently, Lam et al. described a case of complicated IH in a 2-months old infant presenting with recurrent epistaxis [19], treated with nasal drops of timolol maleate 0.5%. This treatment allowed the resolution of bleeding, secondary to ulceration, as shown by nasal endoscopy. Nevertheless, the Authors reported that a lip and oral vestibulum mucosal involvement was detected during the follow-up; thus, the patient underwent MRI, confirming the extension of the IH to oral mucosa, upper jaw and lip, and excluding intracranial involvement. The patient, then, was scheduled for oral propranolol administration which was performed with initial benefit (data on follow-up are lacking). This report underlines the potential role of topical timolol maleate in the management of superficial IHs, and in co-administration with oral propranolol for complicated ones. Such reported cases of the literature are resumed in a comparative table (Table 1).

Despite IHs frequently involve head and neck, their occurrence in the palatal mucosa is uncommon; complications, such as bleeding/ulceration or mass-effect, are often present at diagnosis. Respiratory problems or dysphagia may occur if the upper airway or pharynx are involved. The need for urgent intervention for ulcerated and obstructive IHs is widely acknowledged, and propranolol has emerged as the first-line therapy for complicated HIs, due to its well-known efficacy and safety profile. Response rates for oral propranolol, administered at a dose of 2 to 3 mg/kg/day for a mean duration of six months, range from 96% to 98%. Furthermore, complete or near-complete regression is observed in approximately 60% of cases [7].

Palatine localization of IH seems prone to a more complex diagnostic process, which may be responsible for late identification, as occurred in the patient reported by Lam et al. In their case, indeed, epistaxis was present since the first days of life, but a final diagnosis was obtained at age 3 months. Moreover, a diagnostic color-Doppler ultrasound (US) is not always feasible, and the

Table 1 Comparison of reviewed cases

Author	Age at Clinical presentation	Prematurity	Localization	Complications	Imaging	Histology	Treatment	Age at treatment onset (months)	Need for NICU stay during initial treatment administration
Țarcă et al., 2019 [17]	3-month-old	yes	Soft palate, tongue, pharynnx, epiglottis	Dysphagia, Breathing impairment	CT-scan	yes	Oral Propranolol	>3 months	Yes
Ishikawa et al., 2020 [16]	2.5 month-old	37w	Hard palate	Feeding impairment, Ulceration	MRI	yes	Oral Propranolol	9 weeks	yes
Zuhir et al., 2024 [18]	2 months	36w	cheek, nose, oral mucosa, periorbital	Facial distortion (improved with therapy)	MRI	no	Oral Propranolol	2 months	no
Lam et al., 2024 [19]	2 months	/	Nose septum, upper lip and oral vestibulum	Bleeding	MRI	no	Topical timolol + Oral propranolol	2 months (timolol); >3 month (propranolol)	no
Pensabene et al., 2025	At birth	no	Hard Palate	Bleeding, anemia, Feeding impairment	MRI	no	Oral Propranolol	10 days	yes

The table resumes and compares main clinical characteristics of reviewed cases (age at presentation, localization of the lesion, complications occurred), the diagnostic procedures and the need for NICU stay

US investigation of deeper tissues could be challenging, given the presence of multiple bones. All the described patients, in fact, underwent a higher level imaging, frequently MRI, which allowed a proper anatomical detail on the lesion nature and extension. In this case, MRI ruled out arteriovenous malformation due to the absence of a "tangle-like" appearance. While bone involvement is rare in infantile hemangiomas (IH), it can occur in bone hemangiomas, complicating the diagnosis in our case. Therefore, congenital or bone hemangiomas could not be excluded based on imaging alone. However, clinical findings suggested IH as the more likely diagnosis, given its common occurrence in the head and neck, unlike congenital hemangiomas (CH), which typically appear on the limbs. Additionally, paediatric bone hemangiomas are more common in the vertebrae and ribs and usually develop in older children or adolescents rather than newborns.

In the cases reported by Țarcă and Ishikawa, patients underwent immunohistochemical investigation in order to confirm the diagnosis of IH. In the presented case, we decided to not perform biopsies and the subsequent immunohistochemical investigation given the risk ox exacerbating blood loss and the potential difficulties in airway management in case of hemorrage. As noted in other cited studies, also in our case propranolol administration played a therapeutic and diagnostic role, as a weaker response to the drug would be expected in cases of congenital hemangioma (CH).

Despite being in good general condition, most patients required hospitalization in a safe health care setting, in light of the risk of bleeding (in our patient suckling and enteral feeding caused mucosal ulceration and blood loss, leading parenteral nutrition to be provided during the first days) and breathing impairment, as occurred in the patient described by Țarcă et al., in addition to that of severe anemia requiring transfusion.

The use of propranolol in managing atypical hemangiomas is well described, but its administration in our patient was concerning, since its use is not recommended in newborns, according to AAP guidelines [7]; nevertheless, some authors have demonstrated its safe and effective use even in patients for whom guidelines did not recommend it [22]. The administration of oral propranolol during the NICU stay, as performed in the present experience, shows some advantages in the management of complicated IHs and of the possible treatment-related adverse effects. In fact, it allows a closer and more precise monitoring of vital signs. Moreover, in the current case the parenteral nutrition was easily managed, as well as blood transfusion, which were promptly carried out within the hospital setting. In such context a more accurate diagnostic imaging with MRI has been more suitable, and helpful to better understand the extension of the lesion to the nearest organs.

Our findings further reinforce the safety and efficacy of early propranolol initiation in the treatment of IHs, even in neonates. This is particularly crucial in patients requiring propranolol before 45 weeks of corrected gestational age, who may be more vulnerable to unfavorable effects including hypoglycemia or bradycardia. Furthermore, the present report underlines the need of a multidisciplinary and individualized approach in managing newborns with complicated and high risk HIs. This should include dermatologists, pediatric surgeons, otorhinolaryngologists and neonatologists, and must be tailored to the specific characteristics and the eventual adverse events occurring in each single patient. The continuation of propranolol treatment, until the end of the first year of life, is expected to consolidate the therapeutic outcomes and promote complete regression of the lesions. Future research should explore optimal protocols for initiating beta-blocker therapy in neonates, particularly in those with atypical IH presentations or associated complications and the need for personalized treatment plans.

Abbreviations

IH	Infantile Hemangiomas
NICU	Neonatal intensive care unit
MRI	Magnetic resonance imaging
QoL	Quality of Life
CH	Congenital Hemangioma
RICH	Rapidly involuting CH
PICH	partially involuting CH
NICH	non-involuting CH
PRISMA	Preferred Reporting Items for Systematic reviews and Meta-Analyses
PHACE	Posterior fossa brain malformations, facial segmental infantile Hemangioma, cerebrovascular Arterial anomalies, Cardiac abnormalities or Coarctation of the aorta, Eye or Endocrine anomalies
LUMBAR	Lower body with Urogenital anomalies, IH Ulceration, spinal cord Malformations, Bony defects of the spine and lower extremity, Anorectal malformations, Arterial anomalies and/or Renal anomalies
US	Ultrasound
AAP	American Academy of Pediatrics

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Authors' contributions
MP conceptualized and critically performed the literature review, revised the manuscript and gave the final version of the paper. CC and MPa wrote the manuscript. MG, GS, MDP, MS took care of the patient and contributed in drafting the paper. GC and MDP revised the manuscript and gave final approval for the paper to be submitted. All authors approved the final manuscript as submitted.

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Data availability
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from both parents at admission of their newborn. The study was approved by the Mother and Child Department of the University of Palermo, ethics committee Palermo 1 (Palermo, Italy). All procedures performed in this report were in accordance with the ethical standards of the institutional and national research committee, and with the 1964 Helsinki declaration and its later amendments, or comparable ethical standards.

Consent for publication

Written informed consent was obtained from patient's parents for publication of this case report and accompanying images.

Competing interests

We declare that Giovanni Corsello and Gregorio Serra, co-Authors of the present manuscript, are respectively Editor-in-Chief and Associate Editor of Italian Journal of Pediatrics.

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References

1. Acikgoz A, Sakallioglu U, Ozdamar S, et al. Rare benign tumours of oral cavity- capillary hemangioma of palatal mucosa: a case report. Int J Paediatr Dent. 2000;10:161–5.
2. Neville BW, Damm DD, Allen CM, et al. Oral and maxillofacial pathology. 3rd ed. St Louis: Saunders; 2008.
3. Léauté-Labrèze C, Harper JI, Hoeger PH. Infantile haemangioma. Lancet. 2017;390(10089):85–94. https://doi.org/10.1016/S0140-6736(16)00645-0. (Epub 2017 Jan 13 PMID: 28089471).
4. Barnes L Tumours and tumour-like lesions of the soft tissues. In: Barnes L, ed. Surgical pathology of the head and neck. New York, NY: Marcel Dekker, 1985:725–880.
5. Chiller KG, Passaro D, Frieden IJ. Hemangiomas of infancy: clinical characteristics, morphologic subtypes, and their relationship to race, ethnicity, and sex. Arch Dermatol. 2002;138:1567–76.
6. Pensabene, et al. Quality of life improving after propranolol treatment in patients with Infantile Hemangiomas. Ital J Pediatr. 2022;48(1):140. https://doi.org/10.1186/s13052-022-01334-2.
7. 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:e20183475. https://doi.org/10.1542/peds.2018-3475.
8. Joseph J, Wain T. Infantile haemangiomas: identifying high-risk lesions in primary care. Aust J Gen Pract. 2021;50(12):887–92. https://doi.org/10.31128/AJGP-01-21-5815. PMID: 34845464.
9. Rubegni P, Cevenini G, Lamberti A, Bruni F, Tiezzi R, Verzuri A, Barbini P, Manzi P, Fimiani M. Dermatological conditions presenting at the emergency Department in Siena University Hospital from 2006 to 2011. J Eur Acad Dermatol Venereol. 2015;29(1):164–8. https://doi.org/10.1111/jdv.12513. (Epub 2014 Apr 22 PMID: 24754355).
10. Feygin T, Goldman-Yassen AE, Licht DJ, Schmitt JE, Mian A, Vossough A, Castelo-Soccio L, Treat JR, Bhatia A, Pollock AN. Neuroaxial infantile hemangiomas: imaging manifestations and association with hemangioma syndromes. AJNR Am J Neuroradiol. 2021;42(8):1520–7. https://doi.org/10.3174/ajnr.A7204. Epub 2021 Jul 8. PMID: 34244133; PMCID: PMC8367625.
11. Hossain MS, Stamatiou AT, Kleeman KC, Kellogg BC, Wearden PD, Leto Barone AA, Nelson JS. A 1-day-old girl with infantile hemangioma and sternal cleft. Chest. 2024;165(5):e137-42. https://doi.org/10.1016/j.chest.2023.12.010. PMID: 38724152.
12. Serra G, Giambrone C, Antona V, Cardella F, Carta M, Cimador M, Corsello G, Giuffrè M, Insinga V, Maggio MC, Pensabene M, Schierz IAM, Piro E. Congenital hypopituitarism and multiple midline defects in a newborn with non-familial Cat Eye syndrome. Ital J Pediatr. 2022;48(1):170.
13. Ingrid Anne Mandy Schierz, Mario Giuffrè, Marcello Cimador, Maria Michela D'Alessandro, Gregorio Serra, Federico Favata, Vincenzo Antona, Ettore Piro and Giovanni Corsello. Hypertrophic pyloric stenosis masked by kidney failure in a male infant with a contiguous gene deletion syndrome at Xp22.31 involving the steroid sulfatase gene: case report. Ital J Pediatr. 2022;48: 19.
14. Serra G, Antona V, Giuffrè M, Piro E, Salerno S, Schierz IAM, Corsello G. Interstitial deletions of chromosome 1p: novel 1p31.3p22.2 microdeletion in a newborn with craniosynostosis, coloboma and cleft palate, and review of the genomic and phenotypic profiles. Ital J Pediatr. 2022;8:38.
15. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, McKenzie JE. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021;29(372):n160. https://doi.org/10.1136/bmj.n160.PMID:33781993;PMCID:PMC8005925.
16. Ishikawa K, Fujita M, Takeda T, Mitamura S, Nishio T, Funayama E, Hayashi T, Osawa M, Maeda T, Yamamoto Y, Sasaki S. Ulcerated infantile hemangioma of the hard palate: diagnostic treatment with oral propranolol. J Craniofac Surg. 2020;31(6):e600–2. https://doi.org/10.1097/SCS.0000000000006666. (PMID: 32649551).
17. Țarcă E, Cojocaru E, Roşu ST, Butnariu LI, Plămădeală P, Moisă ŞM. Differential diagnosis difficulties related to infantile hemangioma - case report and literature review. Rom J Morphol Embryol. 2019;60(4):1375–9 (PMID: 32239121).
18. Zuhir O, Muhd Noor N, Marsom A. Management of orofacial infantile haemangioma: a case report. Case Rep Dent. 2024;18(2024):4988221. https://doi.org/10.1155/crid/4988221.PMID:39722746;PMCID:PMC11669428.
19. Lam N, Schrepfer T. Efficiency of topical beta-blockers for epistaxis control in ulcerated infantile hemangioma. Cureus. 2024;16(8): e67709. https://doi.org/10.7759/cureus.67709.PMID:39318943;PMCID:PMC11420686.
20. Piccione M, Serra G, Sanfilippo C, Andreucci E, Sani I, Corsello G. A new mutation in EDA gene in X-linked hypohidrotic ectodermal dysplasia associated with keratoconus. Minerva Pediatrica. 2012;64(1):59–64.
21. Serra G, Memo L, Cavicchioli P, Cutrone M, Giuffrè M, La Torre ML, Schierz IAM, Corsello G. Novel mutations of the ABCA12, KRT1 and ST14 genes in three unrelated newborns showing congenital ichthyosis. Ital J Pediatr. 2022;48(1):145.
22. El Hachem M, Gesualdo F, Diociaiuti A, Berti I, Vercellino N, Boccaletti V, Neri I, Porcedda G, Greco A, Carnevale C, Oranges T, Cutrone M, Dalmonte P. Ital J Pediatr. 2017;43(1):40. https://doi.org/10.1186/s13052-017-0357-9. PMID: 28424095; PMCID: PMC5395924.

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