Case Report

Unusual Cause of Pediatric Vaginal Bleeding: Infantile Capillary Hemangioma of the Cervix

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A B S T R A C T

Background: The differential diagnosis for pediatric prepubertal vaginal bleeding is wide. Rare etiologies include vascular malformations and tumors, such as infantile hemangiomas (IHs), which validate the usefulness of exam under anesthesia, vaginoscopy, and tissue diagnosis.
Case: We report a case of an IH in a 6-year-old girl causing vaginal bleeding requiring transfusion. Vaginoscopy revealed a cervical IH of less than 1 cm. Expectant management and oral propranolol were successful management options.
Summary and Conclusion: Rare, even small soft tissue tumors such as IH can lead to impressive blood loss via vaginal bleeding. Accurate tissue diagnosis and a multidisciplinary approach are essential to planning safe, effective treatment, and follow-up.
Key Words: Prepubertal vaginal bleeding, Infantile hemangioma, Vaginoscopy, Propranolol

Introduction

Infantile hemangiomas (IHs), often cutaneous in location, are the most common soft tissue tumors of infants and children with a prevalence of 5-10%.[1] Characteristically, they spontaneously resolve by 7-10 years of age.[1] They generally require no intervention. Rarely, they cause disfiguration, functional impairment, bleeding, or infection. In this report we present a unique case of an IH of the cervix in a 6-year-old girl who presented with vaginal bleeding requiring transfusion.

Case

A 6-year-old girl with previous, unexplained episodes of vaginal bleeding since 6 months of age presented with acute bleeding requiring transfusion. She had been known to have a prolonged period of neonatal withdrawal bleeding, followed by a vaginoscopy at 2 years of age that showed vaginitis, cervicitis, and posterior labial adhesions that were treated with 2 weeks of topical estrogen. A focal lesion was not seen at that time. She continued to have intermittent spotting and was followed and managed by pediatric endocrinology after her vaginoscopy. Her mother denied exposure to lavender oil, tea tree oil, soy, foreign body, and abuse. Although there was no evidence of breast development, she had an extensive workup by pediatric endocrinology for precocious puberty, which only confirmed a prepubertal state. She did not have café-au-lait spots or fibrous dysplasia to suggest a typical presentation of McCune Albright syndrome.

She then presented to an outside hospital with profuse vaginal bleeding and a 5-point hemoglobin drop over 24 hours. Coagulation testing and a pelvic ultrasound examination were normal. A vaginal culture was negative for *Shigella*. Upon transfer to Stanford Children's Hospital, she was transfused and taken for an urgent exam under anesthesia and vaginoscopy. Findings noted a small crescentic hymen without trauma and clots at the introitus. The cervix had a 3-mm hypervascular raised lesion at 10 o'clock, a small aberrant vessel on the anterior lip, and a 1-cm polypoid structure at the external os, extending into the endocervical canal (Fig. 1). These lesions were biopsied. Hemostasis was achieved with vaginal packing that was removed the next morning.

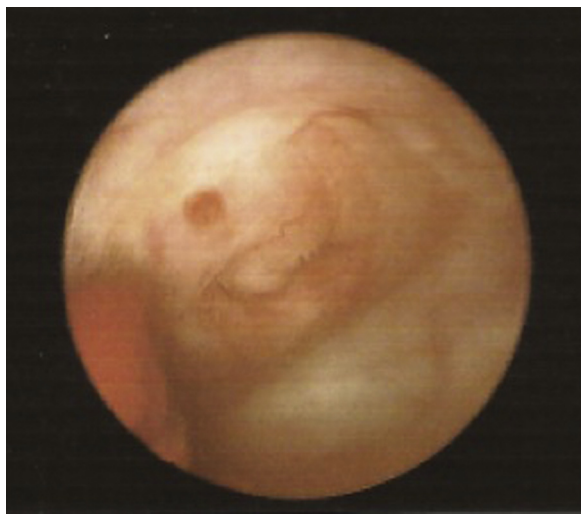

Fig. 1. A raised papule measuring less than 1 cm on the cervix seen on vaginoscopy.

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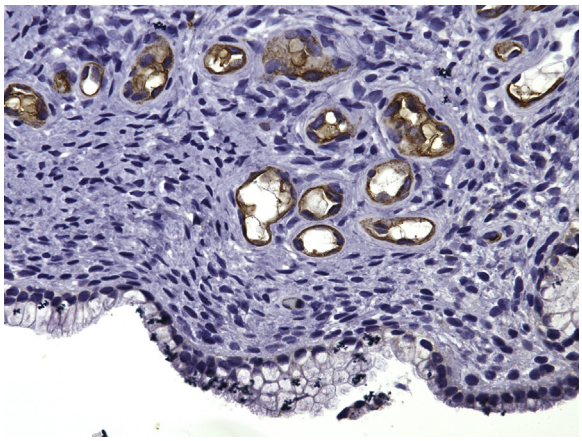

Fig. 2. Glucose transporter-1 positivity is specific for infantile hemangioma (×10).

Pathology of the polypoid lesion was consistent with IH, with capillary vascular proliferation and positive staining for glucose transporter-1 (GLUT-1) (Fig. 2). A subsequent pelvic magnetic resonance imaging (MRI) scan with contrast showed no evidence of a vascular anomaly or pelvic mass. Dermatology consultation recommended oral propranolol. Medication was started with 0.5 mg/kg per dose daily of propranolol, and titrated to a goal of 2 mg/kg per dose daily after 4 weeks.

At her follow-up visits, she was tolerating propranolol therapy well without additional episodes of vaginal bleeding. A persistent 1-cm lesion was noted on repeat vaginoscopy at 18 months. If the lesion is persistent at 2 years, resection will be considered.

Summary and Conclusion

The differential diagnosis for vaginal bleeding in a prepubertal girl is wide and includes vaginal foreign body, trauma, neoplasm, endocrinopathy, and structural anomaly. Initial assessment begins with a thorough history and physical exam, noting the presence or absence of breast development. Most neonatal vaginal bleeding is related to stimulation of fetal endometrium by maternal estrogen in utero and its subsequent withdrawal at birth. Precocious puberty is very unlikely in the case of first bleeding episode in a girl without breast development, excepting the rare circumstance of McCune Albright syndrome and even then, breast development often precedes bleeding. A keen history might include exposure to possible endocrine disrupters, such as lavender or tea tree oil and soy, although these links remain controversial. Abuse certainly should not be missed, but foreign body including retained toilet paper is often the culprit in young girls. Vaginal cultures can be helpful. For example, *Shigella* can cause prepubertal bleeding secondary to vulvovaginitis without concurrent diarrhea. Ultrasound is a reasonable, cost-effective first choice for imaging. MRI has become more widely available and is the most valuable modality to assess vascular anomalies and identify a therapy that would mitigate life-threatening complications. Of note, vascular malformations have decreased signal intensity on T1-weighted images and increased signal intensity on T2-weight images.

A complete differential includes common and rare etiologies. Evaluation should be systematic and cost effective, because an accurate diagnosis does not require expensive tests and imaging. In retrospect, several expensive assays and imaging tests were performed early in the evaluation, which were ultimately unnecessary because of the key findings on physical exam, such as lack of breast development. Moreover, we were able to perform the follow-up vaginoscopy in clinic using the office hysteroscopy device, Endosee, which was well tolerated without sedation, allowed a complete exam, and produced high-quality images for comparison.

Although IH is the most common benign tumor of infancy, as an etiology of vaginal bleeding, there is only 1 case report in the literature of IH of the cervix and another of the vagina.[2,3] In noncutaneous cases, diagnosis must rely on imaging and pathology. MRI is used to delineate the location and extent of IH, and to differentiate it from other high-flow vascular lesions such as arteriovenous malformations. In this case, the lesion could not be appreciated on imaging because of its small size.

Pathological assessment was crucial to our diagnosis. The cervical biopsies taken at the time of vaginoscopy showed a capillary vascular proliferation with GLUT-1 and Wilms tumor 1 positivity, and prospero homeobox protein 1 negativity (Fig. 2).[4,5] GLUT-1 is a sensitive and specific marker for proliferating and involuting IH that is not found in other vascular neoplasms or malformations that enter the histopathological differential diagnosis.[5] Additional IH characteristics include capillary lobules and prominent pericytes, without cytologic atypia or evidence of larger vessels.[6] The differential diagnosis for IH is described in further detail in Table 1.

Table 1
Summary of Differential Diagnosis of IH and Key Characteristics

Evaluation Type	IH	Vascular Malformation	Congenital Nonprogressive Hemangioma	Kaposiform Hemangioendothelioma
Clinical	Early childhood Postnatal involution PHACE syndrome association	At birth or childhood	At birth Subtype non-/rapidly-involuting	At birth Might progress to Kasaback-Merritt phenomenon*
Histology	Capillary lobules Prominent pericytes	Large and small vessels admixed	Capillary lobules, draining veins, mitoses	Canonball nodules Slit-like vessels
IHC	GLUT-1 positive	WT-1 negative	GLUT-1 negative	PROX-1 positive

GLUT-1, glucose transporter-1; IH, infantile hemangioma; IHC, immunohistochemistry; PHACE, posterior fossa of the brain, hemangioma, arterial, cerebro/cardio, eye; PROX-1, prospero homeobox protein 1; WT-1, Wilms tumor 1.

* Kasaback-Merritt phenomenon is a rare, life-threatening entrapment of platelets due to rapidly growing hemangioendotheliomas.

Profuse bleeding is a rare complication of IH and has been mostly noted in the gastrointestinal tract, which might be treated with corticosteroids or might require surgical resection.[1,7,8] Propranolol is the first-line treatment of cutaneous IH resulting in rapid shrinkage, although a minimum of 6 months of therapy is recommended.[7] The mechanism is unclear, but might involve vasoconstriction, downregulation of growth factors including vascular endothelial growth factor (VEGF), and upregulation of cellular apoptosis.[3] Propranolol is safe and well tolerated, although adverse effects have been noted including bradycardia, hypotension, hypoglycemia, and bronchospasm. Duration of therapy is not well established, but visible improvement can begin immediately and resolution can occur as soon as 2 months.[3] In patients who present with prepubertal vaginal bleeding, physicians should consider IH of the vagina or cervix as part of a complete differential diagnosis.

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