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CASE REPORT

Vaginal Bleeding In Prepubertal Girls-A Case Series in Malaysia

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ABSTRAK

Pendarahan vagina di kalangan kanak-kanak perempuan boleh disebabkan oleh masalah kematangan dan juga kanser seterusnya mengakibatkan kanak-kanak dan ibu bapa berasa cemas. Oleh itu, kes-kes ini perlu penilaian dan pengurusan yang teliti. Kajian ini melaporkan lima kes pendarahan vagina di kalangan kanak-kanak perempuan yang melibatkan pelbagai etiologi dan telah menerima rawatan di hospital rujukan tertiari di Malaysia. Kes pertama, kanak-kanak berusia 6 tahun yang belum akil baligh mengalami pendarahan selama 3 minggu. Pemeriksaan di bawah bius mendapati pelbagai polip vagina. Seorang lagi kanak-kanak 6 tahun didapati mempunyai tisu berbentuk donut di saluran urethra dan dirawat dengan krim estrogen dan "sitz bath". Kes seterusnya, kanak-kanak yang mempunyai pertumbuhan payudara dan ultrasound mendapati sista ovari yang memerlukan pembedahan. Selain itu, seorang kanak-kanak berusia 19 bulan mempunyai ketumbuhan besar di dalam vagina. Beliau memerlukan penyiasatan lanjutan, rujukan kepada pakar pembedahan kanak-kanak dan pakar onkologi untuk rawatan kanser "yolk sac". Akhir sekali, seorang kanak-kanak yang berusia 8 tahun mengalami pendarahan pada setiap bulan tanpa tanda kematangan yang lain. Pendarahan vagina kanak-kanak adalah tidak normal dan memerlukan penilaian segera untuk memastikan punca dan seterusnya diberikan rawatan yang sepatutnya. Kes-kes begini adalah sangat penting untuk memastikan tiada unsur penderaan seksual dan kanser. Pemeriksaan mengunakan bius dan vaginoskopi disyorkan

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sekiranya pengimejan diagnostik tidak memberikan keputusan yang muktamad. Rujukan ke pusat rawatan tertiari yang berpengalaman dalam kes-kes begini boleh memberikan hasil rawatan yang baik. Penilaian memerlukan pengambilan sejarah yang bersasar dan menyeluruh beserta dengan pemeriksaan ginekologi yang sesuai untuk golongan pediatrik supaya diagnosis dilakukan dengan tepat dan seterusnya dapat memberikan rawatan yang sewajarnya.

Kata kunci: kanak-kanak perempuan, pendarahan vagina, pra-akil baligh, siri-siri kes, pendarahan kanak-kanak

ABSTRACT

The etiology of prepubertal vaginal bleeding varies from isolated pubertal causes to malignant tumors and generates significant anxiety among girls and their caretakers. Hence, these cases require careful assessment and management. This is a report of five cases of prepubertal vaginal bleeding with various causes and were managed in a tertiary referral center in Malaysia. The first case was a 6-year-old girl who had no pubertal changes with 3 weeks' history of bleeding. She underwent examination under anesthesia and found to have multiple vaginal polyps. Another 6-year-old girl noted to have a doughnut-shaped mass protruding from her urethral meatus. She was treated with estrogen cream and sitz baths. Another child had early breast development while pelvic ultrasound revealed a multiseptated ovarian cyst requiring a cystectomy. A 19-month-old toddler had a large intravaginal mass. She required further investigation, referral to the pediatric surgeon and oncologist for treatment of a malignant yolk sac tumor. Lastly, an 8-year-old girl was noted to have monthly vaginal spotting without any secondary sexual characteristics development. Prepubertal vaginal bleeding is abnormal thus requires prompt assessment to ascertain the cause and administer appropriate management. It is important to rule out sexual abuse and malignancy. Examination under anaesthesia and vaginoscopy is recommended when imaging modality is inconclusive. Referral to tertiary centres experienced in managing such cases ensures good outcomes. Thorough targeted history-taking and pediatric-specific gynecological examination skills are crucial to formulate accurate diagnosis and appropriate management.

Keywords: case series, girls, prepubertal, vaginal bleeding, prepubertal bleeding

INTRODUCTION

Prepubertal vaginal bleeding is not a common complaint. Once it occurs, it is an alarming and concerning symptom. It can cause significant anxiety in the girls and her caretakers thus it is important to ascertain the correct etiology. The causes can vary from idiopathic bleeding toward foreign

body, trauma or malignant neoplasm of the genital tract (Fishman & Paldi 1991). In this review, we discussed five different cases of prepubertal bleeding with different causes presented in Pediatric and Adolescent Gynecology (PAG) Unit in Malaysia.

CASE REPORTS

Case 1

A 6-year-old girl presented with vaginal bleeding for 3 weeks which started with brownish staining then progressed to fresh bleeding. She used 5 to 6 pantyliners daily. No pain in the abdomen or at the perineum. She denied any history of trauma or fall. She was asymptomatic of anemia and had normal micturition and bowel opening. During examination, she was 122 cm tall, weighed 21 kg with body mass index (BMI) of 14 kg/m^2. She was not pale and no neck swelling was noted. Her breast and pubic hair development were Tanner stage 1. Perineal inspection was unremarkable. Her hormonal profile showed pre-pubertal levels with Follicular Stimulating Hormone (FSH) level of 1.8 IU/L, Luteinizing Hormone (LH) level of <0.1/ IU/L and serum Estradiol of 47 pmol/L. Ultrasound pelvis showed small uterus 0.4x1.7x3.1 cm, the right and left ovaries were 0.9x1.4x2.4 cm and 0.8x1.5x3.7 cm, respectively and no other abnormality detected. Parents were advised for examination under anesthesia (EUA) and vaginoscopy to rule out local causes. Intra-operative findings noted a hyperemic area at the hymenal ring and a 0.5x0.5 cm polyp at the posterior vaginal wall (Figure 1). Polypectomy was done. Vaginoscopy revealed multiple polyps at the anterior vaginal wall obliterating the cervix thus multiple biopsies were obtained (Figure 2). She was reviewed two weeks post-operatively and was well and did not experience anymore vaginal bleeding. Histopathological examination (HPE) showed fibroepithelial polyp of vagina. The diagnosis for this prepubertal bleeding was vaginal polyps.

Case 2

A 6-year-old girl was brought by her mother in view of 3 days history of per vaginal bleeding. She was previously well. She denied insertion of any foreign objects into the vagina. She had no pain or vaginal itchiness and no problem with urinary or bowel habits. During examination, there was no secondary sexual characteristics development. No mass palpable per abdomen. Perineal inspection noted a lump at the introitus without any active

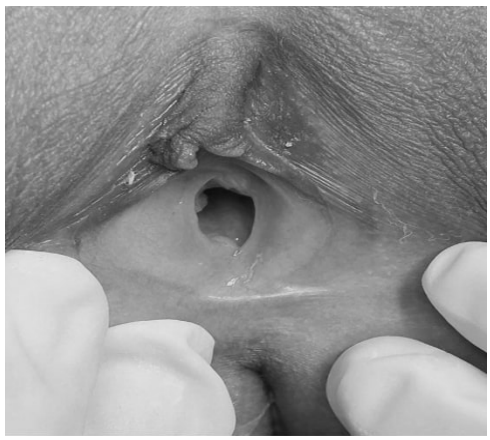

Figure 1: Examination under anesthesia showed hyperemic area at the hymenal ring and a 0.5x0.5 cm polyp at the posterior vaginal wall.

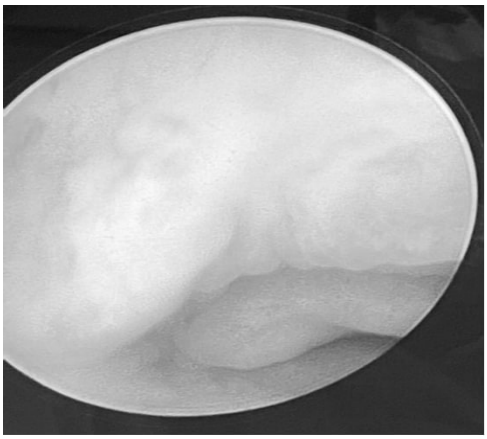

Figure 2: Vaginoscopy revealed multiple polyps at the anterior vaginal wall obliterating the cervix.

bleeding. She was then subjected to EUA. Intra-operative findings revealed a doughnut-shaped mass protruding from the urethral orifice which was consistent with urethral prolapse (Figure 3). The vagina was normal and there was no sign of trauma. She was treated with topical conjugated estrogen cream and advised for sitz bath daily for 10 minutes. Review at 2 and 5 weeks showed no more vaginal bleeding and the mass almost completely resolved (Figure 4). The diagnosis in this case was urethral prolapse.

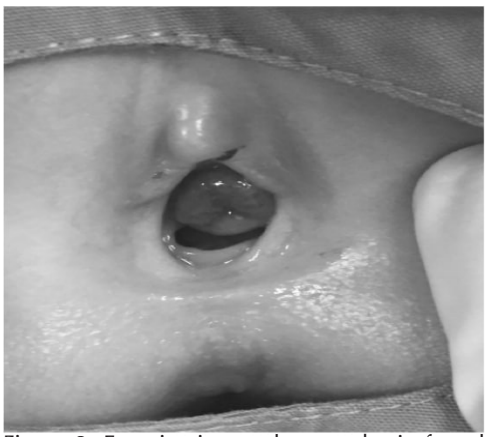

Figure 3: Examination under anesthesia found a doughnut-shaped mass protruding from the urethral orifice which consistent with urethral prolapse.

Case 3

A 7-year-old girl was referred by a pediatrician for vaginal bleeding. The bleeding lasted for 5 days. It was heavy on the first 2 days, requiring 4 pads a day. Her mother also noted she had grown taller in the past one year and remarked that she was almost as tall as her 10-year-old sister. She had noted breast development in her daughter. She denied any abdominal distension or pain and no constitutional symptoms. During examination, she didn't have any syndromic facies. No café au lait spots or any neurocutaneous stigmata was found. Breast examination was Tanner 4 and pubic hair was Tanner 2. Her abdomen was soft and no mass palpable. Perineal inspection was unremarkable. Ultrasound examination revealed uterus 3.5x1.3 cm with endometrial thickening of 4.9

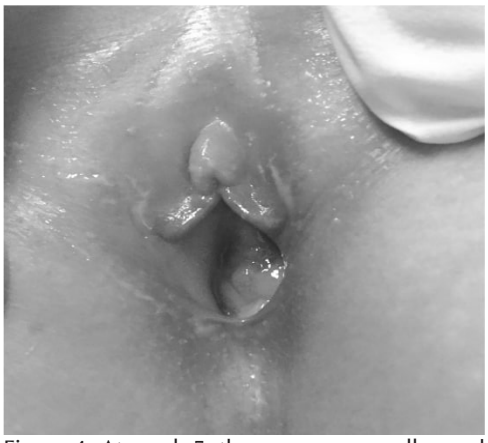

Figure 4: At week 5, the mass was smaller and had almost completely resolved.

mm. Right ovary measuring 1.0x1.8 cm but the left ovary was enlarged about 4.5x4 cm with multiple septation and thick wall. Some of the tumor markers were deranged however it was non-specific. Gonadotrophin-releasing Hormone (GnRH) stimulation test confirmed a peripheral precocious puberty (Table 1). Further imaging by computed tomography (CT) scan showed there was a cystic lesion at the left adnexal region measuring 3.5x1.9 cm without any septa, calcifications, solid component or fat-fluid level. Granulosa cell tumour was suspected; thus, she needed surgery to confirm the diagnosis. After lengthy discussion with the parents, she was subjected for a laparoscopic cystectomy and frozen section examination. Oophorectomy will only be done if the result showed malignant. The result came back as a benign ovarian cyst and she was managed conservatively. Follow-up review noted she was asymptomatic, no more cyst from the ultrasound and tumor markers were in decreasing trend. The diagnosis was autonomous functional ovarian cyst.

Case 4

A 19-month-old girl from Somaliland was unwell for 2 months. She had on and off fever and per vaginal discharge. The vaginal discharge was dark brown in color, noted by the parents when changing diapers. She did not complain of abdominal pain, however experienced difficulty while passing urine. She needed to strain and had poor urine stream. She also had on and off spiking fever especially at night. A month prior to presentation, the child was noted to have yellowish-tinged skin and abdominal distension. She was otherwise active without nausea, vomiting or constitutional symptoms. Examination revealed mild pallor with jaundice. There was a suprapubic mass which was mobile and had smooth surface with regular margins. Ultrasound revealed an intravaginal heterogenous mass. A CT scan of the abdomen noted a large pelvic mass 6.3x6.3x8.0 cm which displaced the uterus superiorly and compressed both the ureters resulting in bilateral hydroureters and hydronephrosis. Serum alpha-fetoprotein (AFP) was

Table 1: Investigation results: Tumour markers and GnRH stimulation test

Tumour markers	**Results**	
Cancer antigen 125 (CA125)	51.0 U/mL	high
Lactate dehydrogenase	381.0 U/L	high
Carcinoembryonic antigen	13.2 ng/mL	high
Alpha fetoprotein (AFP)	2.0 IU/mL	normal
Human Chorionic Gonadotrophin (b-HCG)	<1.0 mIU/mL	normal

Gonadotrophin-releasing Hormone (GnRH) stimulation test	**at 0 minute**	**at 30 minutes**	**at 60 minutes**
Follicular stimulating hormone (FSH)	0.3 IU/L	3.1 IU/L	4.8 IU/L
Luteinizing hormone (LH)	0.1 IU/L	0.6 IU/L	0.8 IU/L
Estradiol	75 pmol/L	-	53 pmol/L

elevated at 11,919 IU/mL. She had an examination under anesthesia and hysteroscopy which showed that there was a fungating vaginal mass and biopsy was taken. HPE report came back as Yolk Sac Tumour of the vagina. Subsequently she underwent chemotherapy with Etoposide, Carboplatin and Bleomycin for 6 cycles and responded well. However, three months later she had a recurrence and the mass had increased in size, causing her to have vaginal bleeding again. She was given a second chemotherapy regime with Vinblastin, Ifosfomide and Cisplatin. However, the response was poor. Subsequently she was planned for a debulking surgery but the surgeons were only able to do limited resection. Sadly, she succumbed to her disease six months post-operatively. In this unfortunate child, the diagnosis was a vaginal malignancy.

Case 5

A 8-year-old girl brought to the clinic by her mother with complain of on and off per vaginal spotting for 2 months. The spotting was about 20 cents coin size and bright red in color. Subsequently, the spotting occurred every month for one to two days. It was so minimal and she didn't need to use any sanitary pads. She denied abdominal pain, urinary or bowel symptoms and any trauma or fall. She didn't have any secondary sexual characteristics development. Hormonal profile showed FSH of 1.0 IU/L, LH of <0.1 IU/L and Estradiol of 57 pmol/L. She had an EUA and noted with normal urethral and vaginal orifices with intact hymen. Vaginoscopy showed normal vaginal wall and cervix without any growth or foreign body. She was also reviewed by pediatric endocrinology and was not suggested as having precocious puberty. The parents were given reassurance. She was monitored in the outpatient clinic and no more vaginal bleeding was noted. Isolated menarche was her final diagnosis.

DISCUSSION

Vaginal bleeding is a common gynecology symptom. However, vaginal bleeding in prepubertal girls is rare (Ng et al. 2020). Clinical assessment of vaginal bleeding in prepubertal girls require a thorough and targeted history taking as well as examination to reach the diagnosis. In order to do appropriate assessment, clinicians need to be equipped with pediatric-specific gynecology examination skills (Howell & Flowers 2016). It is important for the clinicians who are attending to these cases to be familiar with normal variants of pediatric genitourinary anatomy and also able to identify an estrogenised hymen. Furthermore, physical examination and further work up should be done with caution to prevent further trauma to the child (Merritt 1998).

Vaginal examination can be a distressing event for the small girl, thus it is usually limited to perineal inspection by the attending clinician in an outpatient setting. If the source of bleeding is not easily visualised by an external inspection, it is advisable to do an EUA where the situation is under control and an appropriate

and thorough examination can be done (Howell & Flowers 2016). Nasal speculum or vaginoscopy can be used for a better visualisation especially in the upper vagina (Nayak et al. 2014). A recent published paper described the usage of vaginoscopy and warm normal saline as distending media able to visualise small petechiae within the cervix and vaginal wall (Wang et al. 2020). Vaginoscopy is a highly useful and short procedure. It preserves hymenal anatomy and carries low risk of complications. Nevertheless, it is only recommended in patients with unexplained vaginal bleeding (Soderstrom et al. 2016).

An alternative to avoid trauma to the hymen is by using Pediatric Foley specially to look for lesion or foreign body at the level of hymen (Dwiggins & Gomez-Lobo 2014). Small foley catheter can be inserted through the hymen and subsequently the balloon is inflated so that the hymen can be visualised properly. By doing this, any lesion or foreign body near this area can be seen.

The differential diagnose varies, it can be benign or malignant. Benign causes like urethral prolapse and vaginal polyp can present with vaginal bleeding with varying severity. Vaginal bleeding without discharge and presence of intra-labial "doughnut-shaped" mass is a typical presentation for urethral prolapse which can be treated with estrogen cream (Fiogbe et al. 2011). This requires surgical resection only if the estrogen treatment is not efficacious. Vaginal polyp is another rare case where a growth or polyp can be found inside the vagina (Alotay et al. 2015). It is important to get a biopsy for diagnostic confirmation to rule out malignant cause. Simple excision is advisable and recurrence is rare.

Presence of associated ovarian cyst in pubertal girls with vaginal bleeding can be an alarming finding. Juvenile granulosa cell tumour of the ovary can present with precocious puberty (Dwiggins & Gomez-Lobo 2014). As the childhood tumors are aggressive, it is important to determine first the possibility of malignant tumour before proceeding with aggressive surgery like oophorectomy in these young girls. Thus, frozen section is an available option and was done for our patient. Inoperative frozen sections significantly improve the diagnostic of unclear surgical findings (Palakkan et al. 2020). In the patient presented as Case 3, she was more likely to have autonomous functional ovarian cyst as the HPE showed benign ovarian cyst.

Tumor marker tests in children is a challenge because there is variable origin of cell lines that may lead to ovarian malignancy. A study reveals that no single tumor marker provides an accurate prediction of malignancy and a panel of tumour markers which includes AFP, beta human chorionic gonadotrophin (bHCG), lactate dehydrogenase (LDH), cancer antigen 125 (CA125), inhibin A and inhibin B were recommended for preoperative risk stratification in pediatric ovarian neoplasm (Lawrence et al. 2020). Our patient in Case 3 had elevated level of CA125, LDH and carcinoembryonic antigen but the HPE did not conclude as ovarian malignancy. The accuracy

of the suggested panel of tumor markers is currently being investigated (Lawrence et al. 2020).

Autonomous functional ovarian cyst is the most common cause of gonadotrophin-independent precocious puberty in girls. It usually does not require treatment. In a case series reported in Jordon, 89% of 65 ovarian cysts in girls aged 2 to 9 years old and resolved spontaneously within 6 months (Qublan & Abdel-hadi 2000). Surgery can be deferred as long as possible as pseudo-precocious puberty due to these cysts can resolve spontaneously, however it can recur. It is important to conserve normal ovarian tissue for future fertility (Chae & Rheu 2013).

In Case 4, we reported a case of Yolk Sac Tumor of the vagina which was extremely rare and highly malignant. Her clinical presentation was classic with bloody vaginal discharge and huge intravaginal mass. Serum AFP was also raised. Serum AFP is a useful marker and should be taken in girls presenting with huge intravaginal mass. Partial vaginectomy with chemotherapy is the recommended treatment for better prognosis (Alhumidi et al. 2015), however this unfortunate girl did not manage to undergo the surgery. Her late presentation may contribute to the advanced disease thus the tumour was inoperable and risk of recurrence was high.

Isolated menarche is a diagnosis of exclusion when there is no other abnormality detected. The etiology is unclear however it is a self-limiting condition. It is reported to be related to the increased sensitivity of the endometrium to estrogens, similar to increased breast sensitivity to estrogens in premature thelarche (Heller et al. 1979). The major differentiation with precocious puberty is there is no other pubertal signs like accelerated linear growth, advancement of skeletal age and breast development (Pinto & Garden 2016).

CONCLUSION

Pre-pubertal vaginal bleeding is a rare condition but can be a source of fear, anxiety and concern for the girl and the caretakers, regardless whether it occurs as a single, transient or recurring event. The etiology varies thus clinical workout requires careful pediatric-specific gynecological examination followed by relevant investigations and appropriate treatment.

REFERENCES

Alhumidi, A., Al-Shaikh, S., Alhammadi, A. 2015. Yolk sac tumor of vagina: a case report. *Int J Clin Exp Pathol* **8**(2): 2183-5.

Alotay, A.A., Sarhan, O., Alghanbar, M., Nakshabandi, Z. 2015. Fibroepithelial vaginal polyp in a newborn. *Urol Ann* **7**(2): 277-8.

Chae, H.S., Rheu, C.H. 2013. Precocious pseudopuberty due to an autonomous ovarian follicular cyst: case report with a review of literatures. *BMC Res Notes* **6**: 319.

Dwiggins, M., Gomez-Lobo, V. 2017. Current review of prepubertal vaginal bleeding. *Curr Opin Obstet Gynecol* **29**(5): 322-7.

Fishman, A., Paldi, E. 1991. Vaginal bleeding in premenarchal girls: a review. *Obstet Gynecol Surv* **46**(7): 457-60.

Fiogbe, M.A., Hounnou, G.M., Koura, A., Agossou-Voyeme, K.A. 2011. Urethral mucosal prolapse in young girls: a report of nine cases in Cotonou. *Afr J Paediatr Surg* **8**(1): 12-4.

Heller, M.E., Dewhurst, J., Grant, D.B. 1979. Premature menarche without other evidence of precocious puberty. *Arch Dis Child* **54**(6): 472-5.

Howell, J.O., Flowers, D. 2016. Prepubertal vaginal

bleeding: etiology, diagnostic approach, and management. *Obstet Gynecol Surv* **71**(4): 231-42.

Lawrence, A.E., Fallat, M.E., Hewitt, G., Hertweck, P., Onwuka, A., Afrazi, A., Bence, C., Burns, R.C., Corkum, K.S., Dillon, P.A., Ehrlich, P.F., Fraser, J.D., Gonzalez, D.O., Grabowski, J.E., Kabre, R., Lal, D.R., Landman, M.P., Leys, C.M., Mak, G.Z., Overman, R.E., Rademacher, B.L., Raiji, M.T., Sato, T.T., Scannell, M., Sujka, J.A., Wright, T., Minneci, P.C., Deans, K.J., Aldrink, J.H. 2020. Understanding the Value of Tumor Markers in Pediatric Ovarian Neoplasms. *J Pediatr Surg* **55**(1): 122-5.

Merritt, D.F. 1998. Evaluation of vaginal bleeding in the preadolescent child. *Semin Pediatr Surg* 7(1): 35-42.

Nayak, S., Witchel, S.F., Sanfilippo, J.S. 2014. Vaginal foreign body: a delayed diagnosis. *J Pediatr Adolesc Gynecol* **27**(6): e127-9.

Ng, S.M., Apperley, L.J., Upradrasta, S., Natarajan, A. 2020. Vaginal bleeding in pre-pubertal females. *J Pediatr Adolesc Gynecol* **33**(4): 339-42.

Palakkan, S., Augestine, T., Valsan, M.K., Vahab, K.P.A., Nair, L.K. 2020. Role of frozen section in surgical management of ovarian neoplasm. *Gynecol Minim Invasive Ther* 9(1): 13-7.

Pinto, S.M., Garden, A.S. 2006. Prepubertal menarche: a defined clinical entity. *Am J Obstet Gynecol* **195**(1): 327-9.

Qublan, H.S., Abdel-hadi, J. 2000. Simple ovarian cysts: frequency and outcome in girls aged 2-9 years. *Clin Exp Obstet Gynecol* **27**(1): 51-3.

Soderstrom, H.F., Carlsson, A., Borjesson, A., Elfving, M. 2016. Vaginal bleeding in prepubertal girls: etiology and clinical management. *J Pediatr Adolesc Gynecol* **29**(3): 280-5.

Wang, X., Zeng, W., Xu, S., Huang, L., Lai, Y., Yu, Y. 2020. A case report and literature review of vaginal bleeding in prepubertal girl. *Acta Paediatr* **109**(10): 1944-7.

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