Case Report

Stuttering priapism in a pediatric patient with pheochromocytoma-induced thrombocytosis

Sarayuth Boonchai, Surasak Sangkhathat[1,2], Wison Laochareonsuk[1,2], Worapat Attawettayanon[3]

Department of Surgery, Division of Urology, Faculty of Medicine, Prince of Songkla University, [1]Department of Surgery, Division of Pediatric Surgery, Faculty of Medicine, Prince of Songkla University, [2]Translational Medicine Research Center, Faculty of Medicine, Prince of Songkla University, [3]Department of Surgery, Division of Urology, Faculty of Medicine, Songklanagarind Hospital, Prince of Songkla University, Hat Yai, Songkhla, Thailand

Abstract

Priapism is an erection of more than 4 h without sexual stimulation. Ischemic priapism may lead to irreversible erectile dysfunction after a long-lasting period. Stuttering priapism is characterized by a pattern of recurrence that may progress to an unrelenting ischemic crisis, which is a urological emergency. Few reports have revealed that priapism is associated with essential thrombocythemia. The reactive thrombocytosis is uncommonly manifested by pheochromocytoma and rarely causes thrombotic events even if the platelet count is extremely high. We presented priapism related to reactive severe thrombocytosis in a 12-year-old male with pheochromocytoma. The cornerstone of care was prompt medical and surgical intervention by a multidisciplinary team approach to save life and preserve erectile function.

Keywords: Pediatric, pheochromocytoma, stuttering priapism, thrombocytosis

Address for correspondence: Dr. Worapat Attawettayanon, Department of Surgery, Division of Urology, Faculty of Medicine, Songklanagarind Hospital, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand.
E-mail: aworapat@medicine.psu.ac.th

Received: 03.07.2021, **Revised:** 18.09.2021, **Accepted:** 16.10.2021, **Published:** 18.07.2022

INTRODUCTION

Priapism is an inappropriate long-lasting erection without sexual stimulation. In children and adolescents, it is most commonly related to sickle cell disease which is associated with ischemic crisis. Besides hematologic dyscrasias, thrombotic disease states have been cited as precipitants.[1] Several reports have claimed that essential thrombocythemia was associated with ischemic priapism.[2,3] Pheochromocytoma is a catecholamine-secreting tumor that arises from chromaffin cells of the adrenal medulla.[4] Thrombocytosis was reported as a rare manifestation associated with interleukin-6 (IL-6) producing pheochromocytoma.[5] This report is a case of a 12-year-old boy who presented with headache and sweating related to hypertension for 3 years. He had a history of stuttering priapism for the past 6 months. Finally, he developed ischemic crisis priapism, which was managed by cavernosal aspiration followed by the right adrenalectomy.

CASE REPORT

A 12-year-old boy was presented with intermittent headache and sweating for 3 years. Occasionally, he experienced self-limited prolonged unintentional erection for the past 6 months. His blood pressure and pulse rate were 150/90 mmHg and 115 beats/min, respectively.

Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/ua.ua_118_21

How to cite this article: Boonchai S, Sangkhathat S, Laochareonsuk W, Attawettayanon W. Stuttering priapism in a pediatric patient with pheochromocytoma-induced thrombocytosis. Urol Ann 2022;14:283-7.

Hypertension was controlled with doxazosin, metoprolol, and nicardipine. Clinical examination did not show thyroid gland enlargement, abdominal mass, or bruit. The laboratory investigation revealed hemoglobin 10.7 g/dL, white blood cell count 11,590/μL, and platelet count 710,000/μL. The abdominopelvic and thoracic computed tomography showed a 4.2 cm × 4.5 cm × 6.4 cm heterogeneous arterial enhancing mass at the right adrenal gland without evidence of distant metastasis or local invasion [Figure 1]. Subsequently, morning serum cortisol and aldosterone were 18.47 (5.90–26.10) and 21.45 (9.70–62.60), respectively. The serum normetanephrine, metanephrine, and 3-methoxytyramine were 7310.37 pmol/mL (0.00–953.00), <25.35 pmol/mL (0.00–371.00), and <5.98 pmol/mL (0.00–90.00), respectively. The 24-h urine normetanephrine, metanephrine, and 3-methoxytyramine were 9378.03 μg (0.00–659.50), 222.51 μg (0.00–374.70), and 359 μg (0.00–459.80), respectively. During hospitalization, he developed a painful spontaneous erection, lasting longer than 5 h. The penile examination showed rigid tumescence of the corpus cavernosum [Figure 2]. The repeated platelet count was 945,000/μL. After intravenous hydration, the patient was emergently sent to the operating room. The intraoperative corporal blood gas, obtained under anesthesia, revealed pH at 6.83, partial pressure of carbon dioxide (pCO_2) at 79.6 mmHg, and partial pressure of oxygen (pO_2) at 16.3 mmHg, suggestive of ischemic priapism. Immediately, bilateral corporal blood aspiration was performed together with normal saline solution irrigation [Figure 3]. One hundred milliliters of dark blood was obtained and the corpus cavernosum returned detumescent [Figure 4]. Finally, bright red blood was achieved and repeated corporal blood gas revealed pH at 7.46, pCO_2 at 26.5 mmHg, and pO_2 74.2 mmHg. Postoperatively, aspirin (4 mg/kg/day) was prescribed by the hematologist and platelet count was 838,000/μL. Two weeks later, open right adrenalectomy was performed for suspicious pheochromocytoma. Intraoperative blood pressure was elevated during manipulated adrenal mass. Anesthesiologist used sodium nitroprusside to control blood pressure. Postoperatively, the blood pressure was 105/55–120/60 mmHg and platelet count was 300,000/μL. The serum metanephrine, normetanephrine, and 3-methoxytyramine were 393.07 pmol/mL (0.00–953.00), <25.35 pmol/mL (0.00–371.00), and <5.98 pmol/mL (0.00–90.00), respectively. The 24-h urine normetanephrine, metanephrine, and 3-methoxytyramine were 523.56 μg (0.00–659.50), 49.43 μg (0.00–374.70), and 91.49 μg (0.00–459.80), respectively. The pathological result was

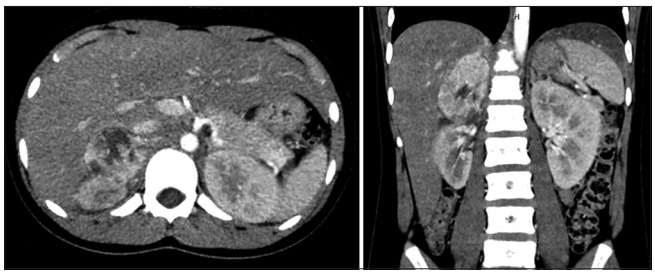

Figure 1: The contrast-enhanced computed tomography of the abdomen revealed a right adrenal mass

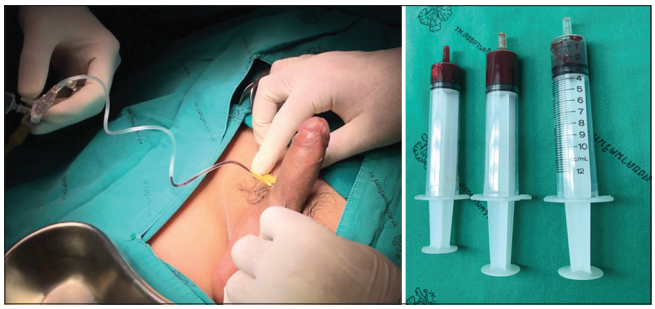

Figure 3: Cavernosal blood aspiration

Figure 2: External male genitalia with preoperative, rigid penile erection

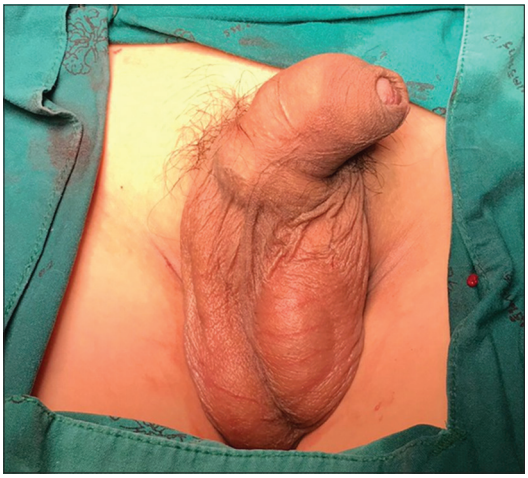

Figure 4: Penile detumescence, immediately postoperation

pheochromocytoma [Figures 5 and 6]. Three weeks after adrenalectomy on follow-up, his blood pressure was 112/72 mmHg without antihypertensive medications. The surgical site healed up and the priapism has not recurred. Morning penile erection was restored. To look for genetic predisposition in this case, a whole-exome sequencing at ×100 depth was performed using DNA from the tumor tissue and blood leukocytes. The study revealed heterozygous missense mutation of VHL at the position chr3:g.10146530C>G (rs1559428077, GRCh38.p13) at the variant depth 64/139 and RET proto-oncogene (RET) at the position chr10:43114671G>A at the variant depth 172/340. Direct nucleotide sequencing confirmed these mutations [Figure 7]. The VHL variant is predicted pathogenic by SIFT and PolyPhen tool and has been reported for its association with pheochromocytoma (CM951287) when RET (rs1799939) has been reported for its association with the disease in ClinVar database.[6]

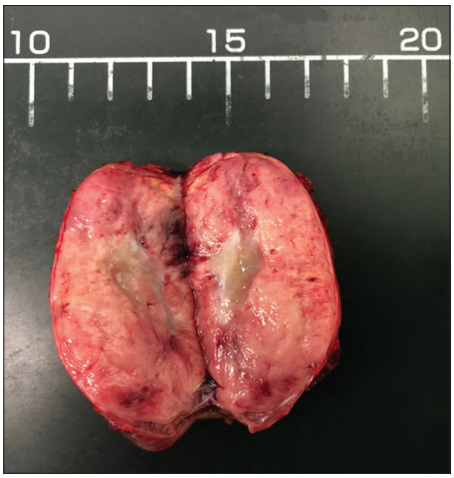

Figure 5: Gross pathology of the right adrenal gland

DISCUSSION

Priapism is an erection unrelated to sexual stimulation that continues for more than 4 h. Stuttering priapism is characterized by a pattern of recurrence and may progress to unrelenting ischemic priapism which is a urological emergency.[1] The management of each acute episode is similar to that for ischemic priapism and should start within 4–6 h because erectile function preservation is directly related to the duration of priapism.[7] Cavernosal blood gas indicated that hypoxia (pO_2 <30 mmHg), hypercarbia (pCO_2 >60 mmHg), and acidosis (pH <7.25) typically suggest ischemic priapism. Interventions beyond 36 h of onset may help relieve erection and pain but have no benefit in preserving potency. The immediate implantation of a penile prosthesis is recommended.[1,7] Treatment options include therapeutic aspirations and intracavernous sympathomimetic drugs, with the latter prohibited for our patient with suspicious pheochromocytoma. Distal and proximal shunt procedures should be considered if necessary. Priapism could be a rare side effect of doxazosin;[8] however, the drug is less likely cause of the condition in this patient because it had been prescribed for a long period.

Only 24% of patients with pheochromocytoma have classic triads.[9] Reactive thrombocytosis was reported as a rare manifestation of pheochromocytoma which induced megakaryocytosis via IL-6–mediated inflammation and endogenous catecholamines.[10] Extreme thrombocytosis may rarely result in thrombotic events.[11] ASA is usually not indicated in reactive thrombocytosis unless platelets are more than 1,000,000/μL and patients are at risk of or have already developed thrombocytosis complications.[12] Regarding pediatric neuroendocrine tumors, laparoscopic

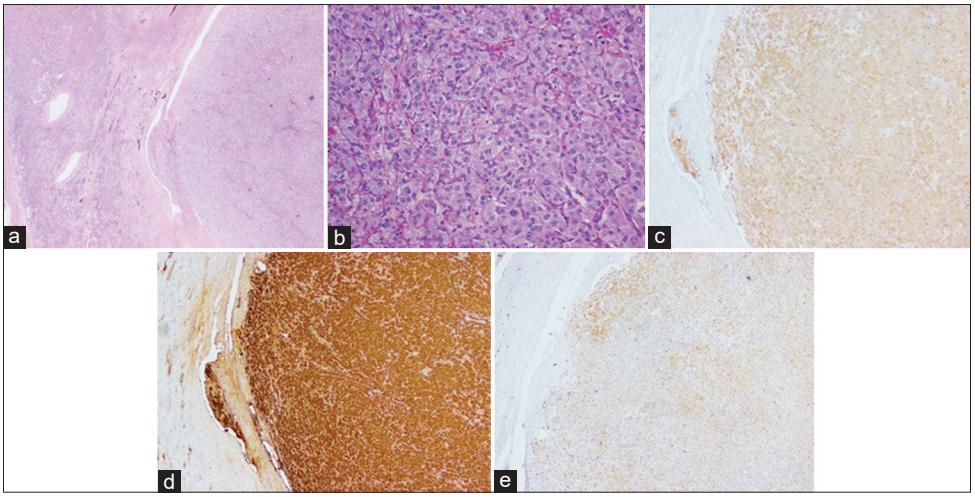

Figure 6: Histopathology of the right adrenal gland. (a: Area of the tumor and normal adrenal gland, b: Zellballen pattern, c: diffused positive synaptophycin stain, d: diffused positive chromogranin stain, e: weakly positive S-100 stain

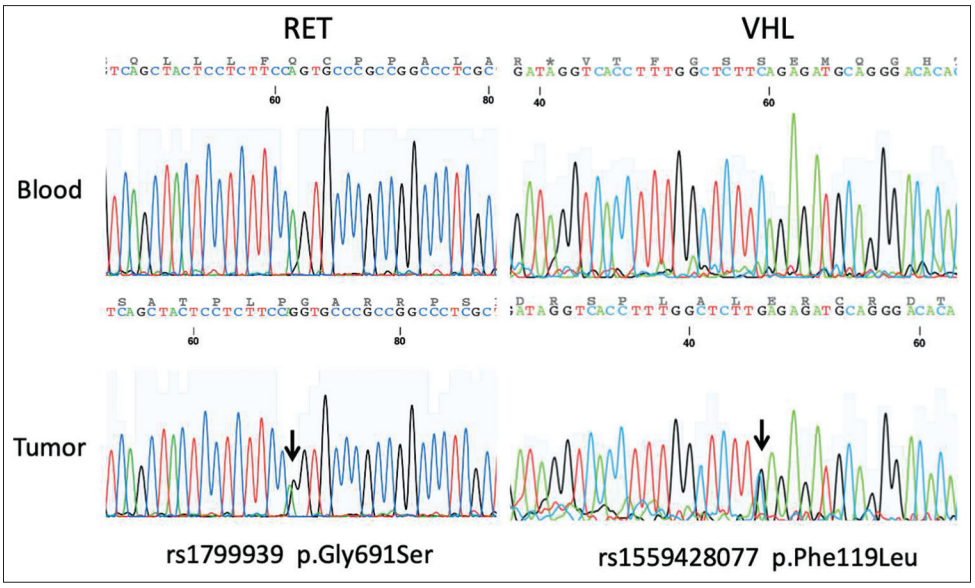

Figure 7: Electropherograms showing somatic mutation of RET (rs1799939) and VHL (rs1559428077) in this patient

resection and adrenal cortical-sparing procedures are now the preferred approaches.[13] However, open adrenalectomy was performed due to concerns of malignancy.

Our patient suffered from pheochromocytoma with severe reactive thrombocytosis which caused stuttering priapism progression to an ischemic crisis. Using appropriate immediate intervention as a guideline,[7] he responded well with adequate cavernosal blood aspiration, resulting in secondary prevention with ASA. Finally, open right adrenalectomy was carried out with histopathological-confirmed pheochromocytoma.

We suggest ASA prophylaxis in children with pheochromocytoma-induced severe reactive thrombocytosis to primarily prevent early thrombotic complications such as ischemic priapism, until an adrenalectomy.[10,14]

CONCLUSION

Stuttering priapism with ischemic crisis is a urological emergency that requires prompt medical and surgical interventions with caution in pheochromocytoma. Correction of the causative factors prevents recurrence and improves subsequent functional outcomes. A multidisciplinary approach is recommended.

Informed consent

A written informed consent was obtained from the patient to publish his medical data and images. Consent approved from ethical and research committees of institute obtained.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal patient identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Levey HR, Segal RL, Bivalacqua TJ. Management of priapism: An update for clinicians. Ther Adv Urol 2014;6:230-44.
2. Bazhenova L, Du EZ, Bhoyrul S, McCallum J, Saven A. Reactive thrombocytosis associated with a pheochromocytoma. Thromb Haemost 2005;94:460-2.
3. Verma SP, Kumar N, Jain M, Tripathi AK. Essential thrombocythemia presenting with recurrent priapism: A case report and review of literature. Asm J Case Rep 2020;21:e924455.
4. Patel D, Phay JE, Yen TW, Dickson PV, Wang TS, Garcia R, *et al.* Update on pheochromocytoma and paraganglioma from the SSO endocrine/head and neck disease-site work group. Part 1 of 2: Advances in pathogenesis and diagnosis of pheochromocytoma and paraganglioma. Ann Surg Oncol 2020;27:1329-37.
5. Yarman S, Soyluk O, Altunoglu E, Tanakol R. Interleukin-6-producing pheochromocytoma presenting with fever of unknown origin. Clinics (Sao Paulo) 2011;66:1843-5.
6. Aghdam MN, Abbaszadegan MR, Tafazoli A, Aslzare M, Mosavi Z. Presence of the RET Cys634Tyr mutation and Gly691Ser functional polymorphism in Iranian families with multiple endocrine neoplasia type 2A. Hormones (Athens) 2016;15:65-72.
7. Salonia A, Eardley I, Giuliano F, Hatzichristou D, Moncada I, Vardi Y, *et al.* European Association of Urology guidelines on priapism. Eur Urol 2014;65:480-9.

8. Spagnul SJ, Cabral PH, Verndl DO, Glina S. Adrenergic α-blockers: An infrequent and overlooked cause of priapism. Int J Impot Res 2011;23:95-8.
9. Baguet JP, Hammer L, Mazzuco TL, Chabre O, Mallion JM, Sturm N, *et al*. Circumstances of discovery of phaeochromocytoma: A retrospective study of 41 consecutive patients. Eur J Endocrinol 2004;150:681-6.
10. Scharf RE. Do we need antiplatelet therapy in thrombocytosis? Contra. Proposal for an individualized risk-adapted treatment. Hamostaseologie 2016;36:241-60.
11. Bholah R, Bunchman TE. Review of pediatric pheochromocytoma and paraganglioma. Front Pediatr 2017;5:155.
12. Alberio L. Do we need antiplatelet therapy in thrombocytosis? Pro. Diagnostic and pathophysiologic considerations for a treatment choice. Hamostaseologie 2016;36:227-40.
13. Kucine N, Chastain KM, Mahler MB, Bussel JB. Primary thrombocytosis in children. Haematologica 2014;99:620-8.
14. Harrison CN, Bareford D, Butt N, Campbell P, Conneally E, Drummond M, *et al*. Guideline for investigation and management of adults and children presenting with a thrombocytosis. Br J Haematol 2010;149:352-75.