Case Report

Cause or Coincidence? Spontaneous Hematometra in Young Women Receiving Depomedroxyprogesterone Acetate: A Small Case Series

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A B S T R A C T

Background: Abdominal pain, secondary amenorrhea, and abnormal uterine bleeding are common gynecologic presentations in adolescence. Rarely this can be associated with an acquired hematometra. Hematometra is a condition of retained blood or clot within the uterus. High-dose progestogenic agents in this age group have been implicated in the accumulation of a hematometra without other explanation.
Cases: We present 4 cases of hematometra after depomedroxyprogesterone acetate (DMPA) therapy in previously menstruating adolescents. All 4 presented with abdominal pelvic pain and/or persistent abnormal uterine bleeding, with the diagnosis confirmed via ultrasound. Suction dilation and curettage was required in each case.
Summary and Conclusion: DMPA is a possible cause of hematometra and should be considered in anatomically normal young women experiencing pain or abnormal bleeding out of character for typical long-term DMPA use.
Key Words: Contraceptive agents, Depomedroxyprogesterone acetate, Hematometra, Adolescence

Introduction

Abdominal pain and abnormal menstruation are common complaints in adolescence. The differential diagnosis is broad.[1] Hematometra refers to the collection of blood or clot within the uterus, generally due to some form of outflow obstruction.[2] The obstruction might be primary (eg, Müllerian anomalies) or secondary (as after pregnancy or surgical instrumentation) and can represent an important cause of abdominal pain and abnormal bleeding. To date, medical therapy has not been cited as a precipitating cause of acquired hematometra in women who had experienced normal menarche. We present 4 cases of secondary hematometra that developed after initiation of depomedroxyprogesterone acetate (DMPA) intramuscular (IM) injection therapy in adolescence (Table 1). Consent was obtained in writing and this case series received institutional review board approval.

Cases

Case A

Patient A is a 15-year-old girl referred for menstrual suppression in the context of global developmental delay. At the time, she was well beyond menarche and had normal pelvic imaging. Ultimately, she was given DMPA 150 mg intramuscular (IM) treatment every 12 weeks. This interval was reduced to 10 weeks when the breakthrough bleeding did not abate. After more than 1 year of therapy and no resolution of the abnormal bleeding pattern, she underwent a pelvic ultrasound examination in which the diagnosis of a hematometra was made. The hematometra persisted on a repeat ultrasound 3 months later (Fig. 1). Patient A was brought to the operating room for an examination under anesthesia. The cervix easily admitted a number 4 Hagar dilator and no obstruction was identified (Fig. 2). A moderate amount of dark blood was evacuated and a 19.5-mg levonorgestrel intrauterine device (LNG-IUS) was placed at the same time. No specimen was sent for pathology. No further DMPA injections were ever given. An ultrasound examination was repeated 4 months postoperatively. She had reaccumulated an (albeit smaller) hematometra despite the LNG-IUS (largest dimension, 4.6 cm) but her bleeding was markedly less. A further 3 months later (at the time of submission of this report), the hematometra has spontaneously regressed with a largest dimension of 2.7 cm but is still visible. It is of possible significance that at the time of dilation and curettage (D&C) and LNG-IUS placement, DMPA continued to be therapeutic and had not been discontinued for sufficient duration to have completely cleared.

Case B

Patient B presented for gynecologic care at the age of 17 years with chronic pelvic pain and dysmenorrhea. Minimal endometriosis was diagnosed at diagnostic

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Table 1
Summary of Cases

Case	Age Entering Care, years	Presenting Concern	Duration DMPA Therapy	Ultrasound Findings	Therapy for Hematometra	Hematometra Recurrence?
A	15	Desire for menstrual suppression (global development delay)	>12 Months	• Pre-DMPA: normal pelvis • Post-DMPA: hematometra	• Exam under anesthesia • Suction D&C • Placement of a 19.5-mg LNG-IUS	Yes • Reaccumulation of hematometra after D&C. Resolved on serial ultrasound
B	17	Cyclic pelvic pain	5 Years	• Thickened endometrium with multiple cystic spaces, ?polyp (hematometra)	• Initial drainage at time of sonohysterogram • Suction D&C • Estrogen therapy postoperatively • Conception within 1 year of D&C, after ceasing estrogen therapy	No • 2 Complete pregnancies since surgical therapy and no interval hormonal therapy for contraception, no pelvic pain
C	15	Frequent menses, pelvic pain	1 Year	• Initially unremarkable • 3 Months after laparoscopy, a large hematometra had accumulated	• Diagnostic laparoscopy: torted right salpinx, mild endometriosis • 3 Months after laparoscopy a suction D&C was performed	Yes • Spontaneous resolution • Placement of a 52-mg LNG-IUS when hematometra resolved • LNG-IUS replaced after 5 years, no recurrence
D	23	Cyclic pelvic pain	7 Years, after diagnostic laparoscopy showed minimal endometriosis	• Large hematometra effacing cervix and ballooning the lower uterine segment • Large bilateral endometriomas	• Suction D&C under anesthesia	Yes • 2nd D&C done • IM leuprolide planned • Patient D was then lost to follow-up

D&C, dilatation and curettage; DMPA, depomedroxyprogesterone acetate; LNG-IUS, levonorgestrel intrauterine device.

laparoscopy. Treatment was started with DMPA IM injection 150 mg every 12 weeks as medical therapy as well as for contraception. She continued to receive DMPA for the next 5 years when she had recurrence of her pelvic pain. Ultrasound imaging showed a small slip of fluid in the uterine cavity with an endometrial lining of 5.9 mm and a small ovarian cyst. A repeat ultrasound examination 5 months later to reassess the ovarian cyst revealed cyst resolution but also a "thickened endometrium with multiple cystic spaces" (Fig. 3). This was radiologically interpreted as a possible polyp and as such a sonohystogram was performed. A 5-French catheter was inserted easily and dark

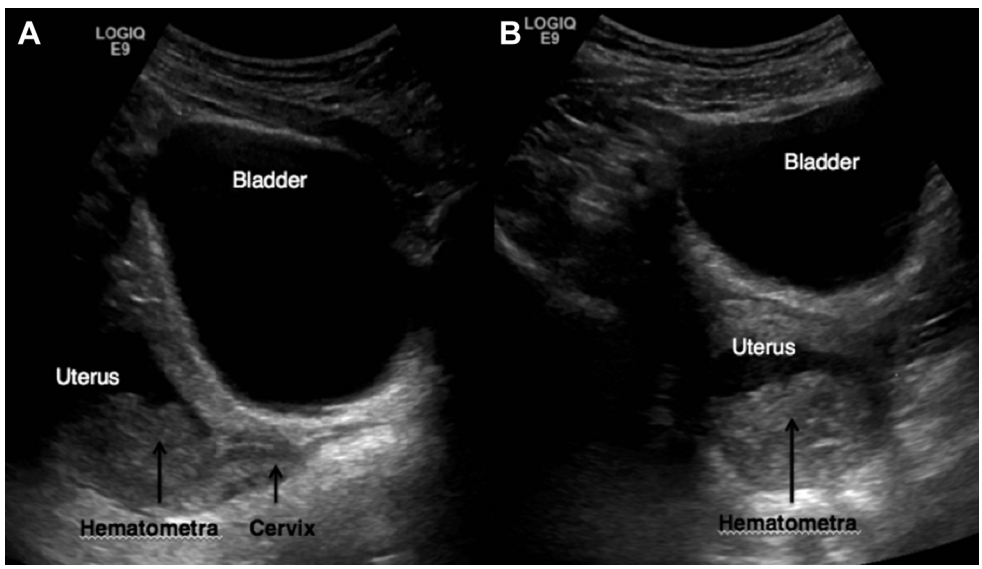

Fig. 1. Pelvic ultrasound (A) sagittal; and (B) transverse.

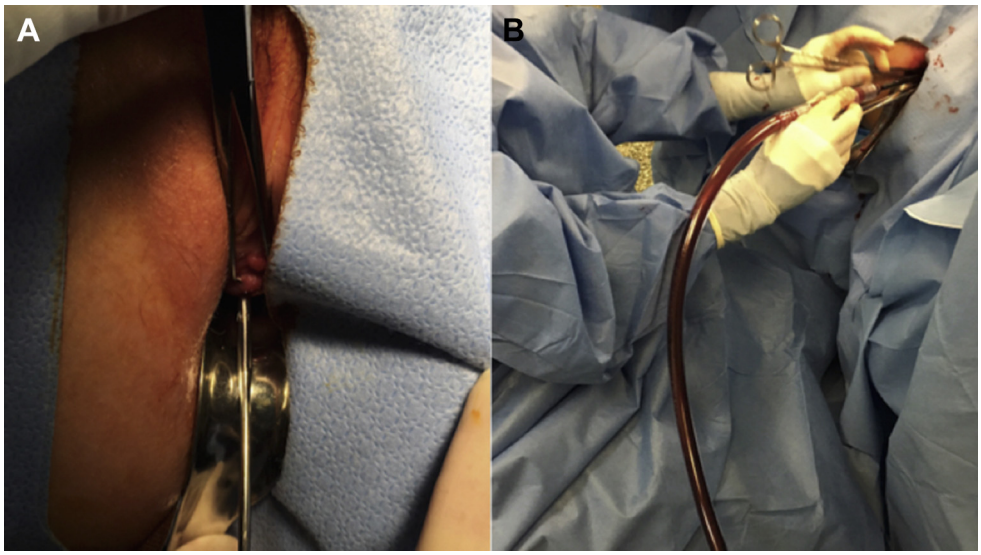

Fig. 2. (A) Easy cervical dilation with Hegar dilator. No evidence of obstruction. (B) Suction curettage to remove uterine hematometra.

blood drained immediately. No polyp was identified. A D&C was performed that same month. No cervical stenosis was noted and a moderate amount of old blood was drained. Oral estrogen therapy was used in addition after the D&C, with the concern at the time being that prolonged DMPA might have caused atrophy and easy bleeding of the endometrium. Patient B ceased both hormonal therapies shortly after the D&C, and she went on to conceive, as planned, within the year. She resumed DMPA postpartum. There was no recurrence of the hematometra. She has subsequently had at least 1 other child.

Case C

Patient C initially presented for gynecologic care at the age of 15 years with frequent menstrual cycles. She went on to develop painful cycles and ultimately started DMPA injections every 12 weeks at the age of 17 years with good initial effect. She developed abnormal bleeding and pelvic pain again after DMPA treatment for 1 year. Ultrasound imaging was negative. She was taken for a diagnostic laparoscopy and a chronically torted right salpinx was identified and detorted. Findings also included pelvic adhesions around the torsion (lysed), hemosiderin deposits, and flame-like hemorrhages. Although no biopsy was performed, the impression was of likely endometriosis. A Hulka tenaculum was used on the cervix during laparoscopy and the cervix accommodated the instrument easily. Within 3 months of the laparoscopy, during DMPA treatment, the patient developed pelvic pain associated with bleeding and was found to have a large hematometra. She was brought to the operating room for a D&C with no noted cervical stenosis. Dark blood was drained, consistent with a hematometra. She reaccumulated a hematometra within

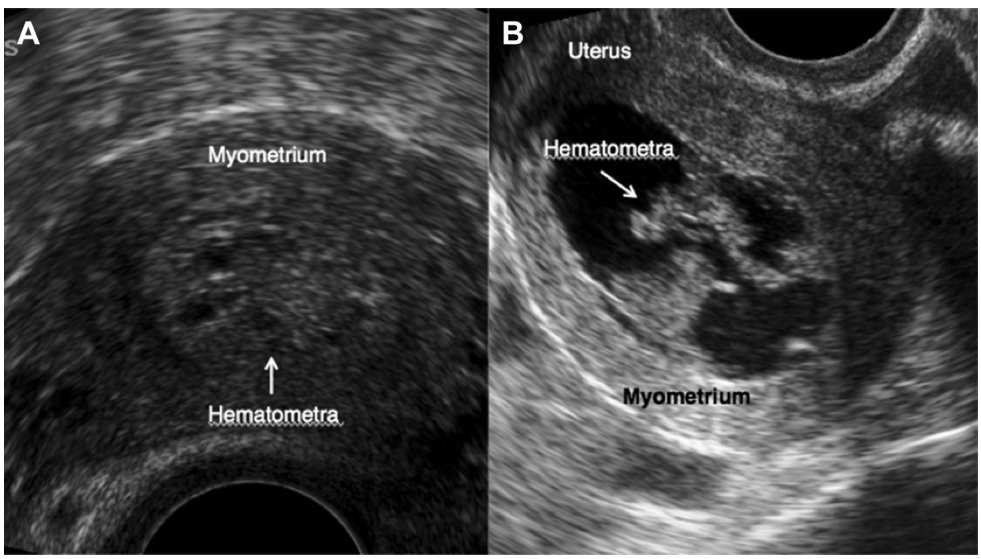

Fig. 3. (A) Pelvic ultrasound (transverse); (B) pelvic sonohysterogram (transverse).

1 month of her D&C. This spontaneously resolved and patient C ultimately had a 52-mg LNG-IUS placement 4 months after D&C for menstrual management. The hematometra has not re-collected and she recently had her LNG-IUS replaced because it reached the end of its 5-year life span.

Case D

Patient D lived in a very remote community. At 16 years of age she had normal flow but intractable cyclic pelvic pain during menses and underwent a diagnostic laparoscopy. Minimal endometriosis was found. She received DMPA and continued to receive it for 7 years. After that, she never menstruated but had ongoing pain, always attributed to the combination of DMPA amenorrhea and endometriosis pain. She was finally assessed with severe abdominal pelvic pain 7 years later. She had a very large hematometra bulging out the lower uterine segment and effacing the closed (but not stenotic) cervix. She also had bilateral endometriomas and stage 4 endometriosis. The hematometra was drained and again the cervix was noted to dilate easily. The endometriosis was planned to be medically managed with leuprolide. Unfortunately she has been lost to follow-up.

Summary and Conclusion

DMPA is typically dosed as a 150-mg IM injection every 12 weeks for contraception and menstrual management.[3] It has been reported to be effective for menstrual suppression, to reduce menstrual blood loss, and reduce cyclic pain (as is seen with primary dysmenorrhea, adenomyosis, and endometriosis). It inhibits the secretion of luteinizing hormone and follicular stimulating hormone thus inhibiting ovulation. It has the added effect of increasing cervical mucous, slowing tubal cilia motility, and thinning the endometrial lining.[4] Peak plasma concentrations can reach up to 7 ng/mL, which is below serum levels in women in the luteal phase not exposed to exogenous hormone.[3,4]

We present 4 cases of hematometra after DMPA therapy in adolescents. They each presented for menstrual management with or without pelvic pain, and proceeded to develop abnormal bleeding or secondary amenorrhea and pelvic pain despite adherence to DMPA injections. The hematometra were all fully evacuated with suction D&C in the operating room. The hematometra reoccurred in 2 of the 4 cases (1 with an LNG-IUS and the other without). In one recurrence, the second blood collection resolved spontaneously and we are hopeful this will occur in the other. Lingering DMPA is postulated. Two of our cases have had an LNG-IUS inserted; patient A, a 19.5-mg LNG-IUS at time of D&C, and patient C, a 52-mg LNG-IUS 4 months after D&C.

We are not sure whether adolescent age is an independent risk factor.

If DMPA is causative in the development of a hematometra, the mechanism remains unclear. One possible explanation might be that of a decidual cast secondary to high levels of progestin. This has been postulated in previously published case reports of adolescents who developed abdominal pain and passed tissue per vagina after initiating combined as well as progesterone-only therapy.[5] It is conceivable that such a cast cannot easily pass through the cervical canal and could lead to functional obstruction. Unfortunately the suctioned uterine contents were not sent to pathology in these 4 described cases. Pathologic description of a decimal cast would bolster this hypothesis. Alternatively it is possible such relatively high doses of systemic progestin allow the cervical mucous to become so thick there is a functional outflow obstruction. Contrary to a previous case report by Ivan et al[6] cervical stenosis was not appreciated at the time of surgery in any of our cases. Alternatively or in combination, DMPA's progesterone-like activity to enhance smooth muscle laxity might have impaired outflow. Finally, 3 of our 4 cases had surgical findings consistent with endometriosis before being given DMPA and the other case has not had laparoscopy. None of our cases had hematometra before DMPA. We are not sure whether endometriosis could be an independent risk factor or just that DMPA was preferentially prescribed to adolescents with symptomatic endometriosis. Regardless, to our knowledge this is the second published report to question an association of DMPA with the acquisition of a hematometra,[5] and the only case series.

DMPA is a possible cause of hematometra and hematometra should be considered in women experiencing pain and or abnormal bleeding out of character for typical long-term DMPA use. Ultrasound imaging should be included as part of the investigations. Surgery was the chosen definitive management therapy, however, medical uterotonics could have been considered, such as misoprostol, ergotamine, or carboprost trimethamine.

We hope to inspire a larger case series to develop a more sophisticated theory and association. A prospective North American Society for Pediatric and Adolescent Gynecology-maintained database with regimented data collection is one way such a rare presentation could be tracked. Alternatively, asymptomatic patients receiving long-term DMPA therapy could undergo serial pelvic ultrasound examinations as part of a prospective cohort study investigating the incidence of hematometra in those individuals.

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