Spotting the culprit; A rare case of hematometra in a menstruating female with Fraser Syndrome

Abstract:

Background:
Fraser syndrome is a rare autosomal disorder that is associated with multiple genetic abnormalities. Discussed here is one abnormality associated with the genital tract.

Case Description:
A 19-year-old female with Fraser syndrome presented to the pediatric emergency department for abdominal distention and pain for two days, noted to have hematometra on CT guided imaging. Decision was made to proceed with total abdominal hysterectomy bilateral salpingoophorectomy.

Conclusion:
This case highlights the rarity of Fraser syndrome with associated hematometra secondary to both internal and external genital abnormalities post-menarche. Hematometra should be a differential diagnosis in patients with syndromes that are associated with genital abnormalities as failure to drain the retained blood and tissue products, can act as a foci for infection.

Introduction:
Fraser syndrome is a rare autosomal disorder with an incidence below 0.043 per 10.000 live born infants and 1.1 in 10.000 stillbirths. It is characterized by cryptophthalmos, syndactyly, and abnormalities of the genitalia and urinary tract. This is a case of a 19-year-old-female with Fraser syndrome presenting with hematometra post-menarche.

Disclaimers:
There are no ethical issues in this manuscript as verbal consent was obtained by the mother of this patient and the patient has been deidentified throughout this manuscript.

Case:

ED Course
A 19-year-old female with a past medical history of Fraser syndrome presented to the pediatric emergency department (ED) secondary to a one-week history of abdominal distention and pain. Due to her condition, she is nonverbal with significant developmental delay and is gastric tube dependent with blindness. In the emergency department, patient was tachycardic to 140 bpm, normotensive 100-110/60-90 mmHg, and demonstrated voluntary and involuntary guarding behaviors as per her family. History was obtained by family who reported the patient would express severe discomfort with tube feeds and enlarging abdominal girth. These symptoms were proceeded by a three-week period of vaginal bleeding which had resolved at time of presentation. There were no changes in urinary or bowel movement habits.

Of note, patient had her first menses 7-months prior to presentation with irregular cycles since menarche. However, one month prior to her ED visit, the patient was found to have heavy

bleeding with clots for three weeks. The patient was evaluated by gynecologist and was given one injection of Depo-Provera to regulate menses. The mother reported that no pelvic examination was done at that time of visit, however, she explicitly stated that she has had pelvic examinations in the past.

On physical examination, there was significant abdominal distention with a mass arising in the pelvis and extending to the xiphoid. She expressed pain diffusely with palpation of the abdomen. A pelvic examination demonstrated significant labial adhesions and vaginal introitus and urethra were not able to be visualized. Secondary sexual characteristics were grossly normal appearing, breasts were normal appearing for 20 year old female. Basic labs were drawn and she was given intravenous (IV) analgesics with IV fluid hydration. Initial blood work demonstrated leukocytosis (white blood count 15.28 x10(3)/mcL) with neutrophil predominance and mild anemia (hemoglobin 9.2 gm/dL). Imaging studies were obtained including transabdominal ultrasound of the abdomen and pelvis and computerized tomography (CT) scan with oral and IV contrast. Imaging demonstrated a very large fluid-filled abdominopelvic mass, potentially representing a massively dilated fluid-filled uterus and mild hydronephrosis (Figure 1 and 2). No other urinary tract abnormalities were noted. Gynecology was initially consulted, and due to the complex nature of the patient's syndrome, as well as concern for significant anatomical variants, GYN-Oncology was then consulted. After thorough review of patient's condition and imaging, the patient was taken to the operating room. Decision was ultimately made to proceed to the operating room based on patient's persistent tachycardia and severe pain.

Hospital Course

At this point, primary differential diagnosis included large volume hematometra versus malignancy of gynecologic origin. Because of the patient's acute presentation and potential impending hemodynamic compromise, the patient was taken to the operating room urgently, in the middle of the night. The plan was to first evaluate the pelvis more adequately with examination under anesthesia (EUA) and perform further procedures as necessary while minimizing surgical risk. In the operating room, EUA was significant for hypertrophic labia with a blind vaginal pouch, a 2-3 cm vaginal opening, absent cervix, and an indistinguishable urethral meatus. In the operating room, the patient remained tachycardiac and hypotensive despite aggressive fluid resuscitation. Due to these findings abdominal approach was necessary to evaluate the contents of the mass and stabilize the patient. The abdominal examination demonstrated large firm mass which grossly distorted the abdomen and was evident below the abdominal wall, extending from the pelvis to the costal margins. Veress needle was used to puncture the skin and enter the mass supraumbilically in the midline. The mass was entered and the contents were consistent with copious dark fluid consistent with chronic hemorrhage. To adequately drain the mass, a small, 2 cm incision was made at this entry site, so that large caliber suction devise could be placed inside the mass. 2000 millimeters (mL) of dark, chocolate, old hemorrhagic fluid was drained. The patients' vitals stabilized, the abdominal incision was closed and the patient was successfully extubated and transferred to the pediatric unit. On post-operative day one, patient's abdominal distention had resolved, and she was tolerating her gastric tube feeds well. She was discharged later that day with plan for outpatient follow up with gyn oncology to plan definitive management.

At outpatient follow up, the high likelihood of recurrent hematometra was discussed. Therefore, patient's parents elected to proceed total abdominal hysterectomy. She then underwent elective total abdominal hysterectomy, bilateral salpingoophrectomy, extensive lysis of adhesions, and bilateral ureterolysis. Surgical findings included a massively distended uterus secondary to recurrent hematometra. The left ovary was completely replaced by a complex mass consistent with hemorrhagic cyst and endometriosis. The left fallopian tube was grossly dilated consistent with hematosalpinx, the right fallopian tube and ovary were overall grossly normal, however abnormally positioned on the superior right pelvic side wall abutting the kidney. The ureters were abnormally positioned and traveling on the lateral uterine walls bilaterally. The uterine cavity was massively ballooned and there was no obvious cervix. A portion of the lower uterine segment/cervical remnant was left in situ secondary to the high risk of both bladder and ureteral injury with removal. Final pathology demonstrated benign pathology with inactive endometrium with acute and chronic inflammation as well as endometriosis involving the left adnexal structures. Her post operative course was uneventful.

Discussion

This 19-year-old female with Fraser syndrome, which is a syndrome characterized by cryptophthalmos, cutaneous syndactyly, malformations of the larynx and genitourinary tract, craniofacial dysmorphism, orofacial clefting, developmental delay, and musculoskeletal anomalies was found to have hematometra after presenting with abdominal distention and pain[4]. As she was post-menarchal, cryptomenorrhea was suspected resulting from entrapped menstrual blood in the uterine cavity causing pain. The CT abdomen/pelvis showed a very large fluid-filled structure representing her enlarged uterus.

Hematometra is the retention of blood in the uterine cavity[1]. It is an uncommon disorder due to partial or complete obstruction of menstrual flow at any portion of the lower genital tract[2]. It is commonly caused by congenital abnormalities such as an imperforate hymen, noncommunicating Müllerian duct, and transverse vaginal septum[1,2]. In older women, it is typically acquired by senile atrophy of the endocervical canal and endometrium, cervical stenosis associated with surgery, radiation therapy, endometrial ablation, and malignant disease of the endocervical canal[2]. Symptoms depend on the age of the patient, her menstrual history, how rapidly the blood accumulates in the uterine cavity, and the possibility of infection[2]. Therefore, common symptoms on presentation are primary or secondary amenorrhea, cyclic lower abdominal pain, abdominal distention, and spotting of dark brown blood[2,3].

Fraser syndrome is a rare autosomal disorder with the incidence below 0.043 per 10.000 live born infants and 1.1 in 10.000 stillbirths[5]. A major diagnostic criterion includes findings of ambiguous genitalia which includes clitoromegaly, hypoplastic or fused labia, and vaginal atresia in females and hypoplasia of the scrotum and a small or even rudimentary penis in males[6]. In males, there also have been reports of low anorectal anomalies[9]. Internal genitalia in females could also be abnormal, such as absent uterus, streak ovaries, absent Mullerian ducts, common urogenital sinus[6]. Some other anomalies that are noted in females include bicornuate uterus, uterine hypoplasia, and synechiae[8].

Conclusion

This case highlights the rarity of Fraser syndrome with associated hematometra secondary to both internal and external genital abnormalities post menarche. There was no imperforate hymen found and she was noted to have a 2-3 cm introitus. Despite high occurrence of abnormal genitalia in Fraser syndrome, no studies have been done to show any abnormalities in the hypothalamic-pituitary-ovarian axis, thus patients may have a functioning menstrual cycle and genital abnormalities are most likely structure in origin rather than hormonal dependent[7], such as the patient described in this case report. Hematometra should be a differential diagnosis in patients with syndromes that are associated with genital abnormalities such as Fraser syndrome, as failure to drain the retained blood and tissue products, can act as a foci for infection and ultimately lead to severe pain and hemodynamic alterations as in our patient. Early evaluation of genital structures including physical examination and examination with imaging including MRI should be considered to identify patients at risk for future hematometra.

Fraser syndrome can be associated with genital abnormalities leading to hematometra and evaluation with identification of patients at risk for development of hematometra should be considered.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

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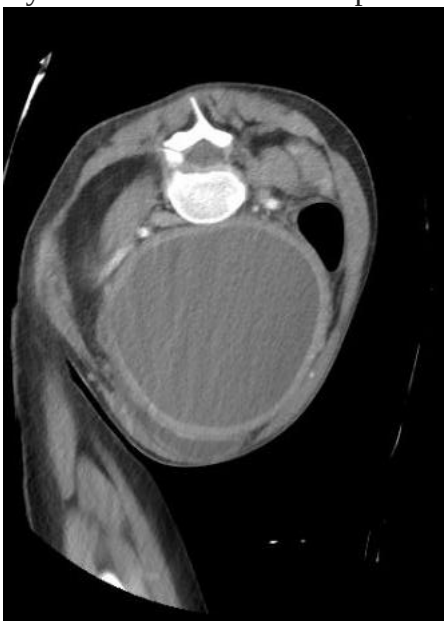

Figure 1: Cross-sectional computed tomography view of the abdomen and pelvis with oral and intravenous contrast

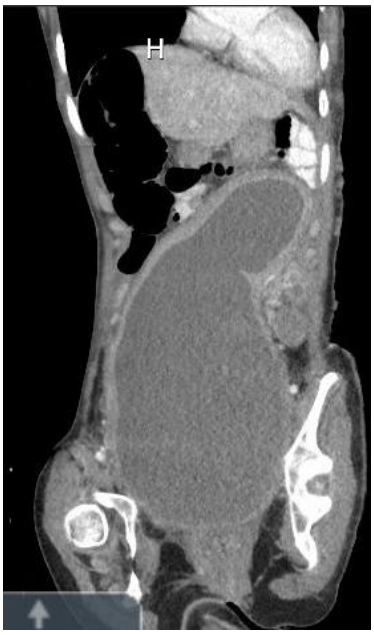

Figure 2: Coronal computed tomography view of the abdomen and pelvis with oral and intravenous contrast