Massive Antepartum Labial Edema

Claudia Hernandez, MD; Rikk Lynn, MD

Vulvar edema occurring during pregnancy requires a careful evaluation for systemic disorders that may place both the patient and fetus at high risk for complications. We present a case of massive antepartum labial edema and factors that may have played a role in initiating the process. Differential diagnoses, associated systemic disorders, potential complications, and treatment options are reviewed for dermatologists confronted with this clinical presentation.

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Severe antepartum vulvar/labial edema is a rare complication of pregnancy. This type of localized edema typically is reported in association with another underlying systemic disease. Dermatologists should be familiar with potential causes as well as diagnostic evaluation and management options for labial edema.

Case Report

A 20-year-old black woman (gravida 2, para 0, aborta 1) at 37 weeks' gestation was hospitalized for massive labial edema at an outside facility. Her medical history was remarkable for an elective pregnancy termination in 2004 and genital herpes since 2002. Her only medication prior to admission was valacyclovir hydrochloride, which she had discontinued for unspecified reasons. She underwent incision and drainage of a suspected right labial boil 2 weeks prior to admission. Swelling of both labia occurred suddenly within hours of the procedure. Vancomycin hydrochloride and clindamycin hydrochloride were initiated, but when no improvement occurred, she was transferred to the university hospital for further evaluation.

From the Department of Dermatology, University of Illinois at Chicago.

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Correspondence: Claudia Hernandez, MD, University of Illinois at Chicago, Department of Dermatology (MC 624), 808 South Wood St, Room 376 CME, Chicago, IL 60612 (claudiah@uic.edu).

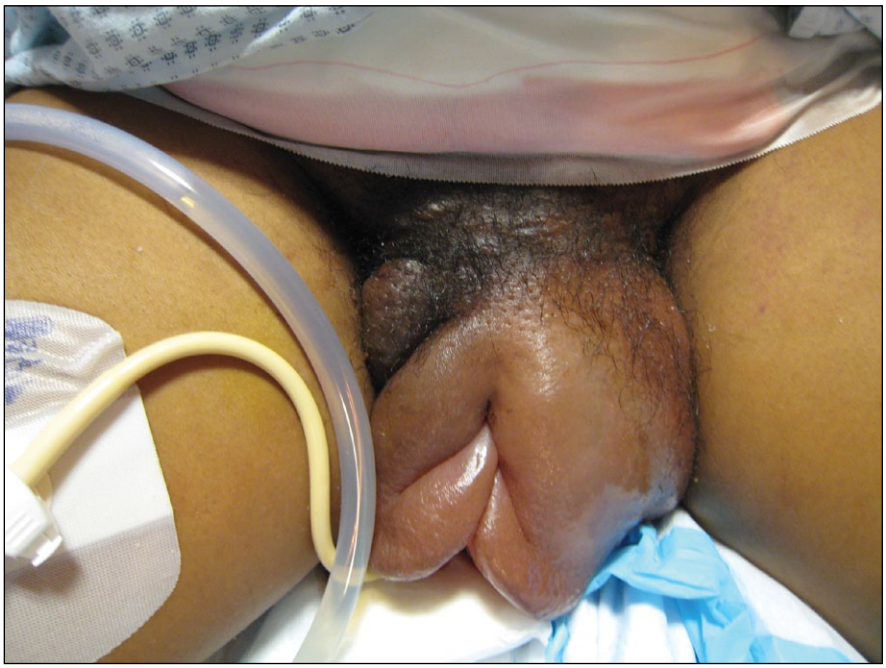
The patient was found to be afebrile and normotensive with stable vital signs. Fetal heart rate was 140 beats per minute. Marked bilateral labial swelling measuring 8×6 cm and 1+ (mild) pitting edema of the lower extremities extending to the upper thighs were noted on examination. No calf tenderness, palpable inguinal lymphadenopathy, erythema, fluctuance, or vesicles were observed. The incision and drainage site was unremarkable and healing well. Lower vaginal vault candidiasis was documented by the admitting obstetrician.

Laboratory examinations revealed the following levels: hemoglobin, 7.6 g/dL (reference range, 14.0–17.5 g/dL); hematocrit, 23% (reference range, 41%–50%); albumin, 1.8 g/dL (reference range, 3.4–5.0 g/dL); and protein, 4.8 g/dL (reference range, 6.0–8.0 g/dL). Her remaining laboratory studies were within reference range including her white blood cell count (4700/µL [reference range, 4500–11,000/µL]).

An infectious disease consultation was obtained and the differential diagnosis for the edema included a retained surgical sponge, herpes reactivation, worsening candidiasis, and dependent edema. Magnetic resonance imaging (MRI) was recommended to visualize any retained surgical sponges. She was started on the following medications: intravenous (IV) vancomycin hydrochloride 1 g every 24 hours, fluconazole 100 mg IV once daily, piperacillin–tazobactam 3.375 g IV every 6 hours, and oral acyclovir 400 mg daily.

The MRI revealed an enlarged edematous vulva without evidence of a retained foreign body. A small collection of fluid was seen at the vaginal introitus, which was believed to represent a small cyst; however, an abscess was not ruled out.

The dermatology department was consulted because of concerns of a possible allergic contact dermatitis. The patient denied any labial pruritus or history suggestive of angioedema. The patient stated her upper thighs were twice their normal size and the labial edema had worsened since admission. Physical examination revealed 2+ (moderate) lower extremity pitting edema and massive labial edema (Figure). Our service felt her presentation was not consistent with an inflammatory dermatosis. An



Severe bilateral vulvar edema affecting both the labia majora and labia minora.

internal medicine consultation was recommended to evaluate her hypoalbuminemic state.

The internal medicine consultant's differential diagnosis of her hypoalbuminemia included nephrotic syndrome causing protein loss, decreased protein production from hepatic disease, or less likely malnutrition. Fluid overload also was noted with input/output of 1000/800 mL over each 8-hour period. Furosemide (40 mg IV) once daily and albumin infusions were initiated with the albumin level improving to 2.1 g/dL. Additional laboratory studies were obtained including 24-hour protein excretion, which was elevated at 298 mg/24 hours (reference range, 200 mg/24 h); urine protein to creatinine ratio was 0.43 (reference range, <0.2); and liver function tests and coagulation studies were both within reference range. All antibiotics and intravenous fluids were discontinued. On the fourth day of hospitalization, worsening painful labial edema necessitated a cesarean delivery with a low transverse incision. The edema began to improve 6 hours after delivery with complete resolution 2 weeks after an uncomplicated postoperative course.

Comment

Edema is defined as the infiltration of abnormal or excess amounts of fluid in the connective tissues of the body. During pregnancy, the total body water increases by 6 to 8 L, with an estimated 4- to 6-L increase in extracellular compartments and 2- to 3-L increase in interstitial compartments. These large volume changes in addition to cumulative sodium retention lead to a decrease in oncotic pressure and increase in capillary pressure causing edematous changes in approximately 8 of 10 pregnant women. An estimated 50% of pregnant women have edema confined to the lower extremities, while the other half experience a generalized form that may include the face and fingers.[1] Mild or moderate labial edema may occur in either pregnant and/or nonpregnant women and is associated with a multitude of conditions including infectious, neoplastic, inflammatory, or even posttraumatic disorders (Table 1). Fortunately severe labial edema remains unusual. Massive vulvar edema that occurs in the immediate postpartum period requires rapid evaluation and close monitoring because of the risk for cardiovascular collapse and maternal death. These cases often are accompanied by fever and leukocytosis, which has caused concern for an endotoxic mechanism.[2]

One suggested mechanism for the development of edema in pregnancy is activation of the renin-angiotensin system. Angiotensin-converting enzyme is important for regulation of blood pressure because it generates the vasoconstrictor angiotensin II from angiotensin I, which in turn is produced by cleavage of angiotensinogen by renin.[3] This mechanism is purported to be important in preeclampsia, and most literature deals with its role in blood pressure maintenance; its role in edema formation in a normal pregnancy remains unclear. Preeclampsia, characterized by maternal hypertension, proteinuria, and generalized edema, is a potential cause of massive vulvar edema. It is believed that poor

Table 1.

Causes of Labial Edema[1,2]

Inflammatory Dermatoses

Contact dermatitis

Atopic dermatitis

Hidradenitis suppurativa

Sarcoidosis (cutaneous)

Sexually Transmitted Diseases (Infectious)

Chancroid

Lymphogranuloma venereum

Trichomonas

Herpes simplex virus

Condyloma acuminatum

Syphilis

Infectious Diseases Miscellaneous

Furuncle

Bartholin abscess

Necrotizing fasciitis

Filariasis

Pregnancy Associated

Preeclampsia

Eclampsia

Obstructed labor

Multiple gestations

Use of birthing chair

Neoplasms Resulting in Venous or Lymphatic Obstruction

Labial or vulvar neoplasm

Intra-abdominal mass

Adenomyoma of round ligament

Ectopic breast tissue

Systemic Diseases

Lymphedema

Hypertension

Nephrotic syndrome

Congestive heart failure

Renal failure

Miscellaneous

Inguinal hernia

Postparacentesis syndrome (Conn syndrome)

Ascites

Nuck hydrocele

Malnutrition

Anemia

uteroplacental perfusion in preeclampsia leads to placental hypoxia releasing placenta products into the maternal circulation, which may stimulate the renin-angiotensin pathway. Angiotensin-converting enzyme inhibitors cannot be used during pregnancy because of fetotoxicity. Use of these medications may lead to impairment of renal function, severe hypertension, proteinuria, polycythemia, congenital malformations, and fetal death due to their effects on fetoplacental circulation.[4]

Table 2.

Cases of Hypoalbuminemia in Pregnant Females With Massive Labial Edema

Clinical Presentation	Gestational Age, wk	Albumin, g/dL[a]
Aged 20 years, cyst incision and drainage, prolonged bed rest, fluid overload, hypoalbuminemia (current case)	37	1.8
Aged 29 years, IDDM, nephropathy, hypertension[8]	34	2.2–2.7
Aged 17 years, anasarca, anemia, preeclampsia[9]	30	1.6
Aged 17 years, proteinuria, preeclampsia[10]	33	Hypoalbuminemia; no value reported
Aged 29 years, IDDM, proteinuria[11]	23	2.3
Aged 14 years, venous obstruction[2]	35	1.7
Aged 23 years, IDDM, hypertension, congenital hydrocephalus[2]	20	1.0
Aged 20 years, premature labor at 34 weeks, tocolytic therapy, fluid overload, uterine obstruction[12]	34	2.7

Abbreviation: IDDM, insulin-dependent diabetes mellitus.
[a]Reference range, 3.4–5.0 g/dL.

A supine position results in a remarkable reduction of venous flow, decreasing cardiac filling and cardiac output in a small percentage of pregnant women.[5] Compression of the inferior vena cava by the enlarging uterus obstructs outflow from the femoral and iliac veins and possibly causes lymphatic stasis. This type of congestive edema typically affects the dependent lower extremities of ambulating women; however, in those on bed rest, such as our patient, the vulvar and sacral areas become the dependent areas of the body.[2,6] Any changes in pressure and volume are quickly noticed in areas with substantial connective tissue. Furthermore, estrogen secretion during pregnancy is believed to possibly alter the physicochemical characteristics of connective tissue mucopolysaccharides, allowing for a substantial increase in water storage. The vulva has large amounts of loose connective tissue and a thin epithelial layer allowing for an expansion of the interstitial space by fluids.[1]

Our patient's labial edema had several potential causes including posttraumatic, obstructive, and nephrotic syndromes with resultant hypoalbuminemia. The classic description of edema formation in nephrotic syndrome includes urinary protein loss resulting in hypoalbuminemia, which causes a decrease in oncotic pressure and a resultant misdistribution of body fluids into the interstitial spaces.[7] Severe hypoalbuminemia has been reported in several cases of massive labial edema (Table 2).

If a dermatologist is confronted with a patient with marked labial edema, performing a complete history and physical examination along with several laboratory tests may assist in patient evaluation. Because hypoalbuminemia is a reported association, serum albumin levels should be drawn along with a serum chemistry profile. Urine studies including a urinalysis, creatinine, creatinine clearance, protein to creatinine ratio, and 24-hour urine protein also should be collected. Liver function

testing and coagulation profile are helpful to determine hepatic function. Excluding angioedema may be warranted according to clinical presentation. C1 inhibitor (protein and function) as well as C4 complement levels should be assessed.[13] Our patient also had herpes simplex virus cultures, which were negative. Gram stain and bacterial, viral, or fungal cultures are appropriate if an infectious etiology is suspected. Histologic evaluation generally is unnecessary because history, clinical features, and laboratory studies should be diagnostic. Radiographic studies such as an MRI or ultrasound may assist in the detection of a retained foreign object or pelvic/intra-abdominal mass that may obstruct venous or lymphatic return.

Because our patient lacked any allergic, infectious, or hypertensive changes, iatrogenic fluid overload combined with hypoalbuminemia likely resulted in low oncotic pressure, which was further compounded by gravid uterus obstruction of venous outflow. The role of incision and drainage in precipitating the edema remains unclear. It is possible that all of these factors contributed to edema formation.

If medical management (ie, diuresis) fails to improve the edema, there are case reports of mechanical drainage of the edema using hypodermic needles and tubing (modified Southey tubes) to collect the fluid.[2,9] However, because of concerns of postprocedure infection, hematoma formation, trauma, and tissue dystocia, this procedure appears to be rarely performed. Cesarean delivery was the preferred method of delivery in some reported cases.[2,8]

Conclusion

Massive vulvar/labial edema remains a challenging diagnosis. This case report is meant to assist dermatologists who are confronted with this condition to rapidly formulate a differential diagnosis, appropriate evaluation, and treatment plan, which should help reduce the risk for deterioration and tissue necrosis of this rare condition.

REFERENCES

1. Davison JM. Edema in pregnancy. *Kidney Int Suppl*. 1997;59:S90-S96.
2. Morris LF, Rapini RP, Herbert AA, et al. Massive labial edema in pregnancy. *South Med J*. 1990;83:846-848.
3. Ito M, Itakura I, Ohno Y, et al. Possible activation of the renin-angiotensin system in the feto-placental unit in preeclampsia. *J Clin Endo Met*. 2002;87:1871-1878.
4. Laube GF, Kemper MJ, Schubiger G, et al. Angiotensin-converting enzyme inhibitor fetopathy: long term outcomes. *Arch Dis Child Fetal Neonatal Ed*. 2007;92:402-403.
5. Metcalfe J, Ueland K. Maternal cardiovascular adjustments to pregnancy. *Prog Cardiovasc Dis*. 1974;16:363-374.
6. Awwad JT, Khalil AM, Aswad NK, et al. Labial edema in pregnancy. a case report. *J Reprod Med*. 1994;39:921-922.
7. Palmer BF, Alpern RJ. Pathogenesis of edema formation in the nephrotic syndrome. *Kidney Int Suppl*. 1997;59:S21-S27.
8. Jakobi P, Friedman M, Goldstein I, et al. Massive vulvar edema in pregnancy. a case report. *J Reprod Med*. 1995;40:479-481.
9. Bracero LA, Didomenico A. Massive vulvar edema complicating preeclampsia: a management dilemma. *J Perinatol*. 1991;11:122-125.
10. Daponte A, Skentou H, Dimopoulos KD, et al. Massive vulvar edema in a woman with preeclampsia: a case report. *J Reprod Med*. 2007;52:1067-1069.
11. Deren O, Bildirici I, Al A. Massive vulvar edema complicating a diabetic pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 2000;93:209-211.
12. Brittain C, Carlson JW, Gehlbach DL, et al. A case report of massive vulvar edema during tocolysis of preterm labor. *Am J Obstet Gynecol*. 1991;165:420-422.
13. Kaplan AP. Urticaria and angioedema. In: Wolff K, Goldsmith LA, Katz SI, et al, eds. *Fitzpatrick's Dermatology in General Medicine*. 7th ed. New York, NY: McGraw Hill Medical; 2008:330-343.