5. Allan SG, Knox J, Kerr F: Interaction between diuretics and indomethacin. Br Med J 283:1611, 1981
6. Kramer HJ, Dusing R, Stinnesbeck B, et al: Interaction of conventional and antikaliuretic diuretics with the renal prostaglandin system. Clin Sci Mol Med 59:67, 1980
7. Smith DE, Brater DC, Lin ET, et al: Attenuation of furosemide's diuretic effect by indomethacin: Pharmacokinetic evaluation. J Pharmacokinet Biopharm 7:265, 1979
8. Chennavasin P, Seiwell R, Brater DC: Pharmacokinetic-dynamic analysis of the indomethacin-furosemide interaction in man. J Pharmacol Exp Ther 215:77, 1980
9. Brater DC: Analysis of the effect of indomethacin on the response to furosemide in man: Effect of dose of furosemide. J Pharmacol Exp Ther 210:386, 1979
10. Tobert JA, Ostaszewski T, Reger B, et al: Diflunisal-furosemide interaction. Clin Pharmacol Ther 27:289, 1980

Toxic Shock Syndrome Associated with Diaphragm Use

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Hymowitz[1] has suggested that if toxic shock syndrome[2,3] is associated with the obstruction of menstrual flow by tampons, the use of a diaphragm during menstruation should be associated with the syndrome. Too few cases of this important possibility have been reported[2-4] to establish it in clinical consciousness or to decide whether such a connection will require a change in instructions for use of diaphragms. The following case is reported and discussed.

Case Report

Mrs. D. is an 18-year-old white woman, gravida 1, para 1, in good health prior to the episode reported. She had a low transverse cesarean section for fetal distress three months prior to admission and had not yet resumed menstruation. Forty-eight hours prior to admission, after unprotected intercourse, she developed a vaginal discharge requiring use of a pad. Twelve hours later she used a diaphragm, left it in place overnight, and failed to remove it the next morning. During the day pelvic and lumbar pain developed, followed by vomiting and a fever as high as 103°F. That evening, 12 hours before admission, the diaphragm was removed with drainage of copious purulent discharge. The edges of the diaphragm and the discharge were blood streaked. She also developed a diffuse macular blanching rash, sparing only the circumoral region.

At the time of admission the following morning her blood pressure was 60/0 mmHg; pulse, 180 beats/min; and temperature, 102°F. Significant physical findings included the rash, conjunctivitis, a pharyngeal infection, and a lack of adenopathy. Pelvic examination showed a vaginal discharge, a very tender, slightly enlarged warm uterus, and normal adnexa.

Cultures of the vaginal discharge were positive for Staphylococcus aureus, resistant to penicillin and ampicillin, and sensitive to methicillin, cepha-

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lothin, erythromycin, colistin, chloramphenicol, tetracycline, sulfisoxazole, and aminoglycoside antibiotics. Cultures of the blood and urine and anaerobic and gonococcal cervical cultures were all negative. Wet mount and Gram stain showed polymorphonuclear leucocytes and gram-positive cocci. The white blood count rose from 11,000/mm^3 on admission to a high of 13,000/mm^3 with a left shift the next day. Urinalysis showed a sterile pyuria. Significant chemical findings included an initial elevation of the fibrinogen to 330 mg/100 mL (control, 220 mg/100 mL), prothrombin time to 15 seconds (control, 11 seconds), and Ivy bleeding time to 11 minutes. The sodium level was 141 mEq/L (normal, 135 to 148 mEq/L); potassium, 3.5 mEq/L (normal, 3.5 to 5.0 mEq/L); chloride, 104 mEq/L (normal, 95 to 108 mEq/L); carbon dioxide, 18 mEq/L (normal, 24 to 32 mEq/L); blood urea nitrogen, 33 mg/100 mL (normal, 7 to 23 mg/100 mL); creatinine, 2.9 mg/100 ml (normal, 0.7 to 1.4 mg/100 mL); glucose, 138 mg/100 mL (normal, 65 to 110 mg/100 mL); SGOT, 81 U/L (normal, 7 to 50 U/L); and bilirubin, 2 mg/100 mL (normal, 0.2 to 1.2 mg/100 mL).

The patient received 1.2 million units of intravenous penicillin every four hours, 80 mg of gentamicin every eight hours, and 300 mg of clindamycin every six hours, as well as fluid replacement and 2 g of methylprednisolone followed by 1 g every six hours. The gentamicin dosage was adjusted after the initial dose through the use of peak and trough levels. The initial antibiotics and steroids were stopped after 24 hours, and treatment continued with 1 g of methicillin every six hours.

The shock, fever, and rash resolved in the following 48 hours. Two days after admission there was circumoral exfoliation. The discharge and electrolyte and renal abnormalities cleared in three days. Laboratory abnormalities corrected in 24 to 48 hours, except for liver function tests. The SGOT peaked at 321 U/L in three days, then returned to normal by discharge after eight days. Other liver function tests followed a parallel course.

After eight days in the hospital, the patient was discharged on 500 mg of cloxacillin every six hours. Repeat cervical and vaginal cultures at the time of discharge were negative, and she had been afebrile for five days. The cloxacillin was stopped two days later upon development of a diffuse maculopapular pruritic rash.

One month later she again developed malaise, a low-grade fever, and a vaginal discharge and was admitted to another hospital. On this occasion, although the sterile pyuria persisted, neither shock nor rash occurred, and all cultures were negative. A monilial vaginitis responded to nystatin vaginal suppositories, and she recovered in three days. The patient has remained well since. Menstruation resumed three months later.

Discussion

This case satisfies the criteria of the Centers for Disease Control for diagnosis of toxic shock syndrome with fever, orthostatic dizziness or hypotension, rash and desquamation, involvement of multiple organ systems, and absence of evidence of other causes, and it was reported to the Tennessee State Health Department. This particular case is unusual because it began with development of a vaginal discharge without vaginal obstruction, developed during a 24-hour period when a diaphragm was in place, and was not associated with menstruation. Whether the discharge represented staphylococcal infection is unknown, but the diaphragm certainly seems to have contributed to the course of events.

Toxic shock syndrome was first described in children[5] and has now been reported in neonates, men, and postmenopausal women. It has been associated with vaginal and cesarean delivery, therapeutic abortion, infected surgical wounds, hydradenitis, lymphadenitis, deep abscesses, and infected skin lesions including burns, abrasions, lacerations, furuncles, and insect bites.[2,3] Even though 85 percent of cases are still associated with menstruation, this percentage has declined in the last two years primarily because of a decline in the number of menstrual cases reported and hypothetically because of changes in tampon availability and use.

Increasing recognition of non-tampon-related cases has argued against simple obstruction as the cause. Search is in progress for alternative explanations, such as the special absorbancy of some forms of tampons and suture material.[6] Staphylococcal septicemia with a scarlatiniform rash has

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been reported sporadically since at least 1927 and probably represents nonmenstrual toxic shock syndrome.

What is new or different remains unknown. New toxin production by staphylococci, new tampon technology, and better disease surveillance are all reasonable hypotheses. However, even as recurrent, mild, and more cases are reported, the sense of something new and different persists.[7]

Vaginal discharges, diaphragms left in for 24 hours or more, and probably even the combination are common. That the combination reported in this case is not seen with any frequency may argue against simple vaginal-cervical obstruction as a sufficient cause of the syndrome.[8] It is sobering nonetheless. Should patients be warned not to use their diaphragms when they have a discharge? Since instructions for using diaphragms encourage leaving them in place for as long as 6 to 12 hours, and leaving them in place overnight is common, should patients be given a maximum time for use (perhaps 24 or 36 hours)? The disease is rare and the combination common. It seems reasonable to add a sentence to instructions recommending that the diaphragm not be left in place over 12 hours with an untreated vaginal discharge.

Finally, all clinicians must be sensitive to a scarlatiniform rash and postural dizziness in association with any potential staphylococcal infection, since the most likely evolution of this entity may be increasing incidence and decreasing association with menstruation.

References

1. Hymowitz EE: Toxic-shock syndrome and the diaphragm. N Engl J Med 305:834, 1981

2. Toxic-shock syndrome—United States, 1970-1982. MMWR 31:201, 1982

3. Toxic-shock syndrome—United States, 1970-1980. MMWR 30:25, 1981

4. Loomis L, Feder H, Jaffe R: Toxic-shock syndrome associated with diaphragm use. New Engl J Med 305:1585, 1981

5. Todd J, Fishant M, Kapral F, et al: Toxic shock syndrome associated with phage-group-I Staphylococci. Lancet 2:1116, 1978

6. Goodpasture HC, Voth DW: Toxic shock syndrome—Additional perspectives. JAMA 247:1464, 1982

7. Bear K: Complex picture emerges for toxic shock syndrome. JAMA 247:2339, 1982

8. Schlech WF, Shands KN, Reingold AL, et al: Risk factors for development of toxic shock syndrome: Association with a tampon brand. JAMA 248:835, 1982