Anaphylaxis From Depot Medroxyprogesterone Acetate in an Adolescent Girl

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BACKGROUND: Anaphylaxis postinjection of depot medroxyprogesterone acetate (DMPA) has been rarely reported in adult women.

CASE: A 16-year-old girl developed anaphylaxis after receiving 150 mg of DMPA intramuscularly. She previously had received four injections of DMPA without any adverse reactions, including two earlier doses from the same lot number. She initially was treated in the clinic and was stabilized in the emergency department, with full recovery. She subsequently underwent allergy testing, which was inconclusive, and decided to use the copper intrauterine device for ongoing contraception.

CONCLUSION: Anaphylaxis, a rare complication of DMPA, can occur even if a patient had no adverse reactions from previous injections from the same lot number.

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Depot medroxyprogesterone acetate (DMPA) is a long-acting form of hormonal contraception that was licensed for use in adolescents in the United States by the Food and Drug Administration in 1992. Given as an intramuscular injection in 12-week intervals, it provides adolescent women with a private and effective form of contraception and, when adhered to, has a failure rate less than 1%.[1] According to data from the most recent National Survey of Family Growth published in 2010, about one in five women in the United States ages 15–44 years had ever used DMPA.[2]

Commonly reported adverse effects from DMPA include irregular menses, reversible decrease in bone mineral density, and often prolonged contraceptive effect after discontinuation.[3] Allergic reactions to this medication are considered rare, and the risk of anaphylaxis, especially after repeated administration, has been previously reported only once, in an adult woman who received two doses of DMPA from different lots.[4] Although it is known that progesterone may modulate allergic responses,[5] the mechanism by which DMPA may trigger anaphylaxis is unknown. Here we describe the case of an adolescent who experienced anaphylaxis after DMPA injection, after having received multiple scheduled doses of DMPA without reporting any previous side effects.

CASE

The patient, a 16-year-old Latina girl, had been seen regularly for family planning services in a mobile clinic program targeting uninsured and homeless adolescents. The mobile clinic, a 36-foot-long vehicle with two examination rooms and known as the "Teen Van," is a community outreach program of Lucile Packard Children's Hospital at Stanford University. The mobile clinic was providing services at an alternative high school at the time. The patient was a healthy teen with no chronic medical problems; no history of surgery; no known history of food, drug, or environmental allergies; and on no other medications. Her family history is positive for a mother with hypothyroidism and diverticulitis, and a brother with asthma. The patient had been receiving DMPA every 12 weeks for a little more than a year without any side effects, and had returned to the clinic for her fifth dose. The patient was given an intramuscular injection of 150 mg DMPA, with this current dose being the third from the same lot number. Before receiving the injection, she had been observed by Teen Van staff for approximately 45 minutes during check-in, waiting, and vital signs. She had no complaints and had exhibited no respiratory distress or any other symptoms of illness. After her injection, she left the clinic and went directly to an appointment with our registered dietitian in a nearby classroom. No food of any kind was consumed, and there was no history of envenomation (eg, spider bites) or exposure to latex items. During the visit with the dietitian, the patient started to have shortness of breath, and the dietitian immediately brought the patient back to the clinic. The patient complained of breathing difficulty and tightness in her throat while holding her hands in front of her neck. On examination, she was peripherally cool and pale with large hives widely scattered over her body. Her breath sounds were clear, and her blood pressure was stable. She was given one dose of epinephrine 0.3 mg by means of an auto-inject Epi-Pen (Dey Pharma) and diphenhydramine (Benadryl, McNeil Consumer Healthcare) 50 mg by mouth. She demonstrated immediate respiratory improvement after receiving the dose of epinephrine. However, the hives remained, and a call to 911 was made. The patient was transferred by ambulance to the Stanford University Hospital emergency department.

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According to the emergency department report, the patient received an intravenous dose of diphenhydramine while in the ambulance. On arrival at the emergency department, she experienced a recurrence of shortness of breath. She was given additional diphenhydramine, 12.5 mg intravenously, epinephrine 0.3 mg intramuscularly, dexamethasone 5.5 mg intravenously, and famotidine 20 mg intravenously. In the emergency department, her blood pressure was 127/62, heart rate was 87, respiratory rate was 30, temperature was 36.7°C, and O_2 saturation was 100%. No urticaria or rashes were noted in the emergency department. The local county poison control center was contacted from the emergency department. The poison control center advised that DMPA levels usually peak in 3 weeks (the half life of 150 mg DMPA given intramuscularly is about 50 days) and that steroid treatment therefore should be continued for 3 weeks. The patient was discharged in stable condition from the emergency department 11 hours after having received the DMPA injection. She was sent home with prednisone for a 3-week course as well as an Epi-Pen and diphenhydramine.

The patient subsequently was referred to the allergy clinic at Stanford Medical Center, where skin testing with DMPA was initially deferred because of concern of the risk of repeat anaphylaxis. The allergy clinic recommended at that time that the patient be evaluated at the adolescent gynecology clinic to determine an appropriate, alternative form of family planning that was not progestin-containing. The patient preferred a low-maintenance and long-acting method and wanted to avoid any risk of recurring anaphylaxis (ie, progestin-containing products). The copper intrauterine device (IUD) was recommended during the gynecology clinic visit, and inserted without complications. Subsequently, however, the patient complained of increased dysmenorrhea after IUD insertion and stated that she would be interested in retrying the DMPA.

The patient was then referred back to the allergy clinic. Both skin prick and intradermal testing were performed with the excipients contained in the DMPA solution (Box 1).

Skin prick tests were performed initially for polyethylene glycol 3350, polysorbate 80, methylparaben, and propylparaben. Initial dilutions were 1:100, then 1:10, and eventually full concentration. The skin pricks for all ingredients were negative after 20 minutes in all concentrations. The positive control was for histamine at 3+. Because the skin prick testing was negative, intradermal testing was then performed because it is a more sensitive testing method, and it is often utilized when allergy is still suspected in light of negative skin prick testing. The intradermal testing was performed first at a dilution of 1:100. Results were negative except for polysorbate 80, which showed slightly equivocal results. Intradermal testing was next performed at a 1:10 dilution, with initially negative results. However, erythematous plaques, with tracking up the arm, developed within 20 minutes at the test site of the polyethylene glycol. Of note, the patient had received four oral doses of polyethylene glycol for constipation several months after the anaphylactic reaction, and had had no adverse reactions. Although the route of administration is quite different (intramuscularly for DMPA compared with orally for polyethylene glycol), it is likely that polyethylene glycol did not provoke the anaphylaxis.

After the equivocal intradermal test results with polysorbate 80, the allergy clinic recommended that intradermal skin testing be performed with DMPA itself, if the patient clearly preferred to go back on DMPA. The recommendation was reviewed with the patient and she decided to not have allergy testing for DMPA, and was fine with continuing using the copper IUD.

Box. 1. Ingredients in Each Single-Dose 1-mL Vial of Medroxyprogesterone Contraceptive Injection

- 150 mg of medroxyprogesterone acetate
- 28.9 mg of polyethylene glycol 3350
- 2.41 mg of sodium chloride
- 1.37 mg of methylparaben
- 0.150 mg of propylparaben
- Quantity sufficient water for injection

COMMENT

A literature search (1966 to present) using "anaphylaxis" and "medroxyprogesterone acetate" (or "DMPA," "Depo-Provera," and other variants) found four previous case reports of anaphylaxis associated with DMPA; the most recent report was from 2004.[4] Although the ingredients of DMPA remain unchanged since earlier case reports, this case is unique in the following ways: the patient's age, multiple exposures to the same lot number, and allergy skin testing performed subsequent to the anaphylactic reaction.

If the patient's response was caused by the active ingredient, the mechanism of action is unknown. There are no known reports of hormone-specific immunoglobulin E levels[6] and mast cell degranulation seems unlikely.[6] DMPA has many effects on the immune system mediated by progesterone and glucocorticoid receptors depending on dose.[7] Although anaphylaxis has been reported in association with the excipients used in DMPA, excipient-free DMPA for clinical use does not exist.

Depot medroxyprogesterone acetate is just one of many types of progestins available for contraceptive use. There are more than 20 types of progestins in a variety of different contraceptive methods, including oral contraceptive pills, the transcutaneous patch, the vaginal ring, the subdermal implant, and the IUD. Unfortunately, there is no literature with consistent recommendations regarding allergy testing for progestins, and allergic cross-reactivity among different progestins can

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occur. One model for considering how progestins may be involved in anaphylaxis is the rare entity known as autoimmune progesterone dermatitis, a skin disorder of recurrent dermatitis.[8] Autoimmune progesterone dermatitis is thought to be caused by an endogenous increase in progesterone levels during the menstrual cycle; associated anaphylaxis has also been reported. Given that our patient preferred a long-acting method of contraception and did not want further allergy testing, and given the possibility of cross-reactivity to other progestins, the severity of her reaction to DMPA, and that subdermal implants and progesterone-containing IUDs are not rapidly removable methods, the patient decided to continue with the copper IUD.

In conclusion, DMPA is a commonly used, generally safe, and effective contraceptive. Providers should be aware of the possibility of acute, life-threatening reactions occurring after DMPA administration, even if patients have not had adverse reactions to previous injections from the same lot number.

REFERENCES

1. Tolaymat LL, Kaunitz AM. Long-acting contraceptives in adolescents. Curr Opin Obstet Gynecol 2007;19:453–60.
2. Mosher WD, Jones J Use of Contraception in the United States: 1982–2008. Vital Health Stat 23 2010;1–44.
3. Roy G. Injectable contraception. Semin Reprod Med 2010;28: 126–32.
4. Selo-Ojeme DO, Tillisi A, Welch CC. Anaphylaxis from medroxyprogesterone acetate. Obstet Gynecol 2004; 103(5 pt 2):1045–6.
5. Farage MA, Berardesca E, Maibach H. The possible relevance of sex hormones on irritant and allergic responses: their importance for skin testing. Contact Dermatitis 2010;62:67–74.
6. Slater JE, Raphael G, Cutler GB Jr, Loriaux DL, Meggs WJ, Kaliner M. Recurrent anaphylaxis in menstruating women: treatment with a luteinizing hormone-releasing hormone agonist–a preliminary report. Obstet Gynecol 1987;70:542–6.
7. Vermeulen M, Pazos P, Lanari C, Molinolo A, Gamberale R, Geffner J, et al. Medroxyprogesterone acetate enhances in vivo and in vitro antibody production. Immunology 2001;104:80–6.
8. Kakarla N, Zurawin RK. A case of autoimmune progesterone dermatitis in an adolescent female. J Pediatr Adolesc Gynecol 2006;19:125–9.

Placental Mesenchymal Dysplasia Presenting as a Twin Gestation With Complete Molar Pregnancy

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BACKGROUND: Placental mesenchymal dysplasia is a rare abnormality characterized by placentomegaly, grapelike cystic vesicles, and villous hyperplasia. The clinical and ultrasonographic presentation may mimic molar pregnancy, provoking incorrect diagnoses and unnecessary therapeutic interventions.

CASE: A 36-year-old nulliparous woman presented for prenatal ultrasonography that indicated the presence of one gestational sac containing both fetus and cystic mass, concerning for partial molar pregnancy. Amniocentesis returned a 46,XX karyotype, suggesting a twin gestation with complete mole. The patient was monitored closely and, because of fetal growth restriction, was induced successfully at term and delivered a healthy newborn. Histopathologic findings of the placenta were consistent with placental mesenchymal dysplasia.

CONCLUSION: Although placental mesenchymal dysplasia is often confused with molar pregnancy, it is important to consider both in a differential to avoid inappropriate treatments.

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Placental mesenchymal dysplasia is a vascular abnormality that shares many ultrasonographic and gross characteristics with molar pregnancy, including a thickened placenta with diffuse, cystic areas.[1] However, unlike molar pregnancy, placental mesenchymal dysplasia has no known malignant potential. Because treatments for each condition differ substantially, ranging from early termination of pregnancy and consideration of chemotherapy for the latter to expectant observation and delivery with the former, it is critical that providers entertain the diagnosis of placental mesenchymal dysplasia in women presenting with an abnormal pregnancy. Here we present a case of a pregnant woman who presented with classic findings of viable pregnancy and concominant placental abnormality who following pathology exami-

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