Keloid Formation From Levonorgestrel Implant (Norplant System) Insertion

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Levonorgestrel implants (Norplant System) are a widely used, highly effective system of contraception.[1] More than 0.5 million women worldwide have used levonorgestrel implants.[2] The complications of this method are well documented and can be divided into systemic and local reactions.[1,3] The local reactions related to insertion include infection, itching, rash, pain, and expulsion of the implants.[4] This article presents the case of a patient who had a particularly unusual dermatologic reaction to a levonorgestrel implant device, and the literature is reviewed to determine whether a certain subset of women receiving levonorgestrel implants should be given additional counseling about this potential complication.

Case Report

A 25-year-old African-American woman came to the Family Practice Clinic requesting a levonorgestrel implant insertion. The patient received counseling on the benefits of this method, the procedure, alternatives, and risks. A family practice resident under the direct supervision of a faculty member skilled in the procedure performed the insertion using the method recommended by the manufacturer.[3] Briefly, this involved the following steps: (1) the medial aspect of the patient's upper arm was prepared using povidone iodine and alcohol, then draped in a sterile fashion; (2) using a sterile surgical pen, the area of insertion was marked 10 cm proximal to the medial epicondyle; (3) five mL of 2 percent lidocaine with epinephrine was infiltrated below the skin in a fanlike pattern; (4) a 3-mm incision was made at the insertion site to allow the subdermal entrance of the trocar; (5) using the trocar, six devices encapsulated in an inert silicone rubber (Silastic) were inserted in the recommended fanlike fashion in the subdermal space; (6) the wound was closed with sterile adhesive strips, and a pressure dressing was applied; and (7) the patient was given instructions on wound care.

Twenty-four hours after insertion, the patient was seen in the emergency department complaining of diffuse redness, swelling, and blistering of the skin overlying the inserted device. Because we were concerned about cellulitis, the patient was prescribed dicloxacillin 500 mg every 6 hours for 10 days. She came to the Family Practice Clinic 1 week later with resolution of the redness and blisters. The wound site was clean, and there was no drainage, fluctuance, or tenderness of the insertion site. On a follow-up appointment 3 months later, the patient complained of persistent itching at the site of insertion. On physical examination she had a fan-shaped area of hyperpigmentation over the implant site. The patient was prescribed 0.1 percent triamcinolone cream and advised to come in for follow-up care. Three months later the patient returned complaining of itching and pain at the insertion site. Physical examination was remarkable for a fan-shaped keloid over the implant site, as well as at the wound site. The patient decided at this point to have the implant devices removed. The six silicone capsules were removed without difficulty, and the keloid was injected with aqueous triamcinolone acetate. Further history from the patient revealed a positive family history of keloid formation in her mother. The patient denied any history of keloid formation; however, she had no history of surgery or of a serious skin wound. Six months later, the patient returned for a follow-up examination, and there was a resolution of the keloid at the implant site.

Discussion

Insertion site complications related to the use of levonorgestrel implants (Norplant System) are well documented. The local adverse reactions that have been reported include infection, expulsion, discomfort, pain, dermatitis, excoriation of

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the superficial skin, itching, visibility of the devices, numbness, recurrent swelling, scarring, blister and bullous edema formation, and hematoma.[1,3-5] The frequency of such complications has been variable. Klavon and Grubb[4] described the 1-year experience among 2674 patients using levonorgestrel implants from 19 centers in seven countries. The percentage of women who had insertion site complications varied substantially among centers (from no reported complications to 18.0 percent [mean = 4.7 percent]). There was no clear pattern of complications among the different countries. Reports from other investigators corroborate this range of insertion site complications. Although one might expect that insertion site complications should be closely related to the time of insertion, this association is not the case for a substantial number of users. From the data presented by Klavon and Grubb,[4] many insertion site complications occur weeks to months after placement. A substantial proportion of insertion site infections and implant expulsions were reported after the first 2 months of use, whereas 35.7 percent of local reactions were reported after 4.5 months of use.

An awareness of the frequency of insertion site complications, distribution of time of onset, and potential sequelae will aid clinicians in better client counseling and in complication management. Insertion site complications are not simply a nuisance to the patient and physician. A substantial number of women will proceed to have the contraceptive implant device removed because of the complication. In a report by Sivin,[1] placement-related problems accounted for between 4.5 and 7.5 percent of medically related terminations, whereas in the Dominican Republic this problem accounted for one-sixth of medically related removals. In a subsequent report that encompassed more than 20,000 woman-years of use, Sivin[1] found that skin conditions represented the cause of between 3.8 to 10.5 percent of all medical terminations.

The experience of the physician performing the insertion does not appear to play an important role in adverse side effects, as the complication rate is not higher among the earlier cases in most centers.[4]

Our patient had a particularly unusual insertion site complication, i.e., the formation of blisters followed by a keloid. Whether these are truly distinct reactions or fall within a continuum or progression of a local reaction remains unclear. Zuber, et al.[5] reported three cases of skin-associated complications after the insertion of a Norplant System device. In two of these patients a blister initially appeared. In the first patient the implant was removed on the 10th day after insertion, and the patient's skin was healed within 4 weeks. In the second patient an ulceration appeared that was treated with local débridement. The implants were not removed and the patient developed a wide band of scar tissue over the implant site. In the third patient a blister did not form. An area of ulceration appeared after 2 weeks, however, which by 3 weeks enlarged and led to the removal of the implants. Six weeks later the insertion site was healed with minimal scarring.

The cause of the described blister formation and ulceration is unclear. Based on a review of the literature the cause is likely to be multifactorial. Zuber, et al.[5] reviewed possible mechanisms for skin reactions that included the following possibilities: (1) the addition of epinephrine to the local anesthetic could result in increased adverse side effects through an unknown mechanism of action; (2) a reaction to the polymethylsiloxane (Silastic) implant could have occurred, which seems most plausible, although implants made of the same material for other medical devices have a low rate of reported reactions; (3) reaction could have been driven by the other materials used in the procedure (i.e., sterile adhesive strips, povidine iodine, adhesive tape); and (4) the implants could have been improperly placed. Ideally, the implants should be placed in the subdermal space. Klavon and Grubb[4] noted that placement of the implant capsules with the proximal ends close to the insertion site incision seems to predispose to infection and expulsion.

There are likely factors other than those noted above contributing to these specific skin reactions. It is possible that those same factors that play a role in the development of skin complications from other types of wounds could be in part responsible for blister formation and subsequent keloid formation. Certain individuals are more susceptible to keloid formation. Those with deeper skin pigmentation (of all races) are more prone to keloid formation than those with fair skin. Keloids are more likely to occur in parts of the body where the concentration of melanocytes

is greatest. The cause of keloid formation could be multifactorial.[6] Increased skin tension, local hypoxemia, growth factors, and a localized immune response appear to be involved in the pathogenesis of a keloid.[6] A familial predilection for keloid formation has been found, and both autosomal dominant and recessive patterns of inheritance have been reported. A positive family history is more likely when a patient has multiple, severe keloid formations.[7] The degree of the risk for keloid formation can be evaluated according to these factors: (1) the patient's history of keloid, (2) the patient's family history of keloid, and (3) the patient's ethnic background. In our case the patient's ethnic background was African-American. Further, her mother had a marked history of keloid formation.

Are patients who have a family history of keloid formation more prone to skin complications with levonorgesterol implant, namely, blister and keloid formation? A review of the literature on the dermatologic complications of insertion reveals very limited data specific to keloid formation.[4] Should these patients be counseled differently from others interested in Norplant prior to the procedure? Given the expense of the procedure and the reported frequency of requests for removal of the devices secondary to the local skin reactions, we believe that this additional information should at least be presented to the patient at the counseling session so that she will be aware of this potential complication and better able to make an informed decision about the use of this device. We do not recommend an absolute contraindication to the use of the implant in patients with risk of keloid formation.

What procedural changes are possible when inserting the implant to avoid keloid formation in those patients who are susceptible? Local steroid injection has been used for a number of years for the treatment of keloids with success. In patients who have a history of keloids, steroid injection into the wound site at the time of surgery has been an effective prophylactic.[6] There is insufficient evidence from the available literature, however, to support this practice in those patients with a history of keloids. If blister formation is a precursor of keloids, steroid injection could be a useful adjunct when blister formation occurs. The evidence from the literature on management of patients with keloids would suggest that this could have a beneficial effect.[6] Alternatives to this practice include the use of antihistamines and topical corticosteroids.

Summary

It is possible that women of certain ethnic backgrounds, specifically those more prone to keloid formation, are also more prone to the insertion site complications of levonorgesterol implants. Failure to recognize the potential for this complication and to provide adequate guidance to the patient could result in unwarranted cost and complications. It is possible that intralesional steroid injection at the first sign of a local reaction will minimize the formation of a keloid; however, specific research will need to be done before a change in practice can be recommended.

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