CASE REPORT

Combined Treatment of Cervical Pregnancy with Methotrexate and Prostaglandins

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About the Author

Grzegorz Raba was born in 1969 in Poland. In 1994, he graduated from the Medical University in Poznan, Poland (MD), and completed his PhD in 1997. Since 2004, he was the Head of the Department of Obstetric and Gynecology in Provincial Hospital in Przemysl, Poland. Since 2012, he is Professor of University of Rzeszow, Poland. He performed the first-in-the-world operation of hysterotomy and evacuation of a deceduate placental hematoma following placental abruption.

Introduction

Cervical pregnancy is the rarest form of ectopic pregnancy. According to different sources, its incidence varies between 1/1,000 and 1/50,000 [1]. Risk factors for the implantation in the area of the cervical canal can include structural uterine abnormalities, intrauterine adhesions, myomas, as well as a post-traumatic injury to the mucous membrane of the cervical canal. The risk accompanied by cervical pregnancy is related to the interaction of proteolytic enzymes released by the trophoblast on the wall of large blood vessels. This results in massive, life-threatening hemorrhages. Contemporary diagnostic methods,

mainly high-resolution ultrasonography, made it possible to implement conservative treatment methods of cervical pregnancies and decrease the proportion of resulting hysterectomies from 90 % to some 15 % [1]. Methods of treatment preserving fertility include systemic or local administration of cytotoxic drugs (methotrexate, actinomycin D, and cyclophosphamide), as well as application of prostaglandin preparations (PGF₂-alpha) to the cervical canal in order to prevent severe bleeding.

Case Report

A 22-year-old woman was admitted to hospital with lower abdominal pain and vaginal bleeding. She had a history of a single miscarriage at 9 weeks' gestation, no children. She was admitted in a good general condition: blood pressure: 122/84, pulse rate: 86/min, body temperature: 36.8 °C. Gynecological examination showed a normally sized body of the uterus, unchanged adnexa, dilated cervix, with

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external uterine os closed, and light bleeding; and marked motion tenderness in the area of the fornices of the vagina. Laboratory tests for blood cell count, coagulation markers, concentrations of D-dimers, and electrolytes remained normal: level of serum hCG: 74000 IU/ml. An ultrasound examination was performed; however, the endovaginal probe did not confirm the presence of a gestational sac in the uterine cavity. In the area of the uterine cervix, 8 mm below the internal uterine os, a gestational sac of 18-mm diameter containing structures of a fetus was identified: CRL 6w 0d. Doppler examination confirmed the presence of fetal cardiac activity: FHR 98/min. Because the patient wished to maintain fertility and due to her young age, the decision was made to try implementing conservative treatment. After contraindications had been excluded, a dose of 1.5 mg/kg of body weight methotrexate was administered intravenously. 24 h later, cessation of vaginal bleeding and a decrease in the serum hCG level to 38000 IU/ml were observed. The follow-up ultrasound showed the presence of the gestational sac in the cervical area, lack of fetal cardiac activity. Over the next 2 days intravenous prostaglandin (Dinoprost) injections at a dose of 5 mg/day were administered, then proceeding to the instrumental removal of the fetal egg from the cervix. Under general anesthesia, the cervix was dilated to 10 mm, with subsequent aspiration of the gestational sac. Site curettage was performed in order to remove the potential remnants. Light vaginal bleeding occurred after the surgery. Patient was discharged in a good general condition on the third day after the surgery. Menstruation resumed 43 days following the surgery. 5 months later the patient was diagnosed with another pregnancy, properly situated, and progressing normally (Fig. 1).

Fig. 1 Cervical pregnancy, at 6 weeks' gestation

Discussion

Because of the risk of massive, life-threatening hemorrhages, cervical pregnancy is, in most cases, treated by a surgical removal of the uterus [2]. Due to rare incidence of this pathology, the available literature does not recommend a uniform management protocol. It is impossible to perform a randomized study in order to explicitly define a single therapeutic approach which would be appropriate and safe for a patient, and thus decrease the risk of removal of the uterus which, particularly for young, childless women, is highly significant. For the time being, the choice of therapeutic treatment in the case of cervical pregnancy is still based on reports of single cases. The exchange of opinions between centers which have dealt with this pathology provides data on effective medical management in a given clinical condition. Contrary to the present case report, Postawski et al. [3], by applying a similar conservative treatment scheme (methotrexate and prostaglandins), did not manage to stop the growth of the live fetus, as well as were faced with greater bleeding after the evacuation of the fetal egg from the cervix, which forced them to place hemostatic sutures and compress the site by means of Foley's catheter. However, those authors used prostaglandins intravaginally, contrary to our case, where prostaglandins (Dinoprost) were administered intravenously, which eventually resulted in a better hemostasis. According to the available literature, the most effective treatment of cervical pregnancy up to 12 weeks' gestation is conservative treatment by means of methotrexate [3, 4]. Some authors claim that effectiveness of such treatment is mainly dependent on a smaller penetration of trophoblast cells into the wall of the cervix than in later stages of pregnancy. Over this period, effectiveness of therapy with methotrexate is assessed to be on the level above 94 % [4]. Similar to the case reported by Postawski et al. [3], in our case, a full therapeutic effect of spontaneous abortion after administration of methotrexate was not achieved, and it was necessary to continue treatment by means of prostaglandins. Both of these cases seem to confirm the opinion of ineffective systemic application of cytotoxic drugs when the level of serum hCG is higher than 10,000 IU/ml [3]. Postawski et al. [3], as a continuation of treatment by methotrexate, applied intravaginal misoprostol; we did not administer intravaginal misoprostol, like the above mentioned authors, but intravenous injections of dinoprost. On comparison of the final results, in our case, no vaginal bleeding was observed after the evacuation of the fetal egg, whereas the above mentioned authors were forced to place hemostatic sutures and apply compression by means of Foley's catheter. It is worth noting that in our case, the initial hCG value, and thus the stage of pregnancy, was higher. To date, prostaglandin treatment of cervical

pregnancy was only described by Dall et al. and Spitzer et al. [3]. In the case of cervical pregnancy, prostaglandin preparations administered directly into the implantation site after curettage of the fetal egg, or intracervically, prevented a hemorrhage to occur. In the case presented here, better hemostasis was observed after intravenous administration of prostaglandins, with no need for any additional placement of hemostatic sutures or pressure.

Conclusion

Conservative treatment of cervical pregnancy by means of a combination of drugs—methotrexate and intravenous prostaglandin injections—made it possible to preserve fertility in a woman in a late stage of cervical pregnancy.

This confirms the fact that medical treatment needs to be individualized in every case of cervical pregnancy.

Conflict of interest There is no conflict of interest.

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