

Ovarian Pregnancy with a Copper-7 Intrauterine Device In Situ

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The possibility of ovarian pregnancy with concurrent use of an intrauterine contraceptive device (IUD) has been recognized since 1929.¹ As IUD use has increased during the last two decades, a number of reports have appeared documenting ovarian ectopic pregnancy with the IUD in situ. Among the general population, there is an incidence of 1 ovarian pregnancy per 150 to 200 ectopic pregnancies; however, among IUD users, this incidence increases to 1 per 7 to 9.^{2,3} Although IUDs may actively increase the risk of ectopic pregnancy,^{4,5} the major effect of inert plastic devices is to reduce uterine implantation by 99.5 percent, tubal implantation by 95 percent, and ovarian implantation not at all.³ The increased incidence of ovarian pregnancy in patients with an IUD, therefore, is probably only relative in comparison with the decreased tubal and intrauterine pregnancies.

In recent years, copper-containing devices have been used as the preferred IUD in many patients. Compared with nonmedicated IUDs, copper devices have the advantages that they are less likely to be expelled, produce less menstrual blood loss, are better tolerated by women without children, and are more likely to stay in place after postpartum or postabortion insertion. On the other hand, copper IUDs are more expensive and must be replaced more often than nonmedicated IUDs.⁵

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In this communication, a case of primary ovarian pregnancy involving a Copper-7 (Cu-7) IUD is described, and the pertinent literature is reviewed.

Case Report

A 29-year-old white woman, gravida 2, para 2, presented with nausea and fatigue of one month's duration and severe bilateral upper abdominal pain with radiation to both shoulders of one day's duration. Her menstrual cycles for the previous four months had been irregular and her last menstrual period started 35 days prior to admission. She was known to have had a Cu-7 IUD in situ for 26 months.

On admission, the patient was in moderate abdominal distress, with a temperature of 99.9°F, blood pressure of 118/70 mmHg, heart rate of 76 beats per minute, and respiratory rate of 20 per minute. Direct and rebound tenderness with some voluntary guarding was found in the upper abdomen, with minimal lower abdominal tenderness. Pelvic examination was normal, except for slight tenderness in the right adnexal area. No vaginal bleeding was observed. Hemoglobin level was 12.2 gm/100 mL; hematocrit, 36.4 percent; platelet count, 259,000/mm³; leukocyte count, 10,000/mm³. The hemoglobin level, hematocrit, and platelet count fell the following day to 11.2 gm/100 mL, 33.3 percent, and 227,000/mm³, respectively, with development of right adnexal fullness. Serum pregnancy test (RIA) was positive. Sonogram of the abdomen showed the IUD in situ, free fluid in the peritoneal cavity, and a mass in the right adnexal area containing fetal parts and a fetal heartbeat.

Dilation and curettage (D&C), after removal of

the IUD, obtained a minimal amount of tissue. Laparotomy revealed 500 to 600 mL of blood. The uterus, both fallopian tubes, and the left ovary were normal. A hemorrhagic cystic area at the distal pole of the right ovary was actively bleeding. Wedge resection of the right ovary was performed. The patient recovered well and was discharged from the hospital four days following operation.

Histopathological examination of the uterine curettings showed fragments of midsecretory endometrium and fragments of endometrium with decidual transformation of the stroma.

The hemorrhagic ovarian mass measured 6.0×4.5×3.0 cm. Section demonstrated a 3.0-cm cavity filled with clear fluid. The cavity was lined with a smooth membrane and contained a 1.6-cm embryo. A corpus luteum, 1.5 cm in greatest dimension, was adjacent to the cavity. Microscopic sections showed an edematous stroma and an area of implantation with vascularized chorionic villi adjacent to a corpus luteum. Hemorrhage extended from the area of implantation to the ovarian surface. Sections of the fetus were histologically normal. Growth and infiltration of chorionic tissue precluded distinction between intrafollicular and extrafollicular implantation. The diagnosis was ovarian pregnancy.

Comment

This case of ectopic pregnancy satisfied all of Spiegelberg's widely accepted criteria for ovarian pregnancy⁶: (1) the fallopian tube on the affected side must be normal, (2) the gestational sac must occupy the normal position of the ovary, (3) the gestational sac must be connected with the uterus by the ovarian ligament, and (4) ovarian tissue must be present in the wall of the sac.

The etiology of primary ovarian pregnancy remains unknown. The hypotheses that have been suggested include obstructed ovulation, malfunction of the tubes, favorable surface phenomena, parthenogenesis, or simply chance.⁷ The remote possibility of parthenogenesis could be addressed in future cases of ovarian pregnancy by establishing karyograms of embryonic tissue.

In a review of the literature from 1966 to the present, information was not complete in every

case of ovarian pregnancy associated with IUD use.⁸⁻²¹ The IUD had been in use for 20 months on the average (SD = 19 months, n = 51). The mean length of amenorrhea was 35 days (SD = 20 days, n = 34). In cases that described symptoms, 48 of 50 (96 percent) presented with abdominal pain, and 26 of 40 (65 percent) with vaginal bleeding. Uterine size was normal in 21 of 26 reported cases (81 percent), and adnexal enlargement was found in 24 of 30 cases (80 percent) for which data were available. In the case described in this report, the pregnancy test was positive. This is in agreement with previous descriptions of ovarian pregnancy, which have documented a relatively high incidence of positive pregnancy tests.¹² Although wedge resection has been advocated to increase detection of ovarian pregnancy,^{22,23} the minority of operative procedures used in treating these ovarian pregnancies was wedge resection (11 of 46, 24 percent). In 22 of 46 cases (48 percent) for which information was reported, oophorectomy or salpingo-oophorectomy was the surgical procedure, while cystectomy was performed in 13 of 46 reported cases (28 percent).

Since 1966, 27 percent of the reported cases of ovarian pregnancy associated with the IUD in the United States have involved the Cu-7 IUD.⁸⁻¹⁴ The prevalence of the Cu-7 IUD among IUD users in the United States increased from 0.0 percent before 1974 to 29.2 percent in 1976.²⁴ In 1977, 37.4 percent of IUD users in the United States wore the Cu-7 device (HW Ory, Women's Health Study, personal communication, February 25, 1982). The Cu-7 since its introduction has held a nearly constant proportion of the United States market, varying from 65 to 80 percent of the IUDs distributed each year (RL Alberti, Searle Laboratories, personal communication, March 10, 1982; see also Lis-kin and Fox⁵). Hence, the prevalence of the Cu-7 among IUD users has probably increased in an approximately linear manner to reach a maximum value within the range of the market share held by the Cu-7 IUD. Information is available concerning the percentage of women in the United States using an IUD²⁵ and changes in the population of women aged 14 to 44 years in the United States from 1966 to the present.^{26,27} These data permit an approximation of the proportion of woman-years

Continued on page 394

Brief Summary

Enduronyl[®] Methyclothiazide and Deserpidine

Oral thiazide-rauwolfia therapy for hypertension.

Warning: This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

Indications: ENDURONYL (methyclothiazide and deserpidine) is indicated in the treatment of mild to moderately severe hypertension (see boxed warning). In many cases ENDURONYL alone produces an adequate reduction of blood pressure. In resistant or unusually severe cases ENDURONYL also may be supplemented by more potent antihypertensive agents. When administered with ENDURONYL, more potent agents can be given at reduced dosage to minimize undesirable side effects.

Contraindications: Methyclothiazide is contraindicated in patients with renal decompensation and in those who are hypersensitive to this or other sulfonamide-derived drugs.

Deserpidine is contraindicated in patients with known hypersensitivity, mental depression especially with suicidal tendencies, active peptic ulcer, and ulcerative colitis. It is also contraindicated in patients receiving electroconvulsive therapy.

Warnings: METHYLCLOTHIAZIDE — Methyclothiazide shares with other thiazides the propensity to deplete potassium reserves to an unpredictable degree.

Thiazides should be used with caution in patients with renal disease or significant impairment of renal function, since azotemia may be precipitated and cumulative drug effects may occur.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma.

Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.

Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma.

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

DESERPIDINE — Extreme caution should be exercised in treating patients with a history of mental depression. Discontinue the drug at the first sign of despondency, early morning insomnia, loss of appetite, impotence, or self-deprecation. Drug-induced depression may persist for several months after drug withdrawal and may be severe enough to result in suicide.

Usage in Pregnancy and Lactation: METHYLCLOTHIAZIDE — Thiazides cross the placental barrier and appear in cord blood. The use of thiazides in pregnant women requires that the anticipated benefit be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possible other adverse reactions that have occurred in the adult.

Thiazides appear in breast milk. If use of the drug is deemed essential, the patient should stop nursing.

DESERPIDINE — The safety of deserpidine for use during pregnancy or lactation has not been established, therefore, it should be used in pregnant women or in women of childbearing potential only when in the judgment of the physician its use is deemed essential to the welfare of the patient. Increased respiratory secretions, nasal congestion, cyanosis, and anorexia may occur in infants born to rauwolfia alkaloid-treated mothers, since these preparations are known to cross the placental barrier to enter the fetal circulation and appear in cord blood. They also are secreted by nursing mothers into breast milk.

Reproductive and teratology studies in rats reduced the mating index and neonatal survival indices; the no-effect dosage has not been established.

Precautions: Periodic determinations of serum electrolytes should be performed at appropriate intervals for the purpose of detecting possible electrolyte imbalances such as hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when a patient is vomiting excessively or receiving parenteral fluids. All patients should be observed for other clinical signs of electrolyte imbalances such as dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting.

Hypokalemia may develop with thiazides as with any other potent diuretic, especially when brisk diuresis occurs, severe cirrhosis is present, or when corticosteroids or ACTH are given concomitantly. Interference with the adequate oral intake of electrolytes will also contribute to the possible development of hypokalemia. Potassium depletion, even of a mild degree, resulting from thiazide use, may sensitize a patient to the effects of cardiac glycosides such as digitalis.

Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt, except in rare instances when the hyponatremia is life threatening.

In actual salt depletion, appropriate replacement is the therapy of choice.

Hyperuricemia may occur or frank gout may be precipitated in certain patients receiving thiazide therapy.

Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes mellitus may become manifest during thiazide administration.

Thiazide drugs may increase the responsiveness to tubocurarine.

The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient.

Thiazides may decrease arterial responsiveness to norepinephrine. This diminution is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.

If progressive renal impairment becomes evident as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy.

Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

Thiazides have been reported, on rare occasions, to have elevated serum calcium to hypercalcemic levels. The serum calcium levels have returned to normal when the medication has been stopped. This phenomenon may be related to the ability of the thiazide diuretics to lower the amount of calcium excreted in the urine.

Because rauwolfia preparations increase gastrointestinal motility and secretion, this drug should be used cautiously in patients with a history of peptic ulcer, ulcerative colitis, or gallstones, where biliary colic may be precipitated.

Caution should be exercised when treating hypertensive patients with renal insufficiency since they adjust poorly to lowered blood pressure levels.

Use deserpidine cautiously with digitalis and quinidine since cardiac arrhythmias have occurred with rauwolfia preparations.

Preoperative withdrawal of deserpidine does not assure that circulatory instability will not occur. It is important that the anesthesiologist be aware of the patient's drug intake and consider this in the overall management, since hypotension has occurred in patients receiving rauwolfia preparations. Anticholinergic and/or adrenergic drugs (metaraminol, norepinephrine) have been employed to treat adverse vagocurricular effects.

Adverse Reactions: METHYLCLOTHIAZIDE — **GASTROINTESTINAL SYSTEM REACTIONS:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis.

CENTRAL NERVOUS SYSTEM REACTIONS: Dizziness, vertigo, paresthesias, headache, xanthopsia.

HEMATOLOGIC REACTIONS: Leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia.

DERMATOLOGIC — **HYPERSENSITIVITY REACTIONS:** Purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous vasculitis).

CARDIOVASCULAR REACTION: Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates, or narcotics.

OTHER: Hyperglycemia, glycosuria, hypercalcemia, hyperuricemia, muscle spasm, weakness, restlessness.

There have been isolated reports that certain nonedematous individuals developed severe fluid and electrolyte derangements after only brief exposure to normal doses of thiazide and non-thiazide diuretics. The condition is usually manifested as severe dilutional hyponatremia, hypokalemia, and hypochloremia. It has been reported to be due to inappropriately increased ADH secretion and appears to be idiosyncratic. Potassium replacement is apparently the most important therapy in the treatment of this syndrome along with removal of the offending drug.

Whenever adverse reactions are severe, treatment should be discontinued.

DESERPIDINE — The following adverse reactions have been reported with rauwolfia preparations. These reactions are usually reversible and disappear when the drug is discontinued.

GASTROINTESTINAL: Including hypersecretion, anorexia, diarrhea, nausea, and vomiting.

CARDIOVASCULAR: Including angina-like symptoms, arrhythmias (particularly when used concurrently with digitalis or quinidine), and bradycardia.

CENTRAL NERVOUS SYSTEM: Including drowsiness, depression, nervousness, paradoxical anxiety, nightmares, extrapyramidal tract symptoms, CNS sensitization manifested by dull sensorium, and deafness.

DERMATOLOGIC — **HYPERSENSITIVITY:** Including pruritus, rash, and asthma in asthmatic patients.

OPHTHALMOLOGIC: Including glaucoma, uveitis, optic atrophy, and conjunctival injection.

HEMATOLOGIC: Thrombocytopenic purpura.

MISCELLANEOUS: Nasal congestion, weight gain, impotence or decreased libido, dysuria, dyspnea, muscular aches, dryness of mouth, dizziness, and headache.

Overdosage: Symptoms of thiazide overdosage include electrolyte imbalance and signs of potassium deficiency such as confusion, dizziness, muscular weakness, and gastrointestinal disturbances. General supportive measures including replacement of fluids and electrolytes may be indicated in treatment of overdosage.

An overdosage of deserpidine is characterized by flushing of the skin, conjunctival injection and pupillary constriction. Sedation ranging from drowsiness to coma may occur. Hypotension, hypothermia, central respiratory depression and bradycardia may develop in cases of severe overdosage. Treatment consists of the careful evacuation of stomach contents followed by the usual procedures for the symptomatic management of CNS depression of overdose. If severe hypotension occurs it should be treated with a direct acting vasopressor such as norepinephrine bilaterally injection.

OVARIAN PREGNANCY

Continued from page 390

of IUD use that involve the Cu-7 IUD in the United States since 1966, which is calculated to be 28 percent. This calculation agrees with the observed 27 percent of the cases of ovarian pregnancy with an IUD in situ that involved the CU-7 IUD reported in the United States literature.

The agreement of these calculated and observed values to within 1 percent is well within that expected from the sources of error in the calculation and the imprecision of reporting in the literature. This comparison suggests that the Cu-7 does not increase the risk of ovarian pregnancy relative to inert plastic IUDs. Similar statements have been made by several investigators concerning the relative likelihood of ectopic pregnancy with copper-containing IUDs and with nonmedicated IUDs.^{28,29}

In conclusion, evidence cited in this report suggests that copper-containing or inert plastic devices do not affect the likelihood of ovarian pregnancy. Better understanding of the etiology of primary ovarian pregnancy and the mechanism of action of inert and copper-containing IUDs will allow interpretation of the evidence to date, which suggests that the relationship between IUDs and ovarian pregnancy does not reflect causality. Nonetheless, both copper-containing and nonmedicated IUDs suppress uterine or tubal pregnancies, whereas both types of IUD probably have no effect upon the incidence of ovarian pregnancy. Clinicians, therefore, should be aware of the possibility of ovarian pregnancy in patients who use the intrauterine device.

References

1. Grafenberg E: Die intrauterine methode de konzerplionsuerhting, Proceedings of the Third Congress World League for Sexual Reform, Haine N (ed). London, Keegan, Paul, Treach, Trulener, 1930
2. Tietze C: Wanted—Ovarian pregnancies, letter. Am J Obstet Gynecol 101:275, 1968
3. Lehfeld H, Tietze C, Gorstein F: Ovarian pregnancy and the intrauterine contraceptive device. Am J Obstet Gynecol 108:1005, 1970
4. Tatum HJ, Schmidt FH: Contraceptive and steriliza-

tion practices and extrauterine pregnancy: A realistic perspective. *Fertil Steril* 28:407, 1977

5. Liskin L, Fox G: IUDs—an appropriate contraceptive for many women. *Popul Rep [B]* 4:101, 1982

6. Spiegelberg O: Zur casuistik der ovarialschwangerschaft. *Arch Gynaekol* 13:73, 1878

7. Boronow RC, McElin TW, West RH, Buckingham JC: Ovarian pregnancy: Report of four cases and thirteen-year survey of the English literature. *Am J Obstet Gynecol* 91:1095, 1965

8. Berger B, Blechner JN: Ovarian pregnancy associated with copper-7 intrauterine device. *Obstet Gynecol* 52:597, 1978

9. Wilson SJ, Milano CT, Marinescu A: Ovarian pregnancy and the intrauterine device, report of a case and review of the literature. *Mount Sinai J Med* 46:15, 1979

10. Gray CL, Ruffolo EH: Ovarian pregnancy associated with intrauterine contraceptive devices. *Am J Obstet Gynecol* 132:134, 1978

11. Chidiac A, Buka N, Ravinsky E, Garulli R: Ovarian ectopic pregnancy in association with a copper-7 intrauterine device in situ. *Fertil Steril* 32:127, 1979

12. Evans MI, Angerman NS, Moravec WD, Hajj SN: The intrauterine device and ovarian pregnancy. *Fertil Steril* 32:31, 1979

13. Hallatt JG: Primary ovarian pregnancy: A report of twenty-five cases. *Am J Obstet Gynecol* 143:55, 1982

14. McMorries KE, Lofton RH, Stinson JC, Cummings RV: Is the IUD increasing the number of ovarian pregnancies? *Contemp Ob/Gyn* 13(June):165, 1979

15. Golan A, Menchovsky E, Edelstein T: Primary ovarian pregnancy and the intrauterine contraceptive device: Report of two cases. *S Afr Med J* 52:1130, 1977

16. Buchholz F, Philipp E: Kasuistischer beitrag zur ovarialgraviditat bei intrauterinpressaren. *Med Welt* 29:59, 1978

17. Laufer M, Zilberman R, Antebi SV: Ectopic pregnancy and intrauterine device. *Harefuah* 94:71, 1978

18. Ringrose CAD: The occurrence of non-tubal ectopic

pregnancies in women with an intrauterine device. *J Reprod Fertil* 55:373, 1979

19. Esmer A, Ahat E: Primare ovarialgraviditat bei liegender intrauterinspirale. *Geburtshilfe Frauenheilkd* 40:456, 1980

20. David MP, Avni A, Pausner D, Baratz M: Ovarian pregnancy and IUD. *Eur J Obstet Gynaecol Reprod Biol* 11:173, 1980

21. Exalto N, Vooyes GP, Meyer JWR, Lange WPH: Ovarian pregnancy: A morphologic description. *Eur J Obstet Gynaecol Reprod Biol* 11:179, 1980

22. Helde MD, Campbell JS, Himaya A, et al: Detection of unsuspected ovarian pregnancy by wedge resection. *Can Med Assoc J* 106:237, 1972

23. Campbell JS, Hacquebard S, Mitton DM, et al: Acute hemoperitoneum, IUD, and occult ovarian pregnancy. *Obstet Gynecol* 43:438, 1974

24. Ford K: Use of intrauterine contraceptive devices in the United States. In National Center for Health Statistics (Hyattsville, Md): Advance Data from Vital and Health Statistics, No. 43. DHEW publication No. (PHS)79-1250. Government Printing Office, 1978

25. Piotrow PT, Rinehart W, Schmidt JC: IUDs—update on safety, effectiveness, and research. *Popul Rep [B]* 3:49, 1979

26. US Bureau of Census: Statistical Abstract of the United States; 1978. US Department of Commerce. Government Printing Office, 1978

27. Births, marriages, divorces, and deaths for 1980. National Center for Health Statistics (Hyattsville, Md): In Monthly Vital Statistics Report, Provisional Data, vol 29, No. 12. DHHS publication No. (PHS)81-1120. Government Printing Office, March 18, 1981

28. Tatum HJ, Schmidt FH: Contraceptive and sterilization practices and extrauterine pregnancy: A realistic perspective. *Fertil Steril* 28:407, 1977

29. Ory HW, Women's Health Study: Ectopic pregnancy and intrauterine contraceptive devices: New perspectives. *Obstet Gynecol* 57:137, 1981

Epigastric Bruit: Prevalence and Clinical Significance in a Student Population

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Localized epigastric bruit is the sole physical sign in celiac artery compression syndrome,^{1,2} an

association of abdominal symptoms with extrinsic compression of the celiac axis at its origin from the anterior aspect of the abdominal aorta immediately below the diaphragm. This extrinsic compression may be from either the median arcuate ligament of the diaphragm or from strands of the celiac plexus.³

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