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CASE REPORT

Peripheral Gangrene, a Rare Side Effect of Methergine, Secondary to Antiphospholipid Antibody Syndrome: Case Report

Major Anjali Rani[1] · Preeti Vashistha[2] · Mayank Sharma[3] · Amrita Singh[2]

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Introduction

Methergine is a semi-synthetic ergot alkaloid used for the prevention and treatment of postpartum and postabortal hemorrhage [1]. Methergine acts directly on the smooth muscle of the uterus and increases the tone, rate, and amplitude of rhythmic contractions; thus, it induces a rapid and sustained tetanic contraction of uterus [1, 2]. Peripheral gangrene is a rare complication of methergine, which develops due to vasoconstriction by stimulation of alpha-adrenergic and serotonin receptors[3] and inhibition of release of endothelial-derived relaxation factor. It leads to reduced blood supply of already poorly vascularized distal organs like limbs, fingers and toes. This phenomenon mostly occurs in presence of any preexisting factors like [1, 2]-

1. Patient is having any underlying systemic disease affecting blood vessels, e.g., antiphospholipid antibody syndrome, vasculitis, occlusive peripheral vascular disease, Raynaud's phenomenon, other autoimmune disease, etc.
2. Drug interactions with:- Beta blockers, CYP 3A4 inhibitors, e.g., macrolide antibiotics, HIV protease inhibitors, Azole antifungal, etc.
3. Use of inadvertent large dose of methergine (very rare)

Our aim to report this case is the need of increasing awareness among practicing obstetricians regarding use of methergine. Before its use, we should assess high risk factors, rule out contraindications to prevent the side effect like peripheral gangrene, which is though rare but a very serious complication of methergine.

Case Report

A 25-year-old female Para2, Live2, Abortion1, visited the outpatient department of Obstetrics and gynecology with complaints of per vaginal bleeding and blackening with loss of sensation of fingertips of right hand for 20 days. Patient had a history of heavy vaginal bleeding followed by D&C done in view of incomplete abortion 25 days back at some private hospital, and there was history of administration of high dose of Inj Methergine to manage postabortal hemorrhage with transfusion of 3 units of blood. Her last menstrual period was $2^{1/2}$ month back, and previous cycles were regular

Dr Major Anjali Rani: MBBS MS DNB, Professor, Department of Obstetrics and Gynecology, Institute of Medical Sciences, Banaras Hindu University. Dr Preeti Vashistha: MBBS MS DNB, Assistant Professor Department of obstetrics and gynecology, Era's Lucknow Medical College & Hospital. Dr Mayank Sharma: MBBS MD (Medicine), Senior resident (DM) Department of Critical care medicine, Sanjay Gandhi Postgraduate institute of Medical Sciences Lucknow. Dr Amrita Singh: MBBS MS DNB, Assistant Professor Department of obstetrics and gynecology, Era's Lucknow Medical College & Hospital.

✉ Preeti Vashistha
preeti603@gmail.com

Major Anjali Rani
anjaliraniimsbhu@gmail.com

Mayank Sharma
mayankjnmc2k6@gmail.com

Amrita Singh
amritanitinshankar@gmail.com

[1] Department of Obstetrics and Gynecology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India

[2] Department of Obstetrics and Gynecology, Era's Lucknow Medical College & Hospital, Lucknow, India

[3] Department of Critical Care Medicine, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

with average flow. She had a history of previous two normal vaginal deliveries. On general examination, patient was conscious, oriented, her pulse was 104/min, blood pressure: 100/60 mm of Hg, mild pallor was present, systemic examination was within normal limits. Local examination of upper limb showed radial pulse of right upper limb was feeble than left upper limb, blackish discoloration of distal part of all five digits of right hand was seen (Fig. 1), dry and thickened skin with loss of touch and pain sensation with presence of mild temperature sensation at the affected area of right hand was present. On per abdominal examination, abdomen was soft with no tenderness or organomegaly. On per speculum examination, post-intervention cervical laceration was seen, and mild bleeding through cervical os was present. On per vaginal examination, uterus was 10 weeks size, and forniceal induration with tenderness was present (right > > left). For the evaluation of the cause of fingertip gangrene, further relevant investigations were done with medicine and surgery reference. Diagnosis of Antiphospholipid antibody syndrome was made with the help of specific blood investigations, that is, anticardiolipin antibody and, Anti-β2 glycoprotein antibody IgG and IgM which were positive in high titers. Ultrasound with color doppler of upper limb was done which showed reduced flow in right digital arteries, with biphasic waveform in right brachial, radial, ulnar, digital arteries. After ruling out other causes of peripheral gangrene, diagnosis of methergine-induced peripheral gangrene with antiphospholipid antibody syndrome was made after consultation with medicine and surgery department. Treatment including warfarin overlapped with low molecular weight heparin, vasodilator-nicardipine, platelet aggregation inhibitors-pentoxifylline, antiplatelet-ecosprin was started. Suction and evacuation were done under antibiotic cover with strict asepsis in view of retained product of conception as showed in USG pelvis. Repeat USG with color doppler of right upper limb after 5 days of treatment showed thrombosed third and fourth metacarpal arteries with collateral circulation providing dampened flow to the digital arteries; however, the circulation through the respective digital arteries was insufficient. Rest of the digital circulation showed normal flow. Patient was discharged on day 10 in satisfactory condition with advice to continue above treatment. Repeat anticardiolipin antibody and Anti-β2 glycoprotein anibody IgG and IgM was done after 12 weeks to confirm the diagnosis of APLA syndrome, which came out to be positive in high titres. Patient was under regular follow-up till 6 months; during this period, patient's right hand recovered satisfactorily (loss of fingernails and pulp of around 1 cm^2) (Fig. 2). Satisfactory recovery included preservation of maximal functional capacity, sensations and satisfactory appearance with minimal loss of functional length of fingers.

Discussion

Methergine is effectively used in postpartum and postabortal hemorrhage, but it also causes vasoconstriction by stimulating α-adrenergic receptor [3]. This is a known fact that the distal most part of our body is poorly vascularized as compare to more proximal part, so the vasoconstriction can lead to reduced blood supply of these poorly vascularized distal parts which can cause gangrene. Fingers, toes and limbs are mostly affected. Isolated incidence of methergine-induced digital gangrene is very rare but in presence of underlying hypercoagulable state or vasculitis due to the presence of any autoimmune disease, for example, APLA syndrome, the incidence is more. Because underlying hypercoagulability or vasculitis due to APLA syndrome with methergine induced vasoconstriction collectively causes significant reduced blood supply which are sufficient to develop gangrene [4].

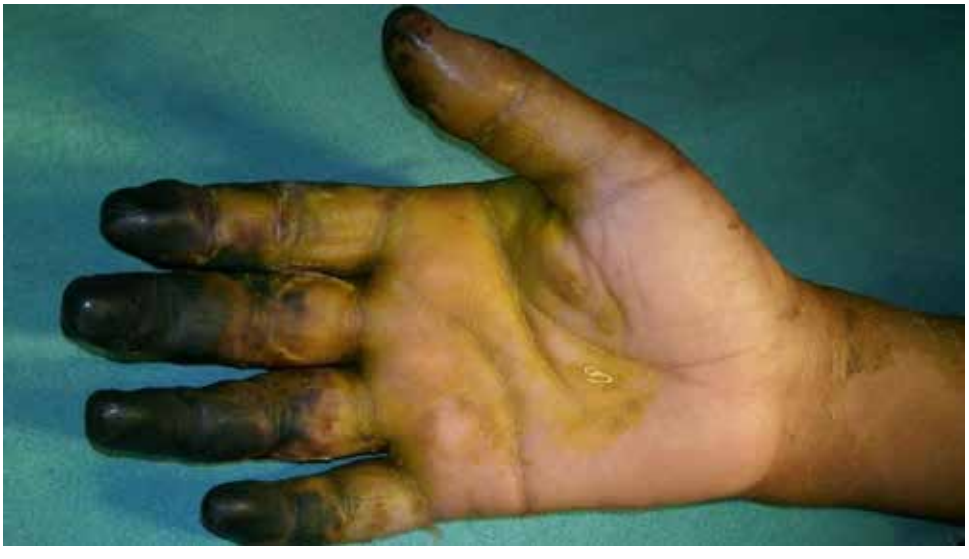

Fig. 1 Peripheral Gangrene of fingers of right hand

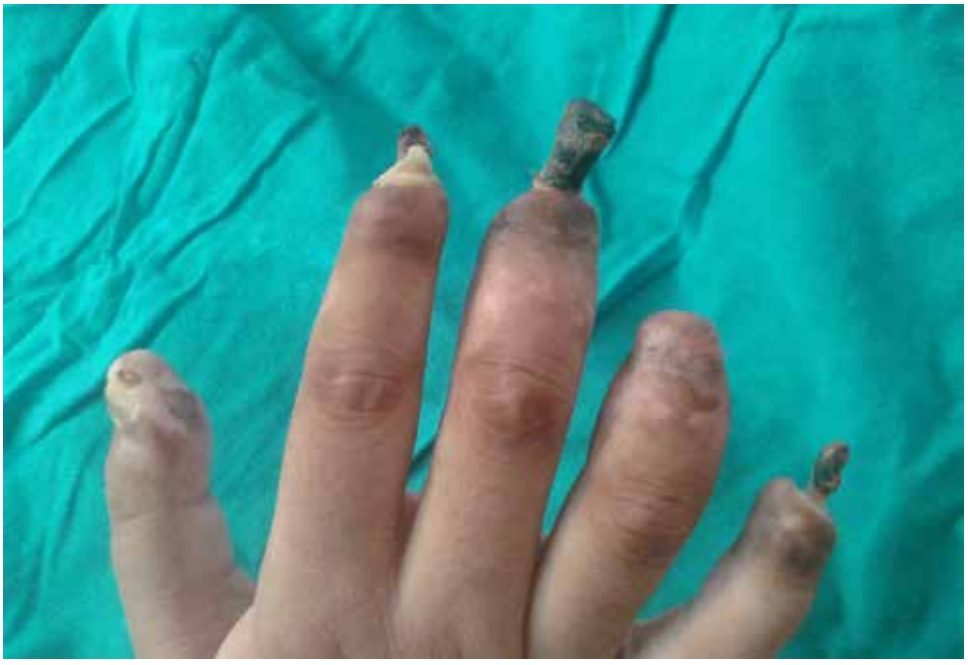

Fig. 2 Recovery of right hand after treatment (Almost 90% functional recovery of right hand)

As far as our best knowledge, no case is reported in the literature with peripheral gangrene as a side effect of methergine, secondary to antiphospholipid antibody syndrome. A case report "Symmetrical peripheral gangrene in Antiphospholipid Syndrome" by Mikio Shiba et al., published in Heart Asia June 2016, reported a case of 75-year-old woman with APLA syndrome developed symmetric peripheral gangrene in all four extremities. In this case report, author concluded that the peripheral gangrene can be caused by variety of disorders like connective tissue disorders, vasculitis, atherosclerosis, thromboembolism, DRUG INDUCED VASOSPASM, myeloproliferative disorders.

Conclusion

Methergine is very effective drug to treat postpartum and postabortal hemorrhage but it can leads to severe complications like gangrene of extremities because of its vasoconstrictive effect. So prior to use of methergine, a proper history to rule out any autoimmune disease, vascular disease, cardiac disease, hypertension is important to prevent these complications. In case of high suspicion of any underlying autoimmune disease, it is better to avoid methergine and use other available options.

Declarations

Conflict of interest The authors declare that they have no conflict of interest regarding the publication of this case report.

Informed Consent Informed written consent was taken from the patient.

Ethical Approval Patient identifiers have been anonymized.

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About the Author

Dr. Major Anjali Rani Professor Department of Obstetrics and Gynecology IMS BHU. She has worked in army as Short service commissioned officer, in Command hospital Chandimandir, Millitary hospital Jullandhar and Tezpur. She has published more than 25 papers in various national and international journals. Presently she is working as Secrectary Varanasi Obs & Gynae society and as Vice President NMO. She has conducted Medical Camps in Leh and Assam. She has special interest in High Risk Obstetrics.