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## Case Report

## Acute chorioamnionitis complicated with symmetrical peripheral gangrene

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## ABSTRACT

**Objective:** Symmetrical peripheral gangrene (SPG) is an uncommon but important clinical syndrome. We present a case of acute chorioamnionitis complicated with SPG.**Case report:** A 33-year-old female (gravida 5, para 2) was admitted with preterm premature rupture of membranes (PPROM) at 20 weeks and four days of gestation. She received cervical cerclage four days ago. Seven days after the diagnosis of PPRM, she developed fever, tachypnea and tachycardia. Termination of pregnancy was decided for clinical diagnosis of sepsis. After the abortus was born, gangrene change on the nose was noticed. Afterwards, this patient developed acrocyanosis of extremities. SPG developed following sepsis with intravascular disseminated coagulation (DIC). After intensive care, the patient underwent hyperbaric oxygen therapy and fasciectomy of the left forearm.**Conclusion:** We suggest awareness of SPG associated with acute chorioamnionitis. Early recognition of SPG, multidisciplinary care, and treatment of its underlying conditions are the mainstays of management.© 2020 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

Symmetrical peripheral gangrene (SPG) is a rare clinical syndrome associated with the presence of symmetrical peripheral ischemic lesion of two or more extremities in the absence of any obstruction of large vascular vessels. SPG is a rare but important cause of significant morbidity and mortality and early recognition of SPG and treatment of its underlying conditions may improve the final outcome for such patients.

SPG was first described as severe symmetrical gangrene of the peripheral extremities in a case report of sepsis complicated with intravascular disseminated coagulation (DIC) by Hutchinson in

1891 [1]. A few other cases have been described, including a case associated with H1N1 infection [2], as a complication of dengue fever [3], in a renal disease patient [4] or occurred following polytrauma [5].

SPG in patient with preterm premature rupture of membranes (PPROM) associated with septic shock and DIC is extremely rare and no such case was found in our literature search. Therefore, we would like to discuss a case of SPG in a PPRM patient complicated with acute chorioamnionitis, septic shock and DIC.

## Case report

A 33-year-old female (gravida 5, para 2) was admitted with PPRM at gestational age of 20 weeks and four days. She received the procedure of cervical cerclage due to cervical incompetence four days ago. There was not any prior history of cold or heat intolerance, tobacco smoking, diabetes, collagen vascular disease or similar family history in this patient. Treatment with the antibiotic regimen, ampicillin 2000 mg Q6H and erythromycin 250 mg Q6H,

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for PPRM was initiated. Seven days after the diagnosis of PPRM (gestational age: 21 weeks and four days), she developed fever, chills, nausea, tachypnea and tachycardia. The laboratory study revealed leukocytosis ( $20.4 \times 10^3/\mu\text{L}$ , normal range  $3.5\text{--}9.1 \times 10^3/\mu\text{L}$ ) and inflammatory parameters were elevated (CRP 16.74, normal  $<0.10$  mg/dL). Clinical diagnosis of sepsis was determined; termination of pregnancy was decided. There was no ergot alkaloids agent used in this case. After the abortus was delivered, septic shock then occurred. In this case, inotropic agent was not prescribed but gangrene change on the nose was first noted. Afterwards, the patient developed acrocyanosis of the extremities and progressed with warm and palpable pulse. Laboratory data revealed thrombocytopenia ( $39 \times 10^3/\mu\text{L}$ , normal range  $157\text{--}377 \times 10^3/\mu\text{L}$ ), prolonged coagulation times (APTT 60.3sec, normal range 30.7–40.5 s), elevated D-dimers ( $>10,000$  ng/mL(FEU), normal range 60–325 ng/mL (FEU)), low fibrinogen (118.7 mg/dL, normal range 194–421 mg/dL) and impaired renal function (Creatinine 8.68 mg/dL, normal range 0.6–1.2 mg/dL). Cultures including blood sampling and the placenta obtained during delivery were performed. Blood culture, endometrium culture and cervical bacterial culture revealed the presence of *Escherichia coli*. Pathology study of placenta demonstrated acute chorioamnionitis. After intensive care, clinical condition and renal function gradually improved. She then received hyperbaric oxygen therapy for peripheral gangrene and regional fasciectomy for left forearm during hospitalization (Fig. 1, Fig. 2). Due to stable condition and the improvement of renal function, she was then discharged and kept on hyperbaric oxygen therapy at the outpatient department.



Fig. 1. Left forearm sharp demarcation by Day 15.

## Discussion

We present a rare case of SPG in a patient with PPRM and acute chorioamnionitis complicated with septic shock and DIC. SPG is a well described but rare syndrome marked by the presence of symmetrical ischemia of the peripheries leading to the development of gangrenous lesions in two or more sites. All this occurs in the absence of any large vessel obstruction or vasculitis. Etiologies of symmetrical peripheral gangrene include the infective and non-infective; however, the exact incidence and pathogenesis of SPG are uncertain [6]. Sepsis induced DIC like condition has been shown to be linked in 85–100% to cases with SPG [7]. Ischemic changes of the distal extremities seen in SPG have been hypothesized to be as a result of low flow state in combination with microvascular occlusion from DIC [7]. Furthermore, factors such as cold-induced vasospasm, the use of vasoconstrictor drugs, diabetes mellitus, and renal failure have been shown to possibly aggravate these ischemic changes [7]. SPG is a sign of serious underlying disease including being an important cutaneous marker for DIC as several cases have shown a strong link between SPG and DIC [8]. Hence, prompt recognition and early treatment of the underlying medical problems and DIC may be beneficial for such patients associated with such disease [8].

Our case received cerclage operation prior to the present PPRM complicated with septic shock and DIC. The most frequent complication of cerclage reported in literature are the premature rupture of the membranes (PROM) followed by slipping suture and premature delivery. Intra-uterine infection are also quite commonly seen [9]. Our case however developed PPRM and acute chorioamnionitis four days after receiving cerclage and was therefore theorized to be secondary to the placement of the cervical cerclage. Unfortunately, culture was not performed before the cerclage in this case so it was unknown whether vaginal microbes were already present or appeared after the cerclage was placed. A recent prospective study investigated the microbiota present in the vagina pre- and post-rescue cervical cerclage to ascertain the correlation between vaginal microbial composition and outcome of rescue cervical cerclage [10]. The study revealed that bacterial composition often remain unaltered following cerclage insertion in most cases (10/14, 71%) [10]. Insertion of a rescue cerclage in combination with antibiotics was also shown to not alter the



Fig. 2. Still gangrene change at fingers (A) and toes (B) by Day 15.

vaginal microbiome in the majority of cases [10]. Furthermore, the study also highlighted the importance of two organisms of which their levels have their respective impact on the clinical outcome for such patients. Firstly, the amount of *Lactobacillus* spp. That are present seemed to correspond with premature cervical dilation and secondly, high levels of *G. vaginalis* prior to rescue cerclage seemed to lead to poorer outcomes [10]. Additionally, high maternal serum CRP levels in PPROM patients may be an accurate predictor of chorioamnionitis [11]. Intrauterine infection and preterm delivery are major complications of PPROM [12]. In women with PPROM, antibiotic prophylaxis against group B streptococcus and *E. coli* are thus recommended [13]. In our case, the blood and endometrium culture revealed the presence of *E. coli*. Cervical cerclage may increase the risk of ascending infection and then cause PPROM. This case emphasizes the importance of time to terminate and appropriate infection control measures before and throughout to prevent adverse clinical outcomes.

Diagnosis of SPG should be suspected in patients with symmetrical bluish discoloration of extremities in the absence of any obstruction of large vessels that supplied the affected extremities. A thorough laboratory work-up of SPG should be done to establish the diagnosis of SPG and to determine any underlying factors that predisposes to such an ischemic syndrome [6]. Treatment of the underlying cause, management of DIC, stabilization of hemodynamics, and early recognition of SPG are key to the successful clinical management of such cases [7]. Sympathetic blockades, vasodilators and  $\alpha$ -blockers have also shown to be potentially beneficial [7]. Such cases should be managed in an intensive care unit setting. A multidisciplinary team should also be involved and all these may further lead to improved mortality and morbidity for such patients. Our case also received hyperbaric oxygen therapy.

Unfortunately, SPG is often associated with poor clinical prognosis with high rates of amputation of limbs reported among the survivors [6] and high mortality are often seen with numbers ranging from one-tenth to one third of SPG patients [7]. The development of SPG may be an ominous prognostic sign in the background of DIC [7]; leukopenia is another factor that may play a role as a poor prognostic marker for SPG [14]. In our case however, no leukopenia was detected and no amputation was performed. After improvement of renal function and stabilization of her condition, she was discharged and kept on hyperbaric oxygen therapy at the outpatient department.

## Conclusion

There is a high association between SPG and DIC. DIC most commonly occurs due to sepsis. In our case, SPG developed in a PPROM patient with acute chorioamnionitis, septic shock and DIC. Therefore, this report serves to raise awareness about the fact that SPG can occur in conjunction with acute chorioamnionitis. To prevent symmetrical peripheral gangrene occurring in so many

cases of PPROM of our clinical practice, it is important to promptly identify pre-gangrenous changes and recognize SPG could be triggered possibly by sepsis or ergot alkaloids agent. Early recognition of SPG, multidisciplinary care, and treatment of its underlying conditions are the current mainstays of successful clinical management.

## Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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## References

- [1] Hutchinson J. Notes of uncommon cases. *Br Med J* 1891;2(1592):8–9.
- [2] Kaulgud RS, Kamath V, Patil V, Desai S. Symmetric peripheral gangrene associated with H1N1 infection. *Int J Prev Med* 2013;4(10):1206–9.
- [3] Modak D, Guha SK. Symmetrical peripheral gangrene: a rare complication of dengue fever. *Indian J Med Sci* 2012;66(11–12):292–5.
- [4] Wilkinson SP, Stewart WK, Parham DM, Guthrie W. Symmetric gangrene of the extremities in late renal failure: a case report and review of the literature. *Q J Med* 1988;67(252):319–41.
- [5] Tan JH, Mohamad Y, Tan CLH, Kassim M, Warkentin TE. Concurrence of symmetrical peripheral gangrene and venous limb gangrene following poly-trauma: a case report. *J Med Case Rep* 2018;12(1):131.
- [6] Ghosh SK, Bandyopadhyay D. Symmetrical peripheral gangrene. *Indian J Dermatol Venereol Leprol* 2011;77(2):244–8.
- [7] Basnet S, Rajagopalan P, Dhital R, Qureshi A. Symmetrical peripheral gangrene associated with low output cardiac failure. *Medicina* 2019;55(7).
- [8] Molos MA, Hall JC. Symmetrical peripheral gangrene and disseminated intravascular coagulation. *Arch Dermatol* 1985;121(8):1057–61.
- [9] Aarnoudse JG, Huisjes HJ. Complications of cerclage. *Acta Obstet Gynecol Scand* 1979;58(3):255–7.
- [10] Brown RG, Chan D, Terzidou V, Lee YS, Smith A, Marchesi JR, et al. Prospective observational study of vaginal microbiota pre- and post-rescue cervical cerclage. *BJOG* 2019;126(7):916–25.
- [11] Asadi N, Faraji A, Keshavarzi A, Akbarzadeh-Jahromi M, Yoosefi S. Predictive value of procalcitonin, C-reactive protein, and white blood cells for chorioamnionitis among women with preterm premature rupture of membranes. *Int J Gynaecol Obstet* 2019;147(1):83–8.
- [12] Schmitz T, Sentilhes L, Lortie E, Gallot D, Madar H, Doret-Dion M, et al. Preterm premature rupture of the membranes: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF). *Eur J Obstet Gynecol Reprod Biol* 2019;236:1–6.
- [13] Doret Dion M, Cazanave C, Charlier C. Antibiotic prophylaxis in preterm premature rupture of membranes: CNGOF preterm premature rupture of membranes guidelines. *Gynecologie, obstetrique, fertilité & senologie* 2018;46(12):1043–53.
- [14] Ghosh SK, Bandyopadhyay D, Ghosh A. Symmetrical peripheral gangrene: a prospective study of 14 consecutive cases in a tertiary-care hospital in eastern India. *J Eur Acad Dermatol Venereol : JEADV* 2010;24(2):214–8.