High fibrin/fibrinogen degradation product and D-dimer levels for the diagnosis of invasive group A streptococcal infections during pregnancy

N. Matsumoto¹*, Y. Mori²

¹Matsumoto Women’s Health Clinic, Saitama (Japan)
²Department of Obstetrics and Gynecology, The Jikei University School of Medicine, Tokyo (Japan)

Summary

Objective: Invasive group A streptococcal (GAS) infections during pregnancy are uncommon, and, thus, their early diagnosis remains challenging. The present study was performed to assess fibrin/fibrinogen degradation product (FDP) and D-dimer levels in pregnant women with invasive GAS infections and establish whether they contribute to a diagnosis. Materials and Methods: Laboratory data, including FDP and D-dimer levels, measured between fulmination and just before delivery in 46 cases, consisting of 45 previously published cases and the present case, were examined. Results: Fetal/neonatal and maternal mortality rates were 61 and 28%, respectively. Laboratory data obtained from 24 cases just before delivery were as follows: white blood cell count > 12,000/μL, 46% of cases; platelet count > 100,000/μL, 55% of cases, and C-reactive protein (CRP) level > 10 mg/dL, 40% of cases. These variables showed no sensitivity for the diagnosis of invasive GAS infections. However, 100% of cases were positive for FDP (> 10 μg/dL) and D-dimer (> 2 μg/dL), the levels of which were extremely high in many cases. Conclusion: FDP and D-dimer levels may contribute to the diagnosis of invasive GAS infections during pregnancy.

Key words: Antepartum; Disseminated intravascular coagulation; Sepsis; Streptococcus pyogenes; Toxic shock syndrome.

Introduction

Perinatal invasive group A streptococcal (GAS) infections, which include perinatal GAS-induced toxic shock syndrome, mainly occur in puerperal women. Although these infections are rare in antenatal women, poorer outcomes have been reported for antenatal cases than for puerperal cases [1]. Therefore, early awareness and the rapid initiation of therapy are important for the management of pregnant women with invasive GAS infections [2]. However, since the primary symptoms appear to be flu-like, an early diagnosis remains challenging for clinicians.

We herein describe a case of invasive GAS infection during pregnancy, in which the baby and mother both survived [3]. In brief, the patient was 41 years old, para 1, and on her 39th week of pregnancy. She presented with chills and a fever (38 °C). Fetal tachycardia was noted and, thus, she was admitted for observation. Her laboratory data on admission were as follows: white blood cell count of 8,200/μL, C-reactive protein (CRP) level of 0.52 mg/dL, and normal levels in other tests, except for very high plasma fibrin/fibrinogen degradation product (FDP) and D-dimer levels of 193 and 75 μg/dL, respectively. Intravenous antibiotics were administered for the febrile condition with no detected infection. Although the patient was not in a state of shock, cardiotocography indicated that the condition of the fetus was deteriorating. Emergency cesarean section was performed, and the baby was born without neonatal asphyxia or any infection. Although the patient developed septic shock after the procedure, she was successfully treated and, as a result, fully recovered. Since her blood culture indicated GAS infection, she was diagnosed with invasive GAS infection during pregnancy.

This case prompted speculation on FDP and D-dimer levels in other patients with similar conditions. Therefore, the present study investigated FDP and D-dimer levels in pregnant women with invasive GAS infections and whether they may contribute to a diagnosis.

Materials and Methods

Forty-five cases of invasive GAS infection during pregnancy from studies published in English or Japanese between 2000 and 2017 were identified [4-40]. Cases in which individual clinical data were not available were excluded. The literature search included PubMed, the Japana Centra Revuo Medicina, and reference lists of previously published cases. The search terms used included: ‘group A streptococcus’, ‘Streptococcus pyogenes’, ‘infection’, ‘pregnancy’, ‘perinatal’, ‘peripartum’, ‘antenatal’, ‘antepartum’, ‘intrapartum’, ‘delivery’, ‘labor’, ‘abortion’, ‘toxic shock’, ‘bacteremia’, ‘sepsis’, and ‘disseminated intravascular coagulation’.

The criteria for invasive GAS infections during preg-
Table 1. — Summary of categorical data for clinical background, symptoms, outcomes and therapies from the 46 cases.

| Factor                                      | n | %      |
|---------------------------------------------|---|--------|
| Maternal age (y)                            |   |        |
| Teens                                       | 1 | 2.2    |
| Twenties                                    | 9 | 19.6   |
| Thirties                                    | 32| 69.6   |
| Forties                                     | 4 | 8.7    |
| Parity                                      |   |        |
| Nulliparous                                 | 8 | 19.4   |
| Multiparous                                 | 37| 80.6   |
| NA                                          | 1 |        |
| Maternal complications                      |   |        |
| Yes                                         | 10| 24.4   |
| No                                          | 31| 75.6   |
| NA                                          | 5 |        |
| Week of pregnancy at fulmination            |   |        |
| Abortion period (< 22 weeks)                | 5 | 10.9   |
| Second trimester (22-27 weeks)              | 4 | 8.7    |
| Third trimester before term (28-36 weeks)   | 18| 39.1   |
| Term (≥ 37 weeks)                           | 19| 41.3   |
| Fulmination period                          |   |        |
| Antenatal (before the onset of labor)       | 45| 97.8   |
| During labor                                | 1 | 2.2    |
| Mode of delivery                            |   |        |
| Emergency cesarean                          | 22| 47.8   |
| Vaginal delivery                            | 17| 37     |
| Abortion                                    | 4 | 8.7    |
| None (maternal death before delivery)       | 3 | 6.5    |
| Mortality                                   |   |        |
| Fetal/neonatal death                        | 28| 60.9   |
| Maternal death                              | 13| 28.3   |
| Fetal/neonatal asphyxia (including death)   |   |        |
| Yes                                         | 34| 91.9   |
| No                                          | 3 | 8.1    |
| NA                                          | 9 |        |
| Symptoms at fulmination period (some are overlapping) | | |
| Fever (>38 °C)                              | 44| 95.7   |
| Respiratory symptoms                        | 20| 43.5   |
| Abdominal pain                              | 32| 69.6   |
| Gastrointestinal symptoms                   | 17| 37     |
| Abnormally strong uterine contractions      | 20| 43.5   |
| Unconsciousness                             | 5 | 10.9   |
| Administration of antibiotics                |   |        |
| Yes                                         | 40| 88.9   |
| No                                          | 5 | 11.1   |
| NA                                          | 1 |        |
| Administration of immunoglobulin            |   |        |
| Yes                                         | 20| 44.4   |
| No                                          | 25| 55.6   |
| NA                                          | 1 |        |
| Blood transfusion                           |   |        |
| Yes                                         | 24| 58.5   |
| No                                          | 17| 41.5   |
| NA                                          | 5 |        |

NA, not available.
Table 2. — Summary of laboratory test values in the 24 available cases whose laboratory tests were carried out during fulmination and just before delivery.

| Item                                      | n     | %    | Median | Range          |
|-------------------------------------------|-------|------|--------|----------------|
| White blood cell count (/μL)              |       |      |        |                |
| ≥ 12,000                                  | 11    | 45.8 | 12,490 | 1,970-45,200   |
| < 12,000                                  | 13    | 54.2 |        |                |
| NA                                        | 0     |      |        |                |
| Hemoglobin concentration (g/dL)           |       |      | 11.4   | 6.7-13.4       |
| ≤ 8                                       | 1     | 7.1  |        |                |
| > 8                                       | 13    | 92.9 |        |                |
| NA                                        | 10    |      |        |                |
| Platelet count (/μL)                      |       |      | 96,000 | 5,000-421,000  |
| ≤ 100,000                                 | 11    | 55   |        |                |
| > 100,000                                 | 9     | 45   |        |                |
| NA                                        | 4     |      |        |                |
| AST (U/L)                                 |       |      | 44.5   | 15-198         |
| ≥ 80                                      | 3     | 37.5 |        |                |
| < 80                                      | 5     | 62.5 |        |                |
| NA                                        | 16    |      |        |                |
| Serum creatinine (mg/dL)                  |       |      | 0.87   | 0.57-1.77      |
| ≥ 1.2                                     | 4     | 36.4 |        |                |
| < 1.2                                     | 7     | 63.6 |        |                |
| NA                                        | 13    |      |        |                |
| C-reactive protein (mg/dL)                |       |      | 6.2    | 0.3-28.2       |
| ≥ 10                                      | 8     | 40   |        |                |
| < 10                                      | 12    | 60   |        |                |
| NA                                        | 4     |      |        |                |
| Fibrinogen (mg/dL)                        |       |      | 130    | 18-720         |
| ≤ 100                                     | 4     | 44.4 |        |                |
| > 100                                     | 5     | 55.6 |        |                |
| NA                                        | 15    |      |        |                |
| FDP (μg/mL)                               |       |      | 352    | 31-1,920       |
| Strong positive (≥ 40)                    | 6     | 85.7 |        |                |
| Positive (≥ 10)                           | 7     | 100  |        |                |
| Negative (< 10)                           | 0     | 0    |        |                |
| NA                                        | 17    |      |        |                |
| D-dimer (μg/mL)                           |       |      | 75     | 2.0-444        |
| Strong positive (≥ 10)                    | 3     | 60   |        |                |
| Positive (≥ 2)                            | 5     | 100  |        |                |
| Negative (< 2)                            | 0     | 0    |        |                |
| NA                                        | 19    |      |        |                |

AST, aspartate aminotransferase; FDP, fibrin/fibrinogen degradation product; NA, not available.
Figure 1. — Histograms of continuous clinical background data from 46 cases of invasive group A streptococcal (GAS) infections during pregnancy. The mean maternal age was 34.5 years, the mean week of pregnancy at fulmination was 36 weeks, and mean parity was 1. (Areas with a deep color indicate maternal death).

Figure 2. — Histograms for laboratory data from 24 available cases in which laboratory tests were performed between fulmination and just before delivery. Positive fibrin/fibrinogen degradation product (FDP) (≥ 10 μg/dL) and positive D-dimer (≥ 2 μg/dL) each had 100% sensitivity. Strong positive FDP (≥ 40 μg/dL) and strong positive D-dimer (≥ 10 μg/dL) had sensitivities of 86 and 60%, respectively. (Each red horizontal bar indicates the cut-off value defined as an apparently abnormal level that needs clinical intervention. Each arrow indicates an abnormal direction. Areas with a deep color indicate maternal death).

Abnormally strong uterine contractions (no body temperature data were available for these cases in the literature). During the analysis of laboratory data, cut-off values for each item were defined as apparently abnormal levels that need clinical intervention. FDP and D-dimer cut-off values were defined as two steps. Accordingly, two cut-off values were defined for FDP (≥ 10 μg/dL and ≥ 40 μg/dL) and D-dimer (≥ 2 μg/dL and ≥ 10 μg/dL) based on the literature for normal ranges from maternal laboratory data [43, 44], disseminated intravascular coagulation (DIC) diagno-
tic criteria by the Japanese Ministry of Health, Labour and Welfare [45, 46], and obstetrical DIC scoring [47].

**Results**

The mean maternal age was 34.5 years (range, 16 to 43 years), the mean week of pregnancy at fulmination was 36 weeks (range, 8 to 40 weeks), and mean parity was 1 (range, 0 to 6) (Figure 1). The duration from fulmination to maternal death was one day or less in 87% (67% cases), two days in two (17%), and three days or more in two (17%). Clinical backgrounds, symptoms, therapies, and fetal/neonatal and maternal mortalities are categorically summarized in Table 1. There were more multiparous than nulliparous women, while the majority of women (76%) had no maternal complications. Among the cases included, 80% developed GAS infection in the third trimester and 41% at term, whereas 11% developed GAS infection during the abortion period. The fulmination period in all cases was before the onset of labor, except in one case in which the disease fulminated during labor. Among the cases included, 7% died before delivery or abortion. Maternal and fetal/neonatal death rates were 28% and 61%, respectively. Despite the exclusion of abortion cases, fetal/neonatal asphyxia or fetal/neonatal deaths were frequently observed, such that only 8% of cases presented with no fetal/neonatal asphyxia. The majority of cases (89%) received antibiotics, whereas only 44% received immunoglobulin.

Laboratory data measured between fulmination and just before delivery were available for 24 cases [6, 8, 10-12, 15, 17, 18, 22, 25, 26, 28-30, 32, 35, 37-40]. A summary of the data obtained and histograms to assess distributions are shown in Table 2 and Figure 2, respectively. Regarding laboratory data, 46% of cases had a white blood cell count $\geq 12,000/\mu L$, 7% had a hemoglobin concentration $\leq 8\ g/dL$, 55% had a platelet count $\leq 100,000/\mu L$, 38% had an aspartate aminotransferase level $\geq 80\ U/L$, 36% had a serum creatinine level $\geq 1.2\ mg/dL$, 40% had a CRP level $\geq 10\ mg/dL$, and 44% had a fibrinogen level $\leq 100\ mg/dL$. On the other hand, positive FDP ($\geq 10\ 40\ \mu g/dL$) and positive D-dimer ($\geq 2\ 40\ \mu g/dL$) both had 100% sensitivity for detecting invasive GAS infections during pregnancy with minimum scores of 31 $\mu g/dL$ and 2.0 $\mu g/dL$, respectively. Moreover, strong positive FDP ($\geq 40\ 40\ \mu g/dL$) and strong positive D-dimer ($\geq 10\ 40\ \mu g/dL$) had sensitivities of 86% and 60%, respectively, for detecting invasive GAS infections during pregnancy. Furthermore, in many cases, the levels of these parameters were extremely high, as shown in Figure 2.

**Discussion**

The present study provides a summary of clinical backgrounds, symptoms, therapies, and severe outcomes among pregnant women with invasive GAS infections. The results of laboratory tests performed between fulmination and just before delivery showed that FDP and D-dimer may be supportive laboratory tests for an early diagnosis of invasive GAS infections during pregnancy in clinical practice.

Severe outcomes of invasive GAS infections during pregnancy were identified and consistent with previous findings [2]. The epidemiological finding of multiparous women being dominant and the results of the present case indicated that a patient’s children may be one of the factors affecting the spread of GAS infection. The fulmination period was commonly observed during the third trimester, including term, but was also observed during the early weeks of pregnancy in several cases. The majority of cases (89%) had received antibiotics. However, in almost 40% of reviewed cases (17 out of 43 cases in which the period of antibiotic initiation was known) [4, 7-12, 14-17, 19, 21, 23-25, 27, 29, 31-33, 37, 39], the initiation of antimicrobial therapy was considered to be late. The present results indicated that inadequate management was attributed to circumstances wherein clinicians initially misdiagnosed patients with a viral infection, such as influenza, while occasionally lacking the insight to anticipate the probability of any bacterial infectious conditions, including GAS infections.

In the present study, laboratory data from tests performed between fulmination and just before delivery were available for 24 cases. However, the interpretation of these data was associated with the following limitations. The condition of patients upon blood sampling varied from febrile to almost septic and/or DIC. Furthermore, data availability was limited, such that only seven cases for FDP [3, 10, 11, 15, 22, 37] and five for D-dimer [3, 11, 18, 22, 30] were available for analysis. In addition, negative data may have been omitted from each publication. Therefore, laboratory data were analyzed and interpreted in consideration of these limitations. Moreover, data for pregnant women with febrile conditions, except for those with GAS infections, were unavailable. Therefore, the sensitivity of each laboratory test item was only estimated. The percentages of items over the cut-off value, which affects sensitivity, are shown in Table 2. Accordingly, positive FDP ($\geq 10\ 40\ \mu g/dL$) and positive D-dimer ($\geq 2\ 40\ \mu g/dL$) each had 100% sensitivity, while strong positive FDP ($\geq 40\ 40\ \mu g/dL$) and strong positive D-dimer ($\geq 10\ 40\ \mu g/dL$) had sensitivities of 86% and 60%, respectively. Moreover, high sensitivity implies a high negative predictive value. Therefore, strong positive FDP/D-dimer test results indicate invasive GAS infections in pregnancy, whereas negative FDP/D-dimer test results suggest their absence. Based on these results, high FDP/D-dimer levels may alert clinicians to the possibility of GAS infections during pregnancy.

FDP and D-dimer are both small fibrin-containing molecules that may be measured in blood plasma. Since D-dimer is the final product of fibrin degradation, it is smaller than FDP. These clinical laboratory tests are frequently used to diagnose DIC, deep vein thrombosis (DVT), and pulmonary embolism (PE). Moreover, D-dimer is especially regarded as a marker of DVT and PE. Therefore, high D-dimer levels necessitate further testing in order to rule out DVT and PE. In perinatal medicine, DVT is not uncommon. Moreover, since leg DVT and PE generally present with
obvious symptoms, they are harder to overlook. However, rare types of perinatal DVT, such as ovarian vein thrombosis and internal iliac vein thrombosis [48], are uncommon and may be asymptomatic. Therefore, the early diagnosis of these conditions remains challenging. Moreover, in perinatal medical practice, bacterial infections have been shown to pathophysiologically induce DVT [49] and DIC. Thus, when examining a febrile maternal patient with high FDP and/or D-dimer levels, clinicians need to rule out DVT and DIC, including invasive GAS infections.

The RADT for GAS infections of the throat is a diagnostic test that rapidly identifies the presence of GAS infections. The RADT has a fairly high sensitivity of approximately 85% [50]. However, since the primary infectious focus of invasive GAS infections during pregnancy is not always the throat, negative RADT test results do not always rule out invasive GAS infections during pregnancy.

The results of laboratory tests performed between fulminance and just before delivery in 24 cases showed that FDP and D-dimer may contribute to the diagnosis of invasive GAS infections during pregnancy. Despite some limitations inherent to the present study, the results obtained are of potential clinical significance, particularly for the diagnosis of invasive GAS infections during pregnancy. Nevertheless, further studies are needed to confirm the results presented herein.

Ethics Approval and Consent to Participate

The subjects of our case gave her informed consent for inclusion before she participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Matsumoto Women’s Health Clinic (approval number: 202001).

Acknowledgments

A summary of this research was presented at the 71st Academic Conference of the Japan Society of Obstetrics and Gynecology, Nagoya, Japan, 2019.

Conflict of Interest

The authors declare no conflict of interest.

Submitted: June 27, 2019
Accepted: September 23, 2019
Published: August 15, 2020

References

[1] Hamilton S.M., Stevens D.L., Bryant A.E.: “Pregnancy-related group A streptococcal infections: temporal relationships between bacterial acquisition, infection onset, clinical findings, and outcome.” Clin. Infect. Dis., 2013, 57, 870-876.
[2] Yamada T., Yamada T., Yamamuro M.K., Katabami K., Hayakawa M., Tomaru U., et al.: “Invasive group A streptococcal infection in pregnancy.” J. Infect., 2010, 60, 417-424.
[3] Mori Y., Matsumoto N., Miyashita Y., Asami T., Arai M., Osada M., et al.: “A case report of a patient with invasive group A streptococcal infection in pregnancy who presented extremely high levels of plasma FDP and D-dimer.” Saitama J. Obstet. Gynecol., 2019, 49, 25. [In Japanese]
[4] Hirose Y., Shibuya H., Okazaki E., Aono K., Tomakana A., Taguchi S., et al.: “Toxic shock-like syndrome with flu-like prodrome: a possible role of ‘enhancing tissue focus’ for streptococcal toxic shock.” J. Infect., 2001, 42, 195-200.
[5] Kako N., Okawa N.: “A case report of group A streptococcal infection suspected during pregnancy 40 weeks.” Iwate Kenritsu Byoin Igakkai Zasshi, 2001, 41, 123. [In Japanese]
[6] Crum N.F., Chun H.M., Gaylord T.G., Hale B.R.: “Group A streptococcal toxic shock syndrome developing in the third trimester of pregnancy.” Infect. Dis. Obstet. Gynecol., 2002, 10, 209-216.
[7] Mita S., Okuda N., Yokota A., Sasaki S., Koshino T., Nakai A., et al.: “A case report of streptococcal toxic shock syndrome led to maternal death.” Tokyo J. Obstet. Gynecol. Soc., 2002, 31, 454. [In Japanese]
[8] Noguchi M., Matsushita S., Sawaguchi K., Noguchi M.: “A case report of maternal fetal death due to fulminant group A streptococcal infection in late pregnancy.” Proc. Conf. Obstetrical Gynecol. Infect., 2003, 20, 104. [In Japanese]
[9] Tsuji S., Takebayashi K., Ono T., Akiyama M., Kimura T., Hirose M., et al.: “A case report of fulminant group A streptococcal infection in 35 weeks of gestation: A survival case of twin pregnancy.” Shiga J. Obstet. Gynecol. Soc., 2003, 2, 27. [In Japanese]
[10] Hanada R., Takagi T., Iijima T., Iwao Y.: “A case report of acute respiratory failure after intrauterine fetal death due to fulminant group A streptococcal infection.” Jokyu, 2004, 23, 430. [In Japanese]
[11] Amano M., Tanaka A., Makihara N., Yamada T., Bo M.: “A case of puerperal septic pelvic thrombophlebitis caused by group A streptococcal infection.” Sansainshikou Shingyo, 2005, 57, 297. [In Japanese]
[12] Nakahori T., Takata H., Sai R., Kanamoto N., Uchida T., Beppu M., et al.: “Group A streptococcal infection in pregnancy—two cases report.” Kurashiki Chuohyoin Nenpo, 2005, 68, 99. [In Japanese]
[13] Verhulsdonk M.T., Hassell D.R., Oei S.G.: “Septic shock as a result of group A beta-hemolytic streptococcal meningitis with empyema and pregnancy.” Int. J. Gynaecol. Obset., 2007, 97, 197-198.
[14] Hommel S., Savoye G., Lorencave-Savale C., Costaglioli B., Baron F., Le Pessot F., et al.: “Pleurmonous gastritis in a 32-week pregnant woman managed by conservative surgical treatment and antibiotics.” Dig. Dis. Sci., 2007, 52, 1042-1046.
[15] Matsumoto R., Morimoto K., Suzuki M., Takao M., Hiramia M., Isonishi S., et al.: “Group A streptococcal infection in pregnant women—two cases report.” Tokyo J. Obstet. Gynecol., 2009, 58, 17. [In Japanese]
[16] Koike K., Nakamura H., Motono Y., Shimizu M., Takano M., Goto R., et al.: “A case of maternal death at third trimester and neonatal death related to group A streptococcal toxic shock-like syndrome.” Tokyo J. Obstet. Gynecol., 2009, 58, 426. [In Japanese]
[17] Sato M., Isomine S., Sakaida K., Kanazawa T., Mizushima T., Goto M., et al.: “A case of perinatal fulminant group A streptococcal infection in the early stage of pregnancy: successful life-saving care.” J. Jpn. Soc. Intensive Care Med., 2010, 17, 39. [In Japanese]
[18] Sugiyama T., Kobayashi T., Nagao K., Hatada T., Wada H., Sagawa N.: “Group A streptococcal toxic shock syndrome with extremely aggressive course in the third trimester.” J. Obstet. Gynecol. Res., 2010, 36, 852-855.
[19] Keyama K., Hirano K., Nakayama A., Kunimi K.: “A case report of perinatal type streptococcal toxic shock syndrome that led to maternal and fetal death.” Modern Trends Obstet. Gynecol., 2010, 59, 175. [In Japanese]
[20] Yamazaki T., Sakashita T., Fujihara H., Kudo M.: “A case of successful management of perinatal type Group A streptococcal toxic shock syndrome.” Sankinjuka Kansensho Kenkyukai Gakujutsu, 2011, 29, 151. [In Japanese].
[21] Nakashima K., Oishi Y., Yoshizawa A., Horikawa M., Nishino T., Sengoku K.: “A case of suspected invasive group A streptococcal infection in the perinatal periods.” J. Hokkaido Obset. Gynecol. Soc., 2012, 36, 28. [In Japanese].
[22] Uegaki K., Ikono S., Nonaka M., Ohata J., Okada M., Okada M., et al.: “Successful treatment of invasive group A streptococcal infection in pregnancy: a case report”. J. Tottori Med. Assoc., 2012, 40, 145. [In Japanese].
[23] Matsumoto A., Okada M., Ishida M., Shinohara K.: “A case report of perinatal type streptococcal toxic shock like syndrome that led to...
maternal and fetal death”. Fukushima Med. J., 2012, 62, 158. [In Japanese]

[24] Yamaoka K., Fukuda T., Kimura M., Hagiyu K., Dannura M., Nakayama M., et al.: “Group A streptococcus-induced toxic shock syndrome in pregnancy: a case report of cesarean section”. Jpn. J. Anesth., 2012, 61, 1380. [In Japanese]

[25] Eriguchi Y., Ri M., Fujimura N., Hashizume M., Ooikawa H., Yahata H.: “A case of invasive group A streptococcal infection”. Jpn. J. Clin. Experimental Med., 2012, 89, 111. [In Japanese]

[26] Sekizawa A., Ichizuki K.: “Group A streptococcal toxic shock syndrome”. Shusanki Igaka, 2013, 43, 69. [In Japanese]

[27] Kuzume A., Suga S., Yamashita H., Mizutani Y., Watanabe T., Sugimot S., et al.: “A case of maternal toxic shock syndrome suspected due to invasive group A streptococcal infection in pregnancy with intrauterine fetal death”. Jpn. J. Perinat. Neon. Med., 2014, 50, 1099. [In Japanese]

[28] Murakami K., Fukuhara K., Hasegawa M.: “Group A streptococcal infection in the second trimester”. Kuwarashiki Chuo-byoin Nenpo, 2014, 76, 121. [In Japanese]

[29] Hori S., Mochizuki S., Hamana S.: “Two survived cases of group A streptococcal toxic shock syndrome (perinatal type)”. Sanfujinkano Jissai, 2014, 63, 273. [In Japanese]

[30] Tarvade S., Lane A.S.: “Ante-partum necrotising myometritis due to streptococcal toxic shock”. J Intensive Care Soc., 2015, 16, 173.

[31] Tokoro N., Kinoshita Y., Kusaba S., Takekawa S., Hatsu D.: “A case of group A streptococcal toxic shock syndrome (perinatal type)”. Shiga J. Obstet. Gynecol., 2015, 7, 55. [In Japanese]

[32] Sato T., Matsuawase Y., Watanabe K.: “A case report of invasive group A streptococcal infection in pregnancy: successful maternal life saving care”. Tokyo J. Obstet. Gynecol., 2009, 58, 17. [In Japanese]

[33] Tsutsui S., Matsukawa J.: “Streptococcal toxic shock syndrome in pregnancy”. Sanfujinkano Jissai, 2015, 64, 153. [In Japanese]

[34] Hasegawa J., Sekizawa A., Yoshimotu J., Murakshi T., Osato K., Ikeda T., et al.: “Cases of death due to serious group A streptococcal toxic shock syndrome in pregnant females in Japan”. Arch. Gynecol. Obstet., 2015, 297, S-7.

[35] Fujita S., Hayashi S., Uchishiba M., Yano K., Imae H., Nakagawa Y.: “A case of invasive perinatal-type group A streptococcal infection treated with continuous hemodialifiration”. Modern Trends Obstet. Gynecol., 2016, 65, 51. [In Japanese]

[36] Imaeda T., Nakada T., Abe R., Tateishi Y., Oda S.: “Veno-arterial extracorporeal membrane oxygenation for Streptococcus pyogenes toxic shock syndrome in pregnancy”. J. Artif. Organs, 2016, 19, 200-203.

[37] Shimozono K., Sumitomo M., Takakura M., Nakagi A., Kawamura Y., Hata S., et al.: “Two cases of resuscitated peripartum streptococcal toxic shock syndrome”. J. Jpn. Soc. Perin. Neon. Med., 2014, 52, 954. [In Japanese]

[38] Alhouisseni A., Layne M.E., Gonik B., Bryant D., Patwardhan S., Patwardhan M.: “Successful continuation of pregnancy after treatment of group A streptococci sepsis”. Obstet. Gynecol., 2017, 129, 907-910.

[39] Irani M., McLaren Jr., Savel R.H., Bogatyryova O., Khoury-Collado F.: “Streptococcal toxic shock syndrome occurring in the third trimester of pregnancy: A case report”. J. Obstet. Gynecol. Res., 2017, 43, 1639-1643.

[40] Kobanawa M., Fujioa Y., Muraoka Y., Iwasa N., Wada M., Higuchino M., et al.: “A survived case of invasive perinatal-type group A streptococcal infection”. Saitama J. Obstet. Gynecol., 2017, 47, 85. [In Japanese]

[41] Breiman R.F., Davis J.P., Facklam R.R., Gray B.M., Hoge C.W., Kaplan E.L., et al.: “Defining the group A streptococcal toxic shock syndrome. Rationale and consensus definition”. JAMA, 1993, 269, 390-391.

[42] Udagawa H.: “Maternal infection. Group A streptococcus”. Sanfujinkano Jissai, 2011, 60, 297. [In Japanese]

[43] Hirai C., Makino S.: “Reference value in pregnancy”. Shusanki Igaka, 2016, 46, 1249. [In Japanese]

[44] Hedengran K.K., Andersen M.R., Stender S., Szecsi P.B.: “Large D-Dimer fluctuation in normal pregnancy: a longitudinal cohort study of 4,117 samples from 714 healthy Danish woman”. Obstet. Gynecol. Int., 2016, 2016, 5361675.

[45] Kaneko T., Wada H.: “Diagnostic criteria and laboratory tests for disseminated intravascular coagulation”. J. Clin. Exp. Hematop., 2011, 51, 67-76.

[46] Asakura H., Takahashi H., Uchiyama T., Eguchi Y., Okamoto K., Kasuwa R., et al.: “Proposal for new diagnostic criteria for DIC from the Japanese Society on Thrombosis and Hemostasis”. Thromb. J., 2016, 14, 42.

[47] Kobayashi T.: “Obstetrical disseminated intravascular coagulation score”. J Obstet. Gynecol. Res., 2014, 40, 1500-1506.

[48] Catanzaire V.A., Low R.N., Wong D.Y.: “Ovarian vein thrombosis during cesarean section: A report of two cases”. J. Reprod. Med., 1997, 42, 315-318.

[49] Patwardhan M., Mulinaris E., Saccomano E., Gallo J.C., Kohan G.: “Post-partum ovarian vein thrombophlebitis with staphylococcal bacteremia”. Case Rep. Infect. Dis., 2015, 2015, 589436.

[50] Cohen J.F., Bertille N., Chiren R., Chalameau M.: “Rapid antigen detection test for group A streptococcus in children with pharyngitis”. Cochrane Database Syst. Rev., 2016, 7, CD010502.

Corresponding Author:
NAOKI MATSUMOTO, M.D., Ph.D.
Matsumoto Women’s Health Clinic, 1-1-26 Chiyoda, Honjo City, Saitama 367-0054 (Japan)
e-mail: research@matsumotoc.org