Serum White Blood Cell Count (WBC) and Plasma C Reactive Protein (CRP) Values could be Markers for Acute Pelvic Inflammatory Disease

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Abstract—Pelvic inflammatory disease (PID) is frequently caused by Chlamydia trachomatis and Neisseria gonorrhoeae. Standard bacterial culture confirmation of these causative microorganisms is time-consuming. This study describes a rapid process for identifying these pathogenic microorganisms of acute severe PID. A total of 33 patients diagnosed with pelvic peritonitis (treated between April 2002 and December 2006) were retrospectively analyzed. At initial consultation laboratory tests of white blood cells (WBC) and plasma C-reactive protein were conducted. At the same time the patients were screened for the presence of Chlamydia trachomatis or Neisseria gonorrhoeae by polymerase chain reaction (PCR) amplification analysis of DNA extracted from endocervical mucus swabs. There were significant clinical differences in the WBC count among the patients positive for Chlamydia trachomatis (low WBC) versus Neisseria gonorrhoeae (high) infections ($p=0.0004$), and for patients positive for Chlamydia trachomatis versus patients negative for both bacteria ($p=0.0043$), and for Neisseria gonorrhoeae positive patients versus patients negative for both bacteria ($p=0.0047$). Plasma CRP values were significantly lower in patients positive for Chlamydia trachomatis compared to patients positive for Neisseria gonorrhoeae ($p=0.012$). Our study provides evidence that WBC counts and plasma CRP values are useful PID screening markers to tentatively differentiate between Chlamydia trachomatis and Neisseria gonorrhoeae.

Keywords — PID, Chlamydia trachomatis, Neisseria gonorrhoeae, WBC, CRP

INTRODUCTION

Pelvic inflammatory disease (PID) in women is an infection syndrome with a polymicrobial origin, especially N. gonorrhoeae and C. trachomatis, and a wide range of symptoms and signs. The various clinical criteria commonly used for the diagnosis of pelvic inflammatory disease, such as the presence of low abdominal pain, bilateral adnexal tenderness, fever, and increased erythrocyte sedimentation rate, have a poor sensitivity and specificity, as demonstrated by more accurate laparoscopic studies. There are numerous pathogenic microorganisms, showing similar clinical symptoms but requiring selection of specific antibiotics, which may cause PID. Standard bacterial cultural confirmation of PID pathogens is time-consuming. Therefore, initial diagnostic and treatment plans for PID are problematic. There are several published PID treatment guidelines, such as those from the CDC and IUSTI, which are useful for difficult PID cases. It would be highly beneficial if the pathogens that cause severe acute PID could be predicted from the initial clinical laboratory data, since proper selection of the initial antibiotic regimen while awaiting culture confirmation would be accomplished promptly and improve patient outcome.

The aim of this study is to evaluate whether patient histories, clinical symptoms and laboratory tests such as white blood cell count and C-reactive protein serum levels differed in Chlamydia trachomatis cases from those infected with Neisseria gonorrhoeae, and from non-Chlamydial, non-gonococcal cases.

METHODS

This was a retrospective study of 33 hospitalized patients diagnosed with “severe acute PID following peritonitis”. These cases were treated between April 2002 and December 2006 at the Ikeda Municipal Hospital of Ikeda, Japan. Patients were forwarded to the Department of Gynecology from either the Departments of Emergency Admissions or Internal Medicine when initial laboratory tests indicated a diagnosis of possible acute pelvic abdominal infection.

Patients were diagnosed as having severe acute PID with pelvic peritonitis when presenting with lower abdominal tenderness, cervical motion tenderness, adnexal tenderness, elevated body temperature (38°C or above) and abdominal rebound tenderness. Trans-abdominal and trans-vaginal ultrasound was performed to further demonstrate PID. Magnetic Resonance Imaging (MRI) was performed on ambiguous cases for confirmation of PID. None required supplementary laparoscopy for diagnosis of PID.

At initial consultation within the Department of Gynecology, laboratory tests for white blood cell (WBC) and plasma levels
of C-reactive protein (CRP) were conducted. The patients were simultaneously screened for the presence of Chlamydia trachomatis or Neisseria gonorrhoeae using detection by polymerase chain reaction (PCR) amplification from DNA obtained from endocervical mucus swabs. We evaluated the correlation between basic laboratory test data pertaining to WBC and CRP and the PCR-verified presence or absence of Chlamydia trachomatis and/or Neisseria gonorrhoeae. The statistical significance of differences was evaluated using the Mann-Whitney U test.

RESULTS

The patient’s ages ranged from 16 to 75 years (median: 28.5 years). Seventeen of the 33 patients (51%) were under 30 years of age. Patients with Chlamydia trachomatis ranged from 19 to 35 years old, and patients with Neisseria gonorrhoeae ranged from 16 to 42 years old. There was no significant difference in age between these two groups.

Four of the 33 patients had other diseases (appendicitis, endometriosis, ischemic colitis, and ovarian cyst) causing their peritonitis, and were thus excluded from further study. Eleven (30%) of the patients were infected with Chlamydia trachomatis, and seven (21%) were infected with Neisseria gonorrhoeae. Only one patient was co-infected with both Chlamydia trachomatis and Neisseria gonorrhoeae. By ultrasound or MRI, we detected salpingitis in two cases positive for Chlamydia trachomatis, and one case of non-gonococcal, non-chlamydial PID. There were no cases of salpingitis with Neisseria gonorrhoeae in this study.

There were significant differences in the WBC counts among the patients positive for Chlamydia trachomatis (median WBC: 8,700 WBC/microliter, range: 5,500-9,800/microliter), and Neisseria gonorrhoeae (median: 21,810/microliter, range: 15,600-27,100/microliter) and the patients negative for both STDs (median: 14,000/microliter, range: 7,520-22,500/microliter), respectively (Figure 1a).

In regards to WBC levels in the blood, we can differentiate between PID patients by those whose WBC counts are over or under 10,000/microliter. We found this to have a positive predictive value of 80%, and a negative predictive value of 94%, for picking up chlamydial infections. WBC results gave a sensitivity of 89% and a specificity of 89%.

The plasma CRP values were significantly lower in patients positive for Chlamydia trachomatis (median: 1.1 mg/dl, range: zero-9.7 mg/dl) compared to patients positive for Neisseria gonorrhoeae (median: 10.4 mg/dl, range: 2.8-25 mg/dl) (p=0.012). However, the difference in plasma CRP values between the patients positive for Neisseria gonorrhoeae and patients negative for both bacteria (median: 10.2 mg/dl, range: zero-32 mg/dl) was not significant (p=0.7654) (Figure 1b).

DISCUSSION

Sexually transmitted organisms, especially N. gonorrhoeae and C. trachomatis, are implicated in many PID cases, cause 30%-50%8-10; however, microorganisms that comprise the vaginal flora also have been associated with PID. Although PID has been epidemiologically linked to bacteria vaginosis.11 Acute PID is difficult to diagnose because of the wide variation in the symptoms and signs. Many women with PID have subtle or mild symptoms.12 Delay in diagnosis and treatment probably contributes to inflammatory sequelae in the upper reproductive tract such as infertility, chronic pelvic pain, ectopic pregnancy, and recurrent infection.13-16 Laparoscopy can be used to obtain a more accurate diagnosis of salpingitis and a more complete bacteriologic diagnosis. However, this diagnostic tool frequently is not readily available, and its use not easy to justify not detect subtle inflammation of the fallopian tubes.17,18 Consequently, a diagnosis of PID usually is based on clinical findings.

According to Sexually Transmitted Diseases Treatment Guidelines 2006,19 Empiric treatment of PID should be initiated in sexually active young women and other women at risk for STDs if they are experiencing pelvic or lower abdominal pain, if no cause for the illness other than PID can be identified, and if one or more of the following minimum criteria are present on pelvic examination; cervical motion tenderness or uterine tenderness or adnexal tenderness. The requirement that all three minimum criteria be present before the initiation of empiric treatment could result in insufficient sensitivity for the diagnosis of PID. The presence of signs of lower genital tract inflammation, in addition to one of the three minimum criteria, increases the also consider the risk profile of the patients for STDs. More elaborate diagnostic evaluation frequently is
needed because incorrect diagnosis and management might cause unnecessary morbidity. These additional criteria may be used to enhance the specificity of the minimum criteria. The following additional criteria can be used to enhance the specificity of the minimum criteria and support a diagnosis of PID; oral temperature > 101°F(>38.3°C), abnormal cervical or vaginal mucopurulent discharge, presence of abundant numbers of WBC on saline microscopy of vaginal secretions, elevated erythrocyte sedimentation rate, elevated erythrocyte sedimentation rate, elevated C-reactive protein, and laboratory documentation of cervical infection with N. gonorrhoeae or C. trachomatis. The majority of women with PID have either mucopurulent cervical discharge or evidence of WBC on a microscopic evaluation of a saline preparation of vaginal fluid. If the cervical discharge appears normal and no WBCs are observed on the wet prep of vaginal fluid, the diagnosis of PID is unlikely, and alternative causes of pain should be investigated. A wet prep of vaginal fluid offers the ability to detect the presence of concomitant infections (e.g., bacterial vaginosis and trichomoniasis).

The most specific criteria for diagnosing PID include the following: endometrial biopsy with histopathologic evidence of endometritis; transvaginal sonography or magnetic resonance imaging techniques showing thickened, fluid-filled tubes with or without free pelvic fluid or tubo-ovarian complex, or doppler studies suggesting pelvic infection (e.g., tubal hyperemia); and laparoscopic abnormalities consistent with PID. A diagnostic evaluation that includes some of these more extensive studies might be warranted in some cases. Endometrial biopsy is warranted in women undergoing laparoscopy who do not have visual evidence of salpingitis, as some women with PID have endometritis alone.

In our cases of severe acute PID caused by Chlamydia trachomatis, the WBC count should not be more than 10,000/microliter. As an additional diagnostic criteria, the plasma CRP values will be significantly lower than for patients with severe acute PID caused by other microorganisms, including Neisseria gonorrhoeae. When the WBC count is greater than 15,000/microliter, Neisseria gonorrhoeae can be highly suspected as the causative agent. And also, in our cases of acute PID caused by Chlamydia trachomatis, the plasma CRP values will be significantly lower than for patients with severe acute PID caused by other microorganisms, including Neisseria gonorrhoeae. Short et al.19 demonstrated that compared with women with gonococcal PID, women with PID due to Chlamydia trachomatis were generally less symptomatic and less likely to have elevated systemic inflammatory markers, including elevated oral temperature (0% vs. 13.9%; P=0.013) or elevated WBC count (22.5% vs. 64.6%; P<0.001). They were less likely to present with cervicitis (52.4% vs. 83.3%; P<0.001) or bilateral adnexal tenderness (77.8% vs. 82.4%; P=0.049) and had statistically significantly lower mean composite pain scores (P=0.020).

Chlamydial species are Gram-negative, aerobic, obligate, intracellular pathogens. Because they are unable to synthesize their ATP, they have to use their host cell’s energy resources. For this reason clamidia were once considered viruses. However even this reason existed, in the same PID situation, inflammatory evaluation for Chlamydia trachomatis seems to be significantly lighter than other microorganisms, including Neisseria gonorrhoeae interestingly. In acute upper genital tract infections, Peipert, et al.25 found that laboratory tests for elevated levels of blood and vaginal WBC, blood ESR, and serum CRP gave diagnostic sensitivities of 57, 70, 71, and 78%, respectively. Their results also indicate that 43% of patients do not show elevated WBC counts; these may include PID patients with chlamydial infections, and this may have resulted in their low sensitivity for diagnosing PID when using WBC counts as a differential criteria.

Lehtinen, et al.5 found that determination of serum CRP levels could not discriminate between those PID cases who had either chlamydia or gonococci, or neither, isolated from their genital tract. However, in our study, we did not consider salpingitis and/or endometritis as a requirement for a diagnosis of acute severe PID. Our study also included PID patients who did not yet show detectable lesions by ultrasound and MRI. It is possible that we are detecting early-phase inflammation by the chlamydial infection, before the detectable lesion are formed, and such chlamydial infections without visible lesions may not correlate with blood WBC counts and serum CRP elevation. This may be because a small number of people can have asymptomatic or subclinical STD for up to a year, such that many patients with laparoscopic evidence of previous PID are not aware they have had PID. On the other hand, WBC counts and CRP values of gonococcal infections might be elevated even at the earliest phases of inflammation.

CONCLUSIONS

We conclude, based upon WBC counts, that there are significant differences between chlamydial and gonococcal infections. Our study suggests that the WBC count and plasma CRP values, determined at initial consultation for pelvic peritonitis associated with acute severe PID, are not useful screening markers but it could be to predict underlying microorganisms, and thus begin treatment. Because this study is relatively small in patient number, we hope to receive future funding to extend it.

REFERENCES


