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False-positive Urine Pregnancy Test Due to Leukocyte Interference

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The hCG One Step Pregnancy Test Device (Urine) (ACON Laboratories, Inc., San Diego, CA, USA) is a rapid chromatographic immunoassay used for the qualitative detection of human chorionic gonadotropin (hCG) in the urine to aid in the early detection of pregnancy. The test uses a combination of antibodies, including mouse monoclonal anti-hCG antibodies and goat polyclonal anti-hCG antibodies, to selectively detect elevated levels of hCG. The assay is conducted by adding a urine specimen to the specimen well of the test device and observing the formation of colored lines. The specimen migrates via capillary action along the membrane to react with the colored conjugate. Since these tests can detect as little as 25 mIU/mL hCG in a urine specimen, the test can be performed as early as 7-10 days after conception. Because of its convenience, this test is frequently used in clinics and laboratories and can even be performed by patients at home. However, many factors can interfere with the test results and cause false-positives, including the presence of serum human anti-mouse antibodies (HAMA) and diseases associated with the excretion of hCG into the urine (e.g., colon or cervical cancer). False-positive urine hCG results have also been reported in patients with nephrotic range proteinuria and those with tubo-ovarian abscess [1-3]. Analytical causes of false-positive or false-negative urine hCG tests include human or technical errors in the performance and/or interpretation of the test results. However, leukocyte interference is not currently listed as a cause of false-positive urine pregnancy tests.

Herein, we report a 40-yr-old woman (gravida 0, para 0) who presented to our hospital due to a survey on artificial reproductive technique (ART). She had been previously diagnosed with endometriosis and underwent laparoscopy surgery for endometriosis last year. However, her symptoms of dysmenorrhea and hypermenorrhea still persisted. A urine pregnancy test was ordered by the clinician, and the test indicated the patient was pregnant. A second urine pregnancy test was conducted, and again, the test results came back positive. However, the result was inconsistent with the patient's actual pregnancy status.

According to the manufacturer's instructions, if the urine appears turbid, it should be centrifuged, filtered, or allowed to stand for a while before testing in order to avoid false outcomes. In this case, the patient's urine sample was judged as clear by visual determination, and the urine hCG one-step pregnancy test was performed following the instructions of the manufacturer without centrifugation. A positive result was obtained. However, the total serum hCG was detected simultaneously, indicating a concentration of 1.32 mIU/mL, which was inconsistent with the results of the urine pregnancy test. In order to rule out the hook effect from the serum sample test, quantitative detection of hCG was performed again, using a dilution model. The outcome of this repeat examination was similar to that of the original. Therefore, we made a preliminary hypothesis that there are additional fac-

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tors that interfere with the method and cause false-positive results in the urine hCG one-step pregnancy test. In order to investigate the cause of this false-positive result, we assumed that the interfering factors might have originated from either the content of the urine or the test kit batch.

First, we examined the content of the urine specimen. Routine analysis of the urine sample showed red blood cells (RBC) (+/-), white blood cells (WBC) (3+), and protein (2+). Sediment analysis by microscopy revealed that the concentration of leukocytes and epithelial cells were 717/μL and 31/μL, respectively. Urine sediments were analyzed using an iQ200 fully automatic urine sediment analyzer (IRIS. International Inc., Chatsworth, CA, USA). With no erythrocytes present in the urine, the appearance of the patient's urine seemed clear. Therefore, we designed a test that was able to demonstrate whether cells in the urine could interrupt the performance of the urine hCG one-step pregnancy test. The urine sample was serially diluted with normal urine from a male to a WBC concentration of 600/μL, 500/μL, 400/μL, 300/μL, 200/μL, and 100/μL. These diluted samples were subjected to the urine hCG one-step pregnancy test, and the results indicated that positive test results occurred in samples having 400 or more cells per μL, while samples with less cells tested negative.

Another possible interference was a problem with the test kit batch, since we also found that different batches of test kits gave different outcomes for the same original urine sample. In this examination, a concentration of 500 or more cells per μL gave a positive result, while the other dilutions tested negative. After centrifugation, all samples showed a consistently negative result.

Based on the results from our experiment, the interfering factor could be the presence of cells in the urine sample or the inconsistency of the manufactured device. In both cases, false-positive results can be avoided by centrifugation. Although the package insert states that centrifugation, filtration, or allowing the sample to stand for a while is only required when the sample appears to be turbid, the determination of turbidity may not be consistent between medical technologists due to variations in eyesight.

False-positive urine pregnancy tests may put patients at risk for unnecessary treatment. It is important to confirm a suspected false-positive urine hCG test using a quantitative serum hCG test. Our findings suggest that, when the urine specimen appears turbid, quantitative serum hCG should be analyzed simultaneously.

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