Indium-111-labeled leukocytes in the detection of abscesses

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The experience of an osteopathic community hospital with indium-111-labeled leukocytes (In-111-WBC) for abscess detection is reported. Thirty-two scans were performed in 28 patients with suspected abscesses. Nine true-positive scans were confirmed at surgery, and 16 scans were categorized correctly as true-negatives. One scan was a false-positive, and 2 were false-negative. The sensitivity of In-111-WBC scanning in this series was 82 percent and the specificity was 94 percent; accuracy was 89 percent. False-negative scans are most likely to occur with septic foci of more than 2 weeks' duration. Twenty-two percent of all scans showed areas of inflammation unrelated to abscesses. In-111-WBC scanning has proved to be a valuable, noninvasive tool in the diagnosis of abscesses, especially acute processes.

The identification of an abscess is a difficult clinical problem. If left untreated, occult abscesses may lead to the patient's death. Traditional imaging modalities for diagnosing abscesses include computed tomography (CT), ultrasonography, and gallium-67 (Ga-67) scintigraphy. Although it is still a relatively new modality, the efficacy of indium-111-labeled leukocyte (In-111-WBC) scintigraphy for abscess detection is well established.¹⁻⁸

This paper reports the experience of an osteopathic community hospital with the use of In-111-WBC scintigraphy in abscess detection.

Materials and methods

From June 1984 to April 1985, 37 In-111-WBC scintigraphic scans were obtained from 33 patients

with suspected abscesses. Each patient's chart was reviewed retrospectively. Five cases were excluded from the final tabulation because of insufficient documentation as to the patient's true condition (that is, presence or absence of an abscess). Therefore, this report is based on the results of 32 scans from 28 patients. The study included 17 females and 11 males, who ranged in age from 15 to 82 years.

At the time of this study, indium-111 oxine was an investigational new drug and approval for its use was obtained from the Food and Drug Administration. (On December 23, 1985, this agent received approval from the FDA for routine clinical use.) Each patient gave informed written consent prior to the procedure. After 40-50 ml. of venous blood were drawn into a heparinized syringe, the leukocytes were prepared and labeled with indium-111 oxine by a commercial radiopharmacy, which used the technique described by Beightol and Baker.⁹ A total of 300-800 μ C. of In-111-WBCs were injected intravenously into each patient. The total time that elapsed between obtaining the blood to injection of the autologous labeled leukocytes averaged about 3 hours.

Using a Siemens LFOV gamma camera with a medium-energy collimator, imaging was performed 18 to 24 hours after injection. Two 20-percent windows were set to detect the gamma photon peaks of indium-111 (173 and 247 keV).

A normal scan demonstrated labeled leukocyte uptake in the spleen, liver, and bone marrow, with uptake being greatest in the spleen and least in the marrow. A scan was considered positive for an abscess if there was an area of abnormal uptake that was equal to or greater in intensity than the uptake in the liver. A scan was considered positive for inflammation, not abscess, if there was an area of abnormal uptake less intense than the liver uptake.

Representative cases are presented for each category.

Results and case reports

Table 1 presents the number of scans with each finding (true-negative, true-positive, false-positive, false-negative, or other [inflammation]), as well as the final diagnosis for each category.

True-negative scans

There were 16 true-negative scans. One negative scan for abscess was confirmed by surgery, 1 by laparoscopy, and 1 by needle biopsy. The remaining 13 scans were confirmed by subsequent clinical correlation. Five patients with normal scans were considered as true-negatives because they became afebrile without antibiotics. Eight patients with normal scans were treated with antibiotics; however, they showed no evidence on other tests to suggest an abscess. Sources for their fevers were documented clinically, and they responded to appropriate therapy and were discharged. They also were considered to be true-negatives.

Case 1. An 18-year-old woman presented with fever and a left adnexal mass on bimanual examination. Culdocentesis was performed, and turbid yellow fluid was obtained. A tubo-ovarian abscess was suspected. An In-111-WBC scan obtained the following

day was normal (Figs. 1A and 1B). One day later, laparoscopy was performed and revealed pelvic inflammatory disease and a left hydrosalpinx. There was no evidence of an abscess. Cultures of the culdocentesis fluid and of fluid obtained at laparoscopy failed to grow organisms.

True-positive scans

Nine scans were positive for abscess; all of these cases were verified by surgery.

Case 2. A 36-year-old male had a history of Crohn's disease, which had been diagnosed 3 years earlier. The patient had had intermittent fever and chills for about 2 months, and there was recent onset of low-back pain and inability to flex the left leg. A plain film of the abdomen revealed gas bubbles in the left lower quadrant, which were suspected to be extraluminal (Fig. 2A). An In-111-WBC abdominal scan demonstrated abnormal uptake in the left lower quadrant that indicated an abscess (Fig. 2B). This finding was corroborated by a CT scan of the abdomen (Fig. 2C). Surgical exploration disclosed severe Crohn's disease of the sigmoid colon and a left psoas abscess secondary to sigmoid colon perforation.

Case 3. A 42-year-old man developed left lower quadrant pain and fever 14 days after sigmoid colon resection for a perforated diverticulum. An In-111-WBC scan performed 4 days later showed a lobulated area of abnormal uptake in the left lower quadrant consistent with abscess, as well as less intense uptake in the descending colon indicating inflammation (Fig. 3A). A barium enema was performed the next day and demonstrated two areas of extravasation of contrast medium from the sigmoid colon, with accumulation of the barium in a large cavity (Fig. 3B). Subsequent surgery revealed an intraperitoneal left lower quadrant abscess, as well as a left rectus muscle abscess, with a fistula between this abscess and the area of previous anastomosis.

False-positive scan

There was 1 scan positive for abscess, but no abscess was found at subsequent surgery.

Case 4. A 69-year-old man went into septic shock on the night following a transrectal prostate biopsy. The patient's vital signs were stabilized; however, he developed severe secondary pancreatitis. Despite appropriate therapy, the patient's leukocyte count and temperature remained elevated, and a pancreatic abscess was suspected. Fourteen days after the onset of symptoms, an In-111-WBC scan demonstrated abnormal uptake in the area of the

Figs. 1A and 1B. Case 1. [A], Anterior abdominal and pelvic images show normal uptake of In-111-WBCs in the spleen, liver, and bone marrow. Uptake is greatest in the spleen and least in the marrow. No areas of abnormal uptake are present. [B], Normal posterior abdominal and pelvic images.

pancreas, which indicated an abscess (Fig. 4). Ultrasonography and abdominal CT scanning showed signs of pancreatitis, with no evidence of abscess. Because of conflicting data, surgery was deferred. The patient's condition gradually improved, and he was discharged. On follow-up CT scanning 5 weeks later, a 4-cm. pseudocyst had developed in the head of the pancreas. Repeat CT scans showed no change in the size of the pseudocyst. Almost 4 months after the onset of symptoms, cystojejunostomy was performed for pseudocyst drainage. There was no evidence of abscess or infection.

False-negative scans

Two scans were negative for abscesses, but abscesses were present on subsequent surgery. In both patients, signs of infection had been clinically manifested for 2 weeks or more prior to the scans (30 days in a patient with a perisplenic abscess and left empyema, and 14 days in a patient with pancreatic abscess). The false-positive scan previously reported and 1 of the false-negative scans both occurred in the same patient.

Case 5. After drainage of a noninfected pancreatic pseudocyst, the 69-year-old male patient discussed in case 4 developed back pain, nausea, fever, and an elevated leukocyte count. Nineteen days after the onset of symptoms, an In-111-WBC scan was negative (Fig. 5A). Because of the discordance between the clinical impression and the scan, a Ga-67 scan was obtained 1 day later; this showed increased activity in the area of the pancreas that was compatible with an abscess (Fig. 5B). Four days later, a pancreatic abscess was found at surgery.

Other findings

In addition, 9 areas of abnormal uptake that indicated inflammation were seen on 7 scans in 6 patients (Table 1). Areas of inflammation adjacent to abscesses were excluded from this group. One true-positive scan for pelvic abscess also showed inflammation in the buttocks at sites of intramuscular injections. One false-negative scan for perisplenic abscess and empyema showed inflammation in a healing surgical wound. One true-negative scan for an intra-abdominal abscess also demonstrated inflammation in the buttocks.

Case 6. A 41-year-old woman was readmitted 6 days after cholecystectomy with abdominal pain and an elevated leukocyte count. An In-111-WBC scan showed no evidence of abscess; however, there was abnormal uptake in both buttocks corresponding to sites of intramuscular analgesic injections (Fig. 6). Abdominal exploration revealed a bile leak

Figs. 2A-2C. Case 2. [A], Plain film of the abdomen shows gas bubbles along the left psoas; these were suspected to be extraluminal. [B], Anterior lower abdominal image of In-111-WBC scan demonstrates abnormal uptake in the left lower quadrant consistent with an abscess. [C], CT scan through the lower abdomen shows enlargement of the left psoas, with gas bubbles present within the muscle.

Figs. 3A and 3B. Case 3. [A], Anterior lower abdominal image of an In-111-WBC scan shows a lobulated area of abnormal uptake in the left lower quadrant indicating abscess. Less intense uptake in the descending colon suggests inflammation. [B], Barium enema shows extravasation of contrast into a large cavity, as well as a track of contrast medium that leads to the left anterior abdominal wall.

from the gallbladder fossa, with no evidence of abscess.

Discussion

Because abscesses are localized collections of leukocytes, it seemed reasonable that leukocytes labeled with isotopes could identify abscesses by their migration. After several unsuccessful attempts by others,¹⁰⁻¹² McAfee and Thakur^{13,14} found indium-111 oxine to be the most suitable isotope for labeling leukocytes. Successful results were first obtained in animal experiments,^{15,16} then Segal and Thakur and associates¹ reported the localization of abscesses in humans utilizing In-111-WBCs.

Fig. 4. Case 4. Anterior abdominal In-111-WBC scan demonstrates increased uptake in the area of the pancreas consistent with abscess. Subsequent surgery did not reveal evidence of abscess or infection.

TABLE 1. CORRELATION BETWEEN FINAL DIAGNOSIS AND RESULT OF SCANS.

Scan result	No.	Final diagnosis
True-negative	16	
True-positive	9	Intraperitoneal abscess (6) Retroperitoneal abscess (2) Groin abscess (1)
False-positive	1	Pancreatitis
False-negative	2	Pancreatic abscess (1) Perisplenic abscess with empyema (1)
Other*	9	Buttock inflammation at sites of intramuscular injection (2) Lung inflammation in adult respiratory distress syndrome (2) Inflammation at exit sites of gastrostomy tubes (2) Inflammation at site of healing surgical wound (1) Inflammation of cecum and terminal ileum in Crohn's disease (1) Thigh inflammation from femoral vein heroin injection in a drug addict. (1)

*These findings were present on 7 scans in 6 patients. Three patients with inflammation had unrelated findings, which also classified them as belonging in another group (1 true-positive, 1 true-negative, 1 false-negative).

Subsequently, these results were confirmed by others.²⁻⁸

Indium-111 has several qualities that make it suitable for leukocyte imaging. First, it has a half-life of 67 hours, which is long enough to allow for

Fig. 5A and 5B. Case 5. [A], *In-111*-WBC scanning of the same patient reported in case 4 was performed 19 weeks after the initial study. Anterior abdominal image shows no areas of abnormal uptake. [B], Anterior abdominal image of *Ga-67* scanning performed the next day reveals abnormal activity in the area of the pancreas.

leukocyte migration to pyogenic processes. Second, indium-111 emits two gamma photons of 173 keV and 247 keV, which can be detected with a gamma camera. Third, in the concentrations used, Indium-111 does not alter cell viability or function.¹⁷

Finally, the radiation dose is acceptable, with the spleen receiving 18 rads/mCi, the liver 1.5 rads/mCi, and the whole body 0.5 rads/mCi.¹⁸

To cross the leukocyte membrane, indium-111 must be combined with the chelating agent oxine (8-hydroxyquinoline). The leukocytes must be removed from plasma, because indium-111 has a higher affinity for transferrin than for oxine and dissociates in plasma. In the absence of plasma, indium-111 oxine diffuses across the leukocyte membrane. The indium-111 then dissociates from the oxine and binds to various cytoplasmic components.¹⁹

In-111-WBC scanning compares favorably to other imaging modalities. In 128 patients studied with *In-111*-WBCs, Seabold and coworkers²⁰ reported a sensitivity of 88 percent, specificity of 90 percent, and accuracy of 89 percent. Carroll and associates⁶ compared *In-111*-WBC scanning with ultrasonography and documented a sensitivity of 84 percent and a specificity of 95 percent for the *In-111*-WBC procedure, versus 81 percent sensitivity and 95 percent specificity for ultrasonography. Studying 170 patients with CT, ultrasonography, and *In-111*-WBC scanning, Knochel and coauthors⁴ reported accuracies of 96 percent, 90 percent, and 92 percent respectively. Sfakianakis and coresearchers⁸ reported a sensitivity of 73 percent and specificity of 98 percent for scanning with *In-111*-WBCs, as compared to 81 percent sensitivity and 91 percent specificity for scanning with *Ga-67*.

Ga-67 scanning for abscess detection has several drawbacks. A considerable amount of gallium is excreted through the gut; therefore, caution must be utilized in evaluating abdominal collections of *Ga-67*. Frequently, 48 to 72 hours are required before interpretation is possible because of high background activity. *Ga-67* also accumulates in certain neoplasms, thus making its uptake equivocal when one is attempting to differentiate a neoplastic from an inflammatory process.

Fig. 6. Case 6. Supine left and right anterior oblique *In-111*-WBC abdominal scans show faint uptake in both buttocks, indicating inflammation.

In-111-WBC scanning for abscesses is not without potential pitfalls. Positive scans have been reported in cerebral infarction, adult respiratory distress syndrome, and cystic fibrosis.²¹ Positive scans have also been described in bowel infarction,²² acute gastrointestinal hemorrhage,²³ hematomas,²⁴ and in pancreatitis.⁷ In-111-WBC uptake, usually faint, has been described around tracheostomy tubes, at the exit sites of drains or intravascular catheters, and in recent surgical wounds.²⁵ Although In-111-WBC uptake in neoplasm is rare, it has been reported.^{2,20,25-27} The above list of false-positives scans is not complete. As well as reviewing the literature, McAfee and Samin²⁵ compiled their own list of false-positives.

False-negative scans also occur with In-111-WBC scanning. Granulocytopenic patients have a potential for false-negative studies, and McDougall, Baumert, and Lantieri² recommended that patients with polymorphonuclear leukocyte counts < 2,000/cu. mm. should probably be studied with labeled donor cells. Perhaps the greatest potential for false-negative scans occurs in abscesses of long duration. For abscesses more than 2 weeks old, In-111-WBC scintigraphy may be falsely negative,^{8,28} and in one study,⁸ 7/26 (27 percent) of false-negative In-111-WBC scans occurred in septic foci of greater than 2 weeks' duration.

In the present series, 32 In-111-WBC scans from 28 patients with suspected abscesses were reviewed. In-111-WBC sensitivity was 82 percent, specificity 94 percent, and accuracy 89 percent. There was 1 false-positive scan in a patient with fulminant pancreatitis. This occurrence has been previously reported.⁷ Anderson and associates²⁹ reported that positive scans are seen only in severe, not in mild, pancreatitis. There were two false-negative scans. In both cases, septic foci had been manifested clinically for longer than 2 weeks prior to scanning, which is consistent with the reports that infections older than 2 weeks may produce scans that are falsely negative.

Twenty-two percent (7/32) of all scans showed areas of inflammation that were unrelated to abscesses. In-111-WBC uptake in inflammation is less intense than the liver uptake, and areas of abnormal uptake must be compared to the liver uptake to avoid false-positive interpretation.

Summary

Indium-111-leukocyte scintigraphy is an accurate, noninvasive test for the detection of abscesses, especially acute processes. The whole body can be imaged when searching for occult infections. In-111-WBC scans are easier to interpret than Ga-67 scans because of the lack of uptake by the

kidney or bowel. Also, diagnostic In-111-WBC scans can be obtained sooner after injection than Ga-67 scans. False-positives and false-negatives results do occur. Although In-111-WBC scanning can detect chronic abscesses, the sensitivity decreases when the abscess is older than 2 weeks.

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