Diagnosis of Sternal Wound Infection by Technetium-99m-Leukocyte Imaging

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An imaging study is needed that can detect sternal wound infections and distinguish between superficial and deep sternal wound infection when a clinical diagnosis is uncertain and a decision regarding surgical intervention must be made. We retrospectively reviewed the ⁹⁹mTc-leukocyte scans of 29 patients referred to rule out sternal wound infection. The presence or absence of deep or superficial sternal wound infection was determined by microbiology and long-term follow-up. Images obtained 4 and 20 hr after injection were reviewed by two nuclear physicians who were blinded to the clinical history. Findings were categorized as normal or abnormal. Abnormal images were further defined as having intense uptake at 4 or 20 hr, increasing uptake between 4 and 20 hr, or other patterns such as focal cold regions, irregular uptake or “bifid” sternum appearance. The patterns of intense uptake at 4 or 20 hr or increasing uptake between 4 and 20 hr were 100% sensitive and 89% specific for the detection of deep sternal wound infection. The images were also useful for determining the extent of infection. Superficial sternal wound infection could not be reliably detected. The results indicate that ⁹⁹mTc-leukocyte imaging is useful for the diagnosis of deep sternal wound infection.


Sternal wound infection occurs in 1%-3% of patients who undergo coronary artery bypass grafting, one of the most common surgical procedures in North America (1-3). Sternal wound infections may be superficial or deep. Superficial sternal wound infections involve the subcutaneous tissue just under the skin wound. Deep sternal wound infections involve the deeper peri-sternal or retro-sternal spaces and may involve the sternum itself. Superficial sternal wound infections require prompt and aggressive antibiotic therapy to prevent progression to a deep sternal wound infection. Deep sternal wound infections require wound debridement and sternectomy to prevent morbidity and death (3).

The diagnosis of sternal wound infection is often difficult. The diagnosis may be made clinically by the presence of erythema, purulent drainage, fever and sternal instability. In some patients, deep sternal wound infection can be distinguished from superficial sternal wound infection by positive cultures of deep sternal wound aspirates. However, in many patients sternal wound infection is occult (2), presenting with low-grade fever and a sternal wound that appears normal or has scant serous drainage. Furthermore, equivocal deep sternal wound cultures may prevent differentiation of deep and superficial sternal wound infections. In patients with occult sternal wound infection, the presence and extent of sternal wound infection must be determined retrospectively or after surgical exploration and debridement.

An imaging study is needed that can detect sternal wound infections and distinguish between superficial and deep sternal wound infection when a clinical diagnosis is uncertain and a decision regarding surgical intervention must be made. This has been difficult for two reasons. First, midline sternotomy disrupts the normal anatomy and physiology of the sternum and the pre-sternal and retro-sternal soft tissues. This leads to abnormalities in computed tomography (4,5), bone scintigraphy (6) and gallium images (7) in the uninfected sternal wound. Second, sternal wound infections can involve bone, soft tissue or both. Unfortunately most modalities optimize imaging of either bone or soft tissue, but not both.

Leukocyte imaging methods have been shown to be efficacious for the detection of occult soft-tissue infection (8,9), osteomyelitis (10-13) and surgical wounds (8,14). There are no reports of the normal appearance of the sternum on leukocyte imaging after midline sternotomy, nor are there data on the efficacy of leukocyte imaging for the detection of sternal wound infections.

We evaluated the efficacy of leukocyte imaging for detecting sternal wound infections. Images were read in a blinded fashion. The resulting image patterns were compared to a retrospective clinical diagnosis determined by the results of sternal wound cultures and clinical outcome after long-term follow-up.

MATERIALS AND METHODS

We retrospectively reviewed the ⁹⁹mTc-leukocyte scans performed at Albany Medical Center between 1/89 and 4/90. This study was reviewed by the Human Studies Committee of Albany Medical Center and was approved as an exempt study.
Patients were divided into a control group of patients who had no prior sternal surgery (n = 37) and a study group consisting of those who had a prior sternotomy (n = 29). In the study group, all of the patients were referred to rule out a sternal wound infection.

Autologous leukocytes were isolated and labeled with $^{99m}$Tc using previously described techniques (15). Blood (50 ml) anti-coagulated with heparin was obtained by atraumatic venipuncture and sedimented at 1× g for up to 60 min. The supernatant was decanted and centrifuged at 150× g for 4 min to pellet the leukocytes. The leukocytes were resuspended in 3 ml of saline/autologous plasma (2:1) containing 30 mCi of $^{99m}$Tc-hexamethylenepropylene-amine oxime (HMPAO) and allowed to incubate at room temperature for 20 min. The cells were re-injected within 15 min of preparation and within 2 hr of the initial venipuncture. Cells isolated and radiolabelled with this technique have shown a trypan blue dye exclusion of >99% and cell motility indices of >95% (16).

Planar images with a general-purpose, low-energy collimator were obtained at 4 and 20 hr after injection. At 4 hr, an anterior chest view was obtained for 600K counts and all other views were obtained for the same time. At 20 hr, an anterior chest view was obtained for 250K counts and all other views were obtained for the same time. An anterior oblique image of the chest was obtained in 26 of the 29 patients referred for evaluation of sternal wound infection.

Images from the study group of patients were reviewed by two nuclear medicine physicians who had no clinical knowledge of the cases. Normal patterns of sternal uptake were determined by comparison with the control group images. Scan appearances were divided into the following patterns: (1) normal, (2) intense uptake at 4 and 20 hr (defined as uptake greater than the liver), (3) increasing uptake between 4 and 20 hr, and (4) other abnormal patterns. The latter group included a midline cold defect in the sternum ("bifid" sternum appearance), focal cold areas not in the midline, or mild increased or irregular uptake which was unchanged or decreased between 4 and 20 hr.

Clinical records were reviewed retrospectively by an infectious disease specialist. Antibiotic therapy, the presence of risk factors for sternal wound infection (age, diabetes, re-exploration, morbid obesity, steroid therapy or immune deficiency) and the days between imaging and bypass surgery were recorded. All patients with suspected sternal wound infection had cultures of deep sternal wound aspirates and cultures of sternal wound drainage. Patients who had a positive culture of a deep sternal wound aspirate or had a strong clinical suspicion of deep sternal wound infection underwent sternal debridement. All patients undergoing sternal debridement had cultures taken of debrided tissue. Sternal wound infection was considered to be present whenever there was a positive culture of either: (1) sternal wound drainage, (2) a deep sternal wound aspirate or (3) debrided sternal wound tissue. Sternal wound infections were further classified as superficial or deep. A sternal wound infection was classified as superficial when: (1) all cultures of deep sternal wound aspirates were negative, and (2) there was at least a 6-mo follow-up period in which there was no progression to a deep sternal wound infection without sternal wound debridement. The second criteria excluded patients whose deep sternal aspirate cultures were false-negative; an occult deep sternal wound infection that is missed clinically will progress to an obvious deep sternal wound infection in the absence of surgical debridement. A sternal wound infection was classified as deep whenever there was a positive culture at sternal debridement. The absence of sternal wound infection was defined by negative superficial and deep sternal wound cultures and the absence of progression to a sternal wound infection during a 9-mo follow-up.

RESULTS

Figure 1 is an example of the normal pattern of sternal uptake in a patient who underwent a midline sternotomy. Figures 2 and 3 are examples of patients with intense tracer uptake at both 4 and 24 hr. Intense uptake was defined as tracer localization within the sternum of substantially greater than the liver uptake. Figure 4 demonstrates a patient with increasing tracer localization between 4 and 20 hr. Figures 5, 6 and 7 demonstrate other patterns of abnormal uptake. Whenever anterior views suggested any degree of sternal uptake, the oblique view, when obtained, helped to confirm that the leukocyte uptake was localized to the sternal region. Figure 7 is an example of a midline cold defect in the sternum, which we refer to as a "bifid" sternum appearance. None of the patients with this scan appearance had evidence of sternal dehiscence.
FIGURE 3. Example of the uptake pattern of intense tracer uptake at 4 hr (A) and 20 hr (B). Uptake is seen diffusely throughout the distal sternal wound. At 20 hr (B), there is increasing activity extending laterally from the distal sternal wound. The midline wound was aspirated and found to be infected. The areas of lateral extension were aspirated and found to be loculations of pus.

Table 1 lists the clinical characteristics and imaging results of the post-sternotomy patients who did not have a sternal wound infection. Three of the patients with normal scans were re-explored for bleeding. Cultures of sternal drainage and deep sternal wound aspirates were negative in all patients without sternal wound infection. Table 2 lists the clinical characteristics, imaging results and microbiology of the post-sternotomy patients with a superficial sternal wound infection. Cultures of deep sternal wound aspirates were negative in all patients with superficial sternal wound infection. One patient in this group underwent surgical exploration and had negative cultures of debrided tissue. Table 3 lists the clinical characteristics, imaging results and microbiology of the post-sternotomy patients with a deep sternal wound infection. Cultures of debrided sternal wound tissue were positive in all patients with deep sternal wound infection. Some patients with deep sternal wound infection had negative cultures of sternal wound drainage or deep sternal wound aspirates. Otherwise there were no discrepancies in the organism cultured from debrided sternal wound tissue and the organism cultured from sternal drainage or from deep sternal wound aspirates. None of the patients with either superficial or deep sternal wound infections were immunosuppressed, morbidly obese or on steroid therapy.

The scan patterns of either intense uptake at 4 and 20 hr or increasing uptake between 4 and 20 hr were 100% sensitive for detecting deep sternal wound infections. The positive predictive value for deep sternal wound infection was 100% for the scan pattern of intense uptake at 4 and 20 hr and 75% for the scan pattern of increasing uptake between 4 and 20 hr. The positive predictive value for deep sternal wound infection of either of these two scan patterns was 83%. The specificity of these two scan patterns for distinguishing deep sternal wound infection from both superficial sternal wound infection and the absence of sternal wound infection was 89%. The specificity of these two scan patterns for distinguishing any infection from the absence of infection was 86%. Other abnormal patterns did not reliably distinguish between the presence or absence of deep sternal wound infection. A normal scan had a positive predictive value of 11% for a superficial wound infection and a negative predictive value of 89%.

In all of the positive studies, leukocyte imaging was able to provide information about the extent of infection along

FIGURE 4. Example of a patient with increasing tracer localization between 4 hr (A) and 20 hr (B). This patient had a deep sternal wound infection.

FIGURE 5. Example of other patterns of abnormal uptake. At 4 hr (A), there is increased uptake in the sternum which is less than the liver uptake. At 20 hr (B), the uptake is irregular and relatively decreased to unchanged from 4 hr (A). This patient did not have a sternal wound infection.

FIGURE 6. Example of focal cold defects of the sternum. At 4 hr (A), there is uptake in the sternum greater than the liver and cold areas in the left lateral upper sternum. At 20 hr (B), uptake in the sternum is now less than or equal to the liver and the focal cold defect in the proximal sternum is more prominent. This patient did not have a sternal wound infection.
FIGURE 7.

Example of a midline cold defect in the sternum referred to as a "bifid" sternum appearance. This image was obtained at 4 hr. This patients did not have a sternal wound infection. This scan pattern was not associated with sternal dehiscence.

the sternal wound. In one patient, the study was used to successfully guide a positive deep wound aspiration.

DISCUSSION

We retrospectively evaluated the efficacy of $^{99m}$Tc-leukocyte imaging to detect sternal wound infection. Several patterns of uptake were noted. By considering intense uptake at 4 and 20 hr and increasing uptake between 4 and 20 hr as positive for deep sternal wound infection, the scan sensitivity was 100% and the specificity was 89%. These results are similar to an overall sensitivity and specificity of 87% and 90% for the detection of occult infection by radiolabeled leukocytes, as reported in a review of the literature (17).

Because there are three diagnostic categories (normal, deep sternal wound infection and superficial sternal wound infection), the sensitivity and specificity of this scan can be calculated in several ways. We have chosen to calculate sensitivity and specificity of the scan to distinguish deep sternal wound infection from other diagnostic categories. The resultant values for sensitivity and specificity are most useful to referring physicians because their main goal is to distinguish patients who require surgical debridement (patients with deep sternal wound infection) from patients who require conservative management (patients with su-
peripheral sternal wound infections or patients without sternal wound infection).

Inflammation imaging is usually performed with leukocytes labeled with \(^{111}\)In-oxine (18) or with \(^{99m}\)Tc-HMPAO (15,19), which are equivalent for the detection of osteomyelitis and occult infection (20-23). The main disadvantage of \(^{99m}\)Tc-leukocytes is that some unbound tracer is excreted by the renal and hepatobiliary routes (15,19) and the resultant intestinal and bladder uptake may reduce the specificity of the scan for abdominal infections (24). However, excreted radioactivity does not interfere with sternal wound imaging. The advantages of leukocyte labeling with \(^{99m}\)Tc-HMPAO include labeling in plasma, a procedure which minimizes neutrophil activation (25), and superior images because of the higher administered dose and more favorable imaging characteristics of \(^{99m}\)Tc (15,19).

We obtained both early and delayed images. Because the positive predictive value of intense uptake at 4 and 20 hr is greater than the positive predictive value of increasing uptake between both 4 and 20 hr, both early and delayed imaging should be obtained.

In this study, there were no false-negatives for deep sternal wound infection. Thus, a negative scan can be used as strong evidence that a patient can be treated conservatively without the use of sternal wound debridement and sternectomy. Similarly, there were no false-positives in the group with intense uptake at 4 and 20 hr. A scan with this positive pattern indicates the presence of a deep sternal wound infection and the need for surgical intervention.

The group with increasing uptake between 4 and 20 hr had two false-positives. Recent surgical wounds may show leukocyte uptake, although most surgical wounds show faint to minimal uptake (14,26). This may have been the cause of the false-positive in one patient who was imaged 8 days postoperatively (Table 1). Intense uptake has been reported in 9% of uncomplicated traumatic fractures (27), and the mechanisms which cause uptake in a fracture also may cause uptake in a sternotomy. However, most uninfected fractures have minimal to mild uptake (12,28) which would not be considered positive for a deep sternal wound infection by our criteria. Hematomas in the surgical wound may occasionally result in a false-positive leukocyte scan (29). Leukocyte localization in the healing wound in the early postoperative period, in the healing margins of the sternum or in a wound hematoma may have resulted in the false-positives in our series.

The leukocyte scan could not reliably detect the presence of a superficial wound infection. Thus a negative scan cannot be used as evidence to stop antibiotic therapy for a clinically suspected superficial sternal wound infection. There are several potential reasons for the absence of leukocyte localization in superficial sternal wound infections. Chronic infection may cause false-negative results (8), although other studies have failed to demonstrate a loss of sensitivity with chronic infections (30). However, none of the patients with a false-negative study had clinical evidence of a chronic infection, and there was no difference in the interval between surgery and imaging between the patients with superficial and deep sternal wound infections (Tables 2 and 3). Granulomatous infections may result in false-negative studies (31), but none of our patients had granulomatous infections. Damage to the leukocytes during the isolation and labeling process (23,32) is an unlikely cause of false-negative studies, as our routine quality control indicates that the leukocytes used were undamaged and viable. Pulmonary uptake adjacent to the sternum can interfere with the ability to detect sternal wound uptake, but this was not observed. Diabetes (10,11,13) had no effect on the sensitivity of leukocyte imaging, despite being risk factors for sternal wound infections. Antibiotic therapy, which may be a cause of false-negative leukocytes studies (33), also had no effect on scan sensitivity.

Mild degrees of leukocyte uptake and irregular uptake were not predictive of sternal wound infection. Leukocytes commonly show mild localization in the bone after trauma and surgical manipulation (27,34), which may be due to focal increased phagocytosis of leukocytes by marrow reticuloendothelial cells (34). Sternal leukocyte uptake after a sternotomy from noninfectious causes may be indistinguishable from leukocyte uptake seen with superficial sternal wound infections, which tend to be localized and of a low grade. This may explain the poor sensitivity of leukocyte imaging for superficial wound infection and the poor positive predictive value of mild irregular uptake. Correlation with bone marrow scanning may be helpful to differentiate between infectious and noninfectious causes of mild or irregular leukocyte uptake after sternotomy (34).

Cold defects, both in the midline (“bifid” sternum) and elsewhere within the sternal wound were observed in this study. The “bifid” sternum appearance was not associated with sternal dehiscence. Cold defects have been associated with osteomyelitis, although usually the pattern is due to fractures, avascular necrosis or surgical procedures (35-37). Bone scanning has demonstrated avascular regions of the sternum in patients with internal mammary grafts (38). Because the internal mammary artery supplies blood flow to portions of the sternum, the sternal blood supply can be compromised when an internal mammary artery is harvested. In this study, all patients had at least one internal mammary artery bypass graft. Thus, it is likely that cold defects in the absence of infection are related to areas of avascular sternum. For this reason, focal cold defects are too nonspecific to be a useful diagnostic finding of sternal wound infection in patients who have had an internal mammary artery harvested for a bypass graft.

The patients in this study were not a randomized sample, but were selected by referring physicians because the clinical diagnosis of sternal wound infection was suspected, but could not be confirmed clinically. Our sensitivity and specificity results may differ in a randomized sample of
post-sternotomy patients or in patients with greater or lesser degrees of uncertainty about the presence of sternal wound infection. However, these results suggest that leukocyte scanning is of value in patients in whom the referring physician cannot confirm or exclude the diagnosis of deep sternal wound infection.

Not all patients underwent surgical exploration and debridement to definitively exclude the presence of deep sternal wound infection. However, confirmation bias is unlikely because patients with occult deep sternal wound infection who are misdiagnosed are not treated with surgical debridement and sternectomy will develop overt sternal or mediastinal infection. We required that there be a 9-mo period without subsequent sternal wound complications to confirm the absence of deep sternal wound infection in patients who did not undergo surgical debridement. This follow-up period minimizes the possibility that a patient with deep sternal wound infection was misdiagnosed.

Sternal wound infection is currently diagnosed by a clinical history, wound appearance, fever, leukocytosis, smear and culture (2,3). However, sternal wound infection may be occult with fever as the sole presenting feature (2). Although a deep sternal wound infection may be diagnosed by positive cultures of deep wound aspirates, cultures may be equivocal. In patients suspected of having an occult deep sternal wound infection or in patients with sternal wound infection and equivocal deep wound aspirates, 99mTc-leukocyte imaging may be an important supporting study.

Plain radiography cannot diagnose sternal wound soft-tissue infection (4), but is limited to detecting sternal osteomyelitis by demonstrating bone destruction, focal osteopenia and periosteal reaction, usually in association with enlargement of retrosternal soft tissues. However, the differentiation of normal postoperative changes from osteomyelitis can be difficult. Furthermore, plain films are normal early in the course of the infection (39) and by the time osteomyelitis is detectable on plain films, there is an increased risk of mediastinitis, morbidity and death (4).

Computerized tomography of the sternum demonstrates clear anatomic detail, subtle erosions, reactive periosteal new bone formation, sharply margined sclerosis, adjacent soft-tissue changes and gas (40). Goodman et al. was able to detect infection in all six patients with prestensternal infection with the findings of severe prestensternal edema, fluid collection or air (4). However, the anterior mediastinum is universally abnormal by computed tomography after sternotomy and deeper sternal wound infections are difficult to diagnose by computed tomography (4,41).

Computed tomography can detect the presence of sternal osteomyelitis by demonstrating severe bone demineralization and bone destruction (5), but this occurs in the minority of cases.

Leukocyte imaging reliably identifies patients who have deep sternal wound infection and require aggressive surgical debridement. The scan is useful in patients with suspected deep sternal wound infection when clinical examination fails to confirm a diagnosis or when deep sternal aspirates of a sternal wound infection are equivocal. The images also provide information as to the extent of infection along the wound and may be useful to guide a deep needle aspiration. Leukocyte imaging is not useful for detecting superficial sternal wound infection. However, this limitation is relatively less important since superficial sternal wound infections may be managed with antibiotic therapy, evaluated clinically and followed.

CONCLUSION
In summary, we found that 99mTc-leukocyte imaging was useful for determining the presence or absence of deep sternal wound infections. When imaging patients, it is important to obtain both 4- and 20-hr images. A scan should be considered positive for deep sternal wound infection when there is uptake substantially greater than the liver uptake at both 4 and 20 hr or increasing uptake between 4 and 20 hr. All other scan patterns, including normal uptake, focal cold areas, decreased midline uptake (“bifid” sternum) and irregular uptake should be considered negative for deep sternal wound infection.

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EDITORIAL

Imaging Inflammation: Current Role of Labeled Autologous
Leukocytes

In the article by Cooper et al. (1), 99mTc-leukocyte scanning is shown to be
accurate in the diagnosis of deep sternal wound infection following
sternotomy for coronary by-pass grafting. This appears to be of real
clinical value and represents another indication for leukocyte scanning to
be added to the long list of specialized clinical settings for which the tech-
nique makes a significant contribution to patient management.

Currently, the main areas of contro-
versy concerning the diagnosis of in-
fecfion with radionuclides are: (1) the
relative value of techniques which la-
bel either leukocytes or the inflam-
matory focus in vivo and do not,
therefore, require autologous blood
handling, and (2), perhaps of lesser
importance compared with item 1, the
relative merits of 99mTc and 111In-la-
labeled cells.

Agents which are thought to di-
rectly label the inflammatory focus
include 67Ga citrate, polyclonal im-
munoglobulin (HIG) (2-4), nanocol-
loids (5,6), porphyrins (7) and more
recently streptavidin (8). Apart from
67Ga, these have not been widely ac-
cepted. In experimental models of in-
flammation, most have given abscess-
to-background ratios no greater than
67Ga or radioiodinated serum album-
min, and considerably less than au-
tologous 111In-labeled leukocytes (9).
Radiolabeled monoclonal antibodies
against neutrophil antigens are now
available for labeling granulocytes in vivo. A considerable fraction of the
antibody circulating in peripheral
blood is not bound to cells, and, al-
though the granulocyte-binding in-
creases with time (10), there is a rela-
tively small radioactivity signal from
the spleen (10,11). These antibodies,
in particular the one first described by
the Swiss group (12) and the Behring
monoclonal antibody, BW 250/183

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