Indium-111 Chloride Imaging in the Detection of Infected Prostheses

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Thirty-three patients with painful joint prostheses and a suspicion of infection were imaged with [^{111}In]chloride. A final diagnosis was established by culture in 19. Of these, 12 were categorized as true positives and three as true negatives. There were two false-positive studies, occurring in patients with knee prostheses. In both, the culture was obtained by aspiration. Two false negatives were in patients with hip prostheses, one of whom had been on long-term antibiotic suppressive therapy. The sensitivity was 86%, specificity 60%, and accuracy 79%. Seventeen of the proven cases had bone imaging prior to [^{111}In]chloride imaging. All 17 static images were positive and were not helpful in differentiating loosening from infection. Using increased uptake on the blood-pool image as a criteria for infection, the sensitivity was 89%, but the specificity was 0. Adding flow studies made little difference in interpreting the blood-pool images. This study shows that [^{111}In]chloride imaging is more accurate in evaluating infection in prosthesis than bone imaging.

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Prosthetic implants have met with great success in alleviating the symptoms of arthritis and avascular necrosis, and achieving the early mobilization of patients with hip fractures. The attendant complications, however, may present a difficult diagnostic situation. Postsurgical complications leading to pain include loosening, infection, heterotopic bone formation, cortical fracture around the implant, hematoma formation, dislocation of the prosthetic components, nonunion of the greater trochanter when osteotomy has been performed, and bursa formation. The etiology is important in determining the appropriate therapy. The focus of this paper is on the detection of infected prostheses utilizing indium-111 (^{111}In) chloride.

MATERIALS AND METHODS

Thirty-three adult patients with painful joint prostheses 2 to 9 yr following surgery were referred to help determine if the cause of the pain was loosening or infection. These included 22 hips, ten knees, and one shoulder. Twenty-nine received 20 mCi of technetium-99m methylene diphosphonate followed by total-body bone imaging and regional views of any positive areas. Flow and blood-pool imaging of the suspected abnormal area were obtained in 23 patients. After obtaining informed consent, each received 2 mCi of carrier-free [^{111}In]chloride. At 24 to 72 hr, regional views were obtained. All images were subsequently interpreted by two observers without knowledge of the final diagnosis. The clinical records were then evaluated and the data were correlated.

RESULTS

Of the 33 patients, 19 underwent a definitive diagnostic or therapeutic procedure. Thirteen had operative procedures and six had aspiration of the joint. A diagnosis of infected prostheses was made on the basis of a positive culture. Fourteen patients with unproven diagnoses did not undergo definitive diagnostic or therapeutic procedures for the following reasons: (a) the clinical impression was consistent with loosening, (b) the patient refused operation, (c) was referred back to referring physician, or (d) failed to return for follow-up appointments.

Indium-111 chloride images were considered positive if any uptake was present other than the normal

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TABLE 1
Distribution of Prostheses Sites, Image Interpretations, and Culture Results in Proven Cases

Item*	Patient	Prosthesis site	Indium	Bone scintigraphy			Culture‡
				Flow	Pool	Static†	
	1	Hip	+	−	None	A	+ S
	2	Hip	+	+	+	TR	+ S
	3	Hip	+	None	None	A,S,T	+ S
TP	4	Hip	+	+	+	A	+ S
	5	Hip	+	None	None	None	+ S
	6	Hip	+	None	None	None	+ S
	7	Knee	+	+	+	F,Tb	+ S
	8	Knee	+	None	None	F,Tb	+ S
	9	Knee	+	+	+	T	+ S
	10	Knee	+	−	+	F,Tb	+ S
	11	Knee	+	+	+	A,S,T	+ As
	12	Hip	+	+	+	A	+ As
	13	Hip	−	None	None	A,S,T	− S
TN	14	Hip	−	None	None	A,S,T	− S
	15	Shoulder	−	None	+	H	− S
	16	Knee	+	+	+	F,Tb	− As
FP	17	Knee	+	+	+	F,Tb	− As
	18	Hip	−	−	−	A,S,T	+ As
FN	19	Hip	−	−	+	A,S,T	+ As

* TP = True positive, TN = True negative, FP = False positive, FN = False negative.
† A = Acetabulum, S = Stem, T = Tip, Tb = Tibia, F = Femur, Tr = Trochanter, H = Head.
‡ S = Surgery, As = Aspiration.

bone marrow activity in the greater trochanter when present. Of the 19 proven cases, there were 12 true positives, three true negatives, two false positives, and two false negatives (Table 1). Figure 1 demonstrates a patient with a true-positive study. The two false-positive studies occurred in patients with knee prostheses (Fig. 2). The sensitivity of [^{111}In]chloride imaging was 86% and the specificity 60%, for an overall accuracy of 79%.

Blood-pool and flow images were considered positive if any abnormality was present regardless of the degree. There were eight true-positive blood-pool images, zero true negatives, three false positives, and one false negative. The false positives occurred in two knee prostheses, (which were also false positives on the indium images), and a shoulder prosthesis. The one false negative occurred in a hip prosthesis, (which was also a false negative on [^{111}In]chloride imaging). The sensitivity

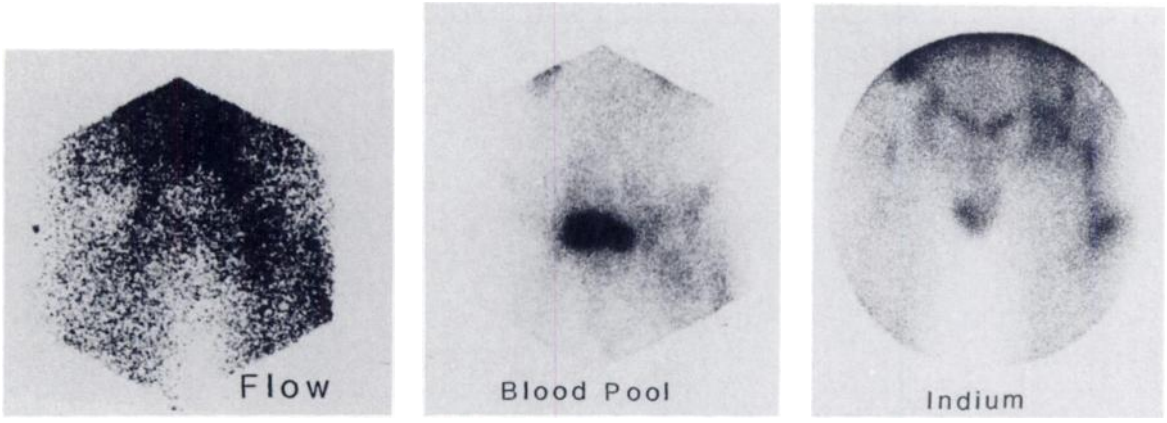

FIGURE 1
True-positive flow, blood pool, and [^{111}In]chloride images in infected left hip prosthesis

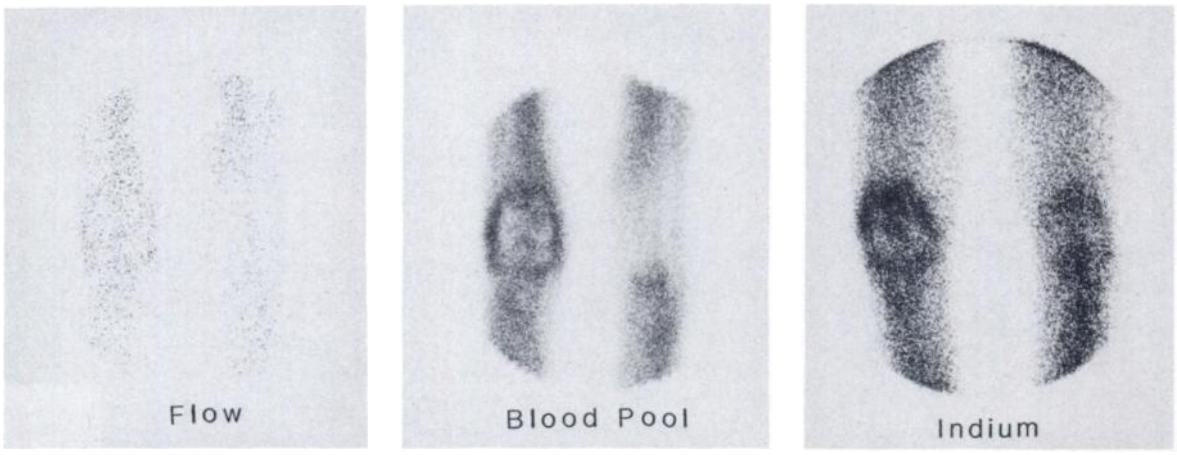

FIGURE 2
False-positive flow, blood pool, and [^{111}In]chloride images in right knee prosthesis

was 89%; however, the specificity was 0. The vascular flow images agreed with blood-pool images except for two cases of documented infection where the flows were interpreted as negative but the blood pool images were positive. The static bone images were positive in all patients when obtained.

Of the 14 unproven cases, [^{111}In]chloride images were positive in eight and negative in six (Table 2). All negative images were clinically felt to be loose. Flow and blood-pool images were performed in 12. They were congruent except for two cases. In one with no diagnostic impression, the flow was negative and blood pool positive ([^{111}In]chloride was also positive). In the other case diagnosed as a possible infection, the flow was positive and the pool negative ([^{111}In]chloride was also positive). The blood-pool images agreed with [^{111}In]chloride images except for three cases of possible infection and one of heterotopic bone.

DISCUSSION

Indium-111 chloride was originally used as a bone marrow imaging agent (*1–3*). Recently it has been demonstrated to be effective in the localization of inflammatory processes and osteomyelitis as well (*4–5*). In vivo it binds tightly to transferrin and albumin and localizes in normal euthyroid bone marrow (*6*). The mechanism of localization in inflammatory disease is not known. Increased capillary permeability to proteins (*7*) and the in vivo labeling of bacteria and leukocytes (*8,9*) are believed to be involved in gallium-67 (^{67}Ga) localization and may possibly play a role in indium localization as well.

TABLE 2
Distribution of Prostheses Sites and Image Interpretations in Unproven Cases

Patient	Prosthesis Site	Indium	Bone scintigraphy			Follow-up p̄ image (mo)	Clinical diagnosis
			Flow	Pool	Static*		
1	Hip	+	−	−	A,S,T	5	Infected
2	Hip	+	+	−	S	3	Infected
3	Hip	+	+	−	A,S,T	3	Infected
4	Hip	+	−	−	Tr	1	Heterotopic bone
5	Hip	+	+	+	A.S.T.	13	Loose
6	Knee	+	+	+	F,Tb	None	Loose
7	Knee	+	−	+	F,Tb	None	Unknown
8	Knee	+	None	None	None	None	Unknown
9	Hip	−	−	−	A,T	12	Loose
10	Hip	−	None	None	A,S,T	11	Loose
11	Hip	−	−	−	A,S,T	13	Loose
12	Hip	−	None	None	A,T	7	Loose
13	Hip	−	−	−	None	6	Loose
14	Hip	−	−	−	A,T	None	Loose

* A = Acetabulum, S = Stem, T = Tip, Tr = Trochanter, F = Femur, Tb = Tibia.

Patients referred for painful joint prostheses first have a three-phase bone scan and, if positive, an [^{111}In]chloride scan is done immediately thereafter. In our series, blood-pool imaging was as sensitive as [^{111}In]chloride in detecting infection but the specificity was entirely lacking. Flow studies tended to agree with blood-pool images. They were not helpful in improving either the sensitivity or the specificity and were in fact slightly less accurate. With [^{111}In]chloride imaging, the two false-positive studies occurred in patients with knee prostheses. Both underwent joint aspiration and subsequently had negative cultures, although this is not an entirely reliable method of excluding infection (*10*). One patient was still felt clinically to have an infected prosthesis but was not operated on because she was a poor candidate for anesthesia, while the second patient had no other evidence of infection despite the continued positivity of the study 7 mo later. The two false-negative images occurred in patients with hip prostheses. One of these patients had been on long-term antibiotic suppressive therapy prior to the radionuclide studies which may have been the reason for the negative images. The reason for the second false negative is unknown. We feel that the specificity is low because relatively few patients with negative images underwent further diagnostic or therapeutic procedures unless the suspicion of infection was great. In partial support of this is that all six patients with negative [^{111}In]chloride images without culture proven diagnosis were all felt to be loose and not infected.

In summary, we found [^{111}In]chloride to be a moderately useful adjunct to bone scintigraphy in distinguishing loose from infected prostheses. Although the accuracy is similar as that reported in the literature for [^{67}Ga]citrate imaging (*11–13*), the interpretation is simpler in that any concentration of indium is considered abnormal and the problem of congruent or noncongruent uptake does not exist.

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