

## Intense accumulation of indium-111 leukocytes in peritonitis carcinomatosa

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In order to detect the infectious foci in a case of terminal recurrent cancer of the sigmoid colon with intense inflammation, In-111 oxine leukocyte scintigraphy was performed. Leukocytes labeled with In-111 oxine quickly localized within the region of peritonitis carcinomatosa and could be imaged after 4 hours. With time, high activity appeared in this area. And 48 hours after injection, the large intestine was clearly seen. However, no activity was seen in the main recurrent tumor. This suggested that the labeled leukocytes had accumulated in regions of inflammation rather than in malignant tissue.

When performing In-111 leukocyte scintigraphy for diseases in which tumor cells and inflammation are mixed, distinguishing the two components is particularly important, and time-sequential scanning is very useful.

**Key words:** In-111 oxine, In-111 leukocyte, Infection, Peritonitis carcinomatosa, Tumor

### INTRODUCTION

THE USEFULNESS of scintigraphy in which leukocytes are labeled with In-111 oxine has been recognized in the detection of abscesses and inflammatory foci. The sensitivity of In-111 labeled leukocytes in detecting abscesses has been estimated to be comparable to that of either ultrasound or CT scanning. The greatest advantage of this technique over other imaging methods is that the level of activity of the affected foci can be assessed. Particularly in cases where the location of infectious foci is unknown, In-111 labeled leukocyte scintigraphy should be considered the examination of choice.<sup>1-3</sup>

In Japan, this technique has not been generally used for the detection of infectious foci; Ga-67 citrate is much more widely used. One of the reasons for this is that the techniques required for *in vitro*

labeling tend to be rather troublesome. Recently, a few reports have mentioned that leukocytes labeled with In-111 oxine can be seen to accumulate in tumors as well as in abscesses, and that it is important to be able to distinguish between these two.<sup>4-6</sup>

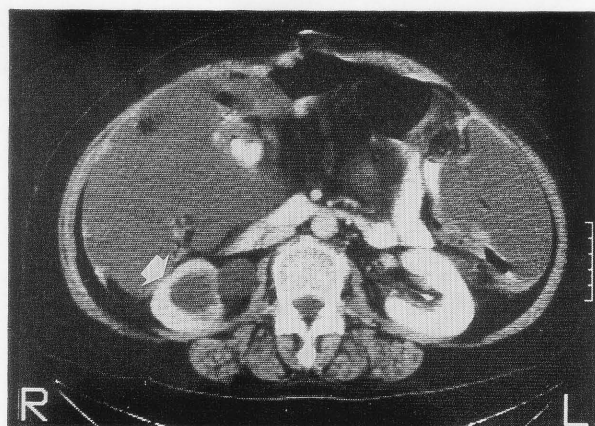
We have had the opportunity to examine a post-operative case of sigmoid colon carcinoma using In-111 labeled leukocyte scintigraphy. The labeled leukocytes accumulated strongly within the region of peritonitis carcinomatosa, and we were able to study the features which distinguish between tumors and abscesses.

### CASE REPORT

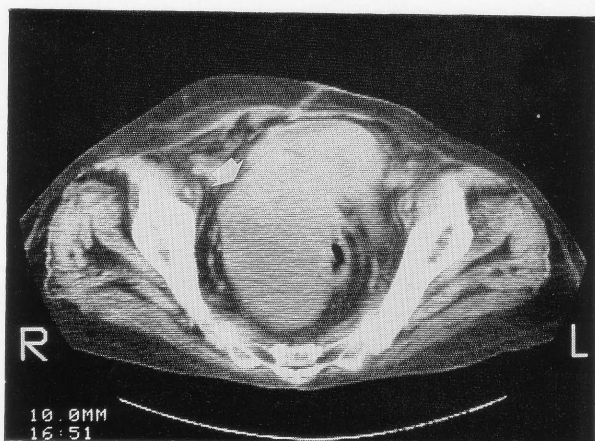
The patient was a 61-year-old woman who had received surgical treatment for cancer of the sigmoid colon one year and ten months previously. One year after surgery, massive ascites developed and malignant involvement of the left ovary was discovered. The patient underwent a second surgical procedure, in which a tumor approximately 25 cm in diameter was removed and intraoperative radiation was administered. Nine months after the second procedure, the patient developed subileus. At that time a CT scan was obtained (Fig. 1). A large quantity of

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(a)

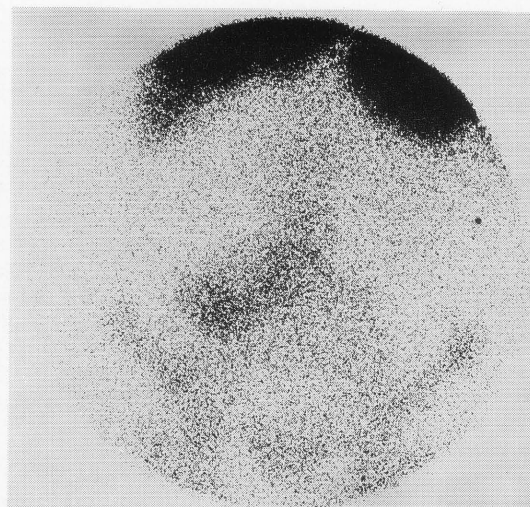


(b)

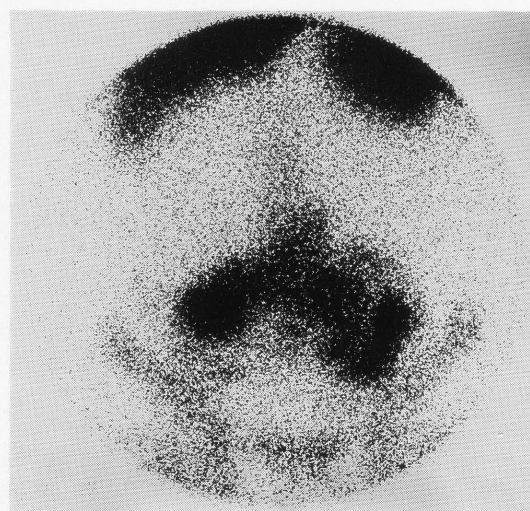
**Fig. 1** Contrasted CT scan showed the local recurrence and peritonitis carcinomatosa. (a) Massive ascites was demonstrated at the level of the kidneys. The right kidney (arrow) was noted to be hydronephrotic due to intrapelvic infiltration as demonstrated at autopsy. (b) The ovarian dilatation (arrow) was due to direct infiltration of recurrent tumor. No uptake of In-111 leukocytes was seen in this area (see Fig. 2(b)).

ascitic fluid and a hydronephrosis of the right kidney were seen. Also, in the lower abdominal quadrant, an invasive tumor was seen surrounding the intestine from the anterior abdominal wall to the anterior aspect of the sacrum. The right ovary was enlarged secondary to direct invasion of a local recurrent tumor. The chest X-ray showed numerous diffuse nodular shadows in both lung fields. The diagnosis was recurrent cancer of the colon with peritonitis carcinomatosa. Two weeks later, the patient developed a fever of about 39°C degrees, suggesting infectious complications, and laboratory findings showed the patient's leukocyte count to be 20,600/microliter, ESR 111 mm/h, and C-reactive protein 6+, confirming the presence of inflammation.

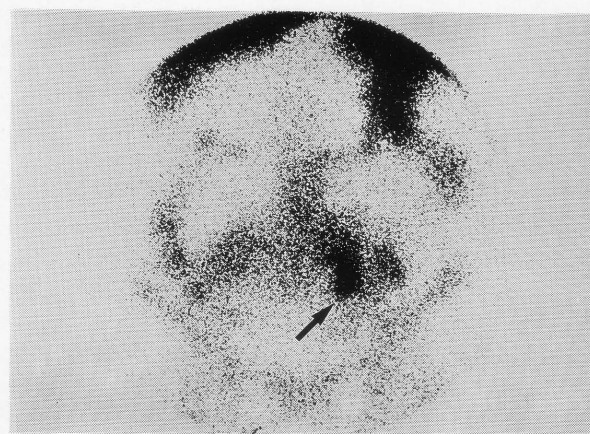
In-111 oxine labeled leukocyte scintigraphy was performed according to the method described by



(a)

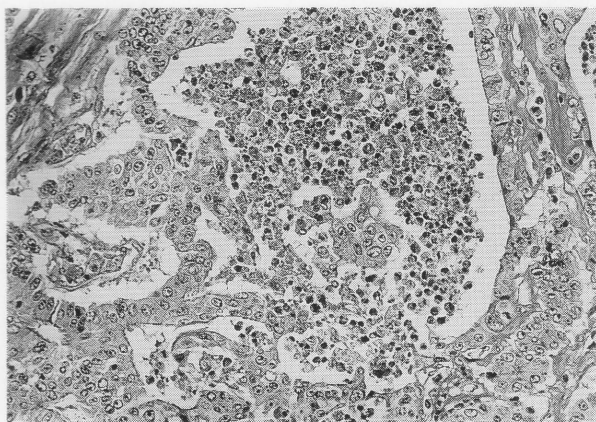


(b)



(c)

**Fig. 2** Anterior view of the scintigram of In-111 leukocytes. (a) The early phase scintigram demonstrated the moderate uptake in the right lower abdominal quadrant. (b) After 24 hours, intense accumulation was seen bilaterally. (c) The tumor-like accumulation was decreased in a 48-hour scan, followed by the appearance of radionuclide activity in the colon and the dermatocolostomy (arrow).



**Fig. 3** On microscopic examination, metastatic nodules in the mesentery were confirmed to be well-differentiated papillotubular adenocarcinoma of the sigmoid colon with prominent infiltration by leukocytes. No abscess was demonstrated. (Hematoxylin-Eosin,  $\times 190$ )

Thakur et al.<sup>7,8</sup> Approximately 700 microcuries of In-111 oxine (Amersham Medical Ltd.) was employed for leukocyte labeling, approximately 600 microcuries of labeled leukocytes were injected intravenously, and scintigraphy was performed at 4, 24, and 48 hours using a PHO/GAMMA LFOV gamma-camera.

A uniform area of activity was seen in the right lower abdomen in a 4-hour image. At 24 hours, the area of activity showed strong intensity, but no accumulation was seen in the lower pelvis. At 48 hours, most of the areas of activity had decreased and a radionuclide activity along the large intestine was clearly delineated. To the inner left of the intestinal lumen, an area of intense activity on what appeared to be a portion of the dermatocolostomy was seen (Fig. 2). The lung foci seen on the chest X-ray failed to show activity.

The patient died one month after the scintigram was obtained. The autopsy showed intense peritonitis carcinomatosa and strong adhesions of the intestinal loops. Recurrent tumor was found in the rectouterine pouch invading the ovary and the bladder. Right-sided hydronephrosis secondary to retroperitoneal spread was also seen. Metastases were found in the lungs, the liver, the adrenals, and the thymus.

Histopathological examination showed the tumor to be a well-differentiated, papillotubular adenocarcinoma. Leukocyte invasion was relatively marked (Fig. 3).

## DISCUSSION

In Japan, Ga-67 citrate scintigraphy is commonly used to search for an inflammatory focus in fever of unknown origin. Ga-67 is thought to combine with

transferrin in the blood, forming a complex which is selectively taken up by leukocytes or bacteria in foci of inflammation.<sup>9</sup> Because Ga-67 citrate is administered by simple intravenous injection, it is easy to handle. However, in Ga-67 citrate scanning there is a long delay before accumulation becomes apparent, and, when the abdomen is to be examined, bowel preparation is required, which may be a severe stress upon the patient. In contrast, In-111 leukocyte scintigraphy has several advantages, despite the fact that autologous leukocytes must be collected, separated and labeled, which is a troublesome process. In-111 labeled leukocytes do not initially distribute within the abdomen, and bowel preparation is not required. Also, the accumulation of In-111 labeled leukocytes in abscesses appears to be much faster. Depending upon the case, areas of high activity may be detectable in as short as three or four hours following intravenous injection, facilitating rapid diagnosis.<sup>7,10</sup> For these reasons, it may be more practical to use In-111 labeled leukocytes than Ga-67 citrate in searching for foci of infection.<sup>8,11</sup> Although several investigators have reported that In-111 oxine labeled leukocytes accumulate in tumors, the mechanism remains to be clarified. Current theories are that the accumulation is due to local increases in blood flow or direct invasion of the tumor by the leukocytes.<sup>4-6</sup> In addition, free In-111 may also form a complex with transferrin in the blood and accumulate due to mechanisms similar to those for Ga-67.<sup>4,11,12</sup> However, leukocytes labeled with In-111 appear to be stable for prolonged periods *in vivo*, and the displacement of In-111, if any, is slight.<sup>7</sup>

In the case of peritonitis carcinomatosa which we examined, labeled leukocytes accumulated in the right lower abdomen within 4 hours after intravenous injection, and high activity were seen bilaterally at 24 hours. Within 48 hours, activity of these areas had reduced, and the In-111 labeled leukocytes were seen to have accumulated in the colon and at the dermatocolostomy. Early accumulation of labeled leukocytes following intravenous injection is thought to be indicative of hyperemia. However, this phenomenon can also be seen in acute inflammation as well as in tumors.<sup>5,10</sup> The significant fact that no activity was seen in the colon at 24 hours, but was clearly visible within 48 hours, suggests that the observed activity was not due to accumulation within the colonic mucosa, but due to the retention of In-111 labeled leukocytes within the lumen.<sup>5,10</sup> The appearance of activity in the colon could be the result either of In-111 from the necrotizing lung tumor entering the digestive tract via the airways, or direct invasion of the tumor into the intestinal tract.<sup>3,5</sup>

In this case study, In-111 labeled leukocytes are

thought to have accumulated in inflammatory components of the peritonitis carcinomatosa and not in the tumor cells. This is because signs of inflammation were obvious, the accumulation of labeled leukocytes was seen early following injection, no activity was noted in the local recurrent tumor and in the metastatic nodules of the lung, and the changes in In-111 distribution were followed. Actually, at autopsy, numerous metastatic nodules in the mesentery with prominent necrosis and leukocyte infiltration was verified, but no abscesses were found.

Although we normally use the 24-hour post injection image in routine diagnosis, in the examination of peritonitis carcinomatosa with a mixture of inflammation and tumor components a single scan was determined to be insufficient.

It is anticipated that In-111 labeled leukocyte scintigraphy will become more widely used in the future. It is essential that abscesses and tumors should be distinguished when scintigraphy is used to diagnose and evaluate the course of illness, and time-sequential scanning is significantly useful in it, as is well illustrated by the case we have presented.

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