

## Visualization of bleeding site on 24-hour imaging in lower gastrointestinal bleeding with $^{99m}\text{Tc}$ -nanocolloid: A case report

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Case Report

## ABSTRACT

Gastrointestinal bleeding can be diagnosed by history taking, physical examination, and diagnostic examinations. However, localization of gastrointestinal bleeding via a nuclear medicine examination can indicate an accurate examination to detect the location of bleeding. Radiopharmaceuticals can be selected according to a patient's condition. Good image results are needed so that the results are conclusive and lead to further examination and management. A 2-years-old girl patient was hospitalized in a paediatric ward due to a large number of loose stools mixed with fresh blood for months after experiencing diarrhoea. The patient was active, absence any decreased appetite, pain, activity disturbances, or significant weight loss. Her parents took her for treatment to several hospitals but no improvement. The patient was referred to the Nuclear Medicine Department to undergo localization of gastrointestinal bleeding study.  $^{99m}\text{Tc}$ -nanocolloid was injected as radiopharmaceuticals, followed by a dynamic and serial static imaging after 30 minutes. No focus of radioactivity extravasation was found. Examination was continued at 1, 2, and 24 hours. Diffuse radioactivity extravasation was found in the descending colon 24 hours after injection of the radiopharmaceutical, and she was confirmed by colonoscopy and biopsy a week later.  $^{99m}\text{Tc}$ -labeled colloid had not been used after a few studies showed that  $^{99m}\text{Tc}$ -red blood cell (RBC) in vitro was better at localizing gastrointestinal bleeding. Usually,  $^{99m}\text{Tc}$ -labeled colloid remains in circulation for only 30 minutes due to rapid distribution to the reticuloendothelial system. The visualization of the bleeding site on 24-hour imaging was unusual. However, these findings suggest that  $^{99m}\text{Tc}$ -labeled colloid can still be used with due regard to the patient's clinical active bleeding and imaging techniques.

## INTRODUCTION

Gastrointestinal bleeding is an abnormal loss of blood in the gastrointestinal tract from the mouth cavity to the anus. A normal volume of blood lost from the gastrointestinal tract is about 0.5-1.5 mL per day.<sup>1</sup> Causes of gastrointestinal bleeding in children vary widely, and its clinical conditions that arise can range from mild with no serious consequences to severe and life-threatening.<sup>1,2</sup> Gastrointestinal bleeding in the upper and lower tract is anatomically delimited by the ligament of Treitz,<sup>3</sup> so lower gastrointestinal bleeding refers to bleeding that occurs in the gastrointestinal tract below (distal to) the ligament of Treitz. Clinical features of lower gastrointestinal bleeding are characterized by the presence of haematochezia, except if intestinal motility is slow.<sup>1</sup>

Lower gastrointestinal bleeding is on the second rank in cases of gastrointestinal bleeding which was a reason for patients visiting the Emergency Department (ED) in America from 2006-2011, accounting for 132,102 cases (30.2%) of all gastrointestinal bleeding cases.<sup>4</sup> There have been few reports on the incidence of lower gastrointestinal tract specifically in children in



Indonesia. A descriptive study at Dr. Sardjito Hospital reported that from 2009-2015, the profile of lower gastrointestinal bleeding in children included 28 of 55 subjects (51%), predominantly occurred in girls (54%), most commonly experienced by children aged 1-6 years (57%), with haematochezia (96%) as the most common clinical sign, diarrhoea as the most common accompanying symptom (29%), and colitis (60%) as the most common etiology from colonoscopy findings.<sup>5</sup>

The lower gastrointestinal bleeding can be diagnosed through history taking, physical examination, laboratory tests, radiological examinations, and colonoscopy.<sup>1</sup> Nuclear medicine and molecular theranostics play a role in confirming the diagnosis and detecting the localization of lower gastrointestinal bleeding. Localization detection of lower gastrointestinal bleeding is a non-invasive study conducted on patients suspected of gastrointestinal bleeding to determine whether the bleeding is active, to localize the bleeding area in patients with overt gastrointestinal bleeding, and to estimate the volume of bleeding for prognostic purposes. This study can be performed using two types of radiopharmaceuticals, namely <sup>99m</sup>Tc-red blood cells (RBCs) and <sup>99m</sup>Tc-sulfur colloid.<sup>6</sup>

In this case report, we present a case of a paediatric patient exhibiting typical symptoms of lower gastrointestinal bleeding. The choice of radiopharmaceuticals and examination procedures was based on the guidelines for detecting the localization of lower gastrointestinal bleeding at Dr. Hasan Sadikin Central General Hospital Bandung, the patient's condition, and the availability of facilities. Findings that differ from theory require further discussion and hopefully serve as a learning experience for colleagues who may need it. This case also has the potential to revolutionize clinical practice. Readers will be informed about the nuclear medicine examination, which is still unfamiliar for diagnosing and localizing bleeding sites in Indonesia. They will also be informed by its different approach, offering valuable insights into a common yet challenging medical issue, especially in the gastrointestinal disease. This study has a promising value in enhancing diagnostic accuracy and patient outcomes in the management of gastrointestinal bleeding.

## CASE DESCRIPTION

A 2-years-old girl had been experiencing fresh bloody stools for one month before treated at the hospital. Complete history taking revealed that she had bloody stools 1-2 times every day. Her complaint was not accompanied by vomiting, abdominal pain, bloating, or pain during defecation. The patient remained active and had a normal appetite and fluid intake. There were no complaints of fever, cough, runny nose, shortness of breath, seizures, or loss of consciousness. There was no history of weight loss greater than 2 kg in one month, trauma, falls, or difficulty in urinating. The patient is the first child of a mother who never had an abortion before (parity status=P1A0), born spontaneously with the assistance of an obstetrician-gynaecologist, weighing 2,700 grams at birth, full-term, and crying immediately after birth. Her history of immunizations is complete, while her growth and development are age appropriate. Before coming to Dr. Hasan Sadikin General Hospital, he was treated with zinc, prebiotics, and antibiotics. Since the previous stool examination revealed bacteria, she was then given another antibiotics and prebiotics. As her condition did not improve, she was advised to go to Dr. Hasan Sadikin General Hospital for further management. She was referred to the Nuclear Medicine Department to undergo an examination of the localization of gastrointestinal bleeding. On the day of examination, the stool was still mixed with blood (Figure 1).



Figure 1. Bloody stool from the patient

Her vital signs and physical examination were within normal limits. The gastrointestinal bleeding localization was performed with <sup>99m</sup>Tc-nanocolloid 3.8 mCi intravenous injection. Imaging with hybrid single photon emission computed tomography (SPECT) and computed tomography (CT) was performed dynamically and serially statically for 30 minutes after the injection of radiopharmaceuticals; no focus of radioactivity extravasation was found. The study was continued at 1, 2, and 24 hours (Figure 2).

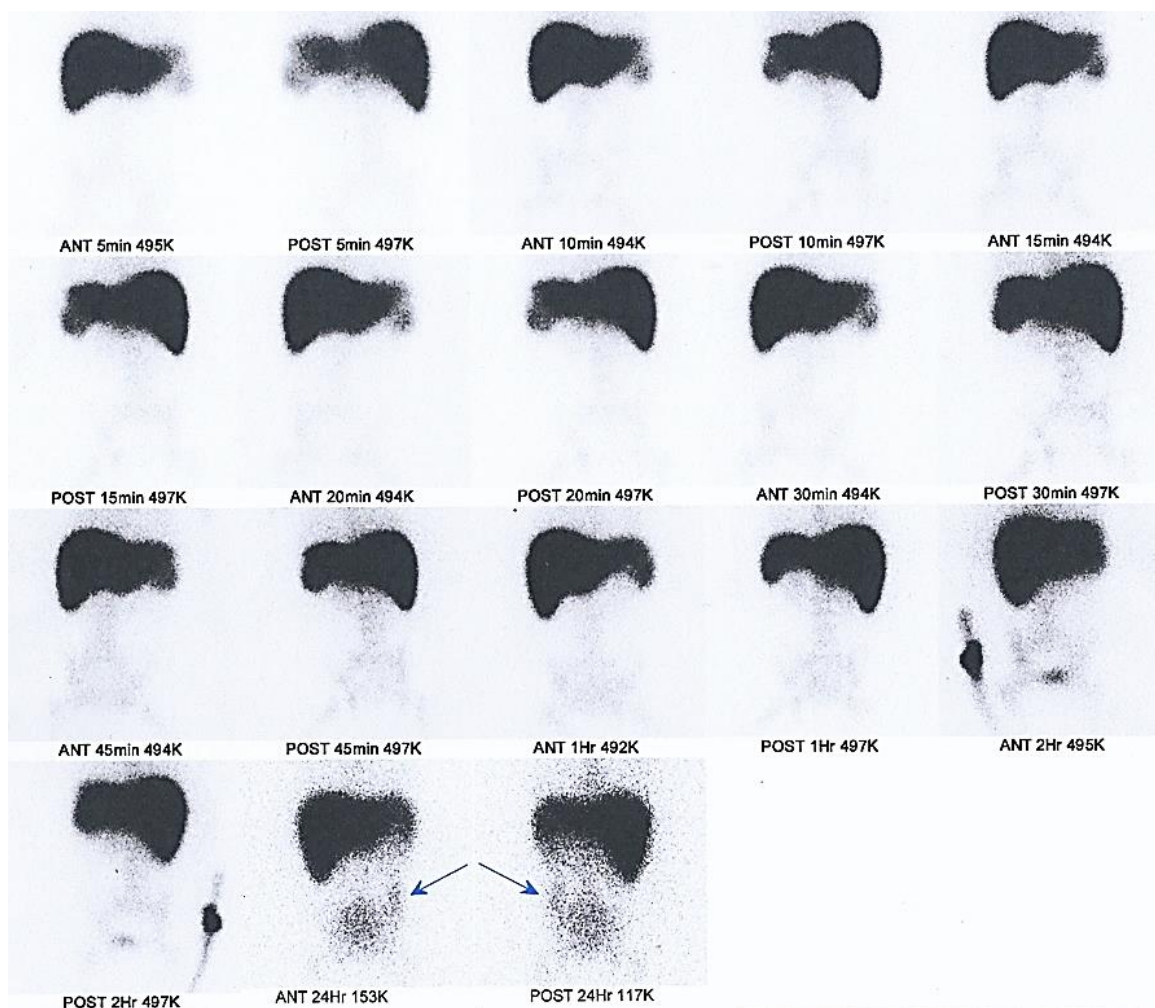


Figure 2. Anterior-posterior view from serial static images. The red square indicates the images in 1-, 2-, and 24-hours acquisitions. The black arrows indicate the site of the bleeding. The 24-hours acquisition took a longer time than the examination the day before due to radiopharmaceutical decay.

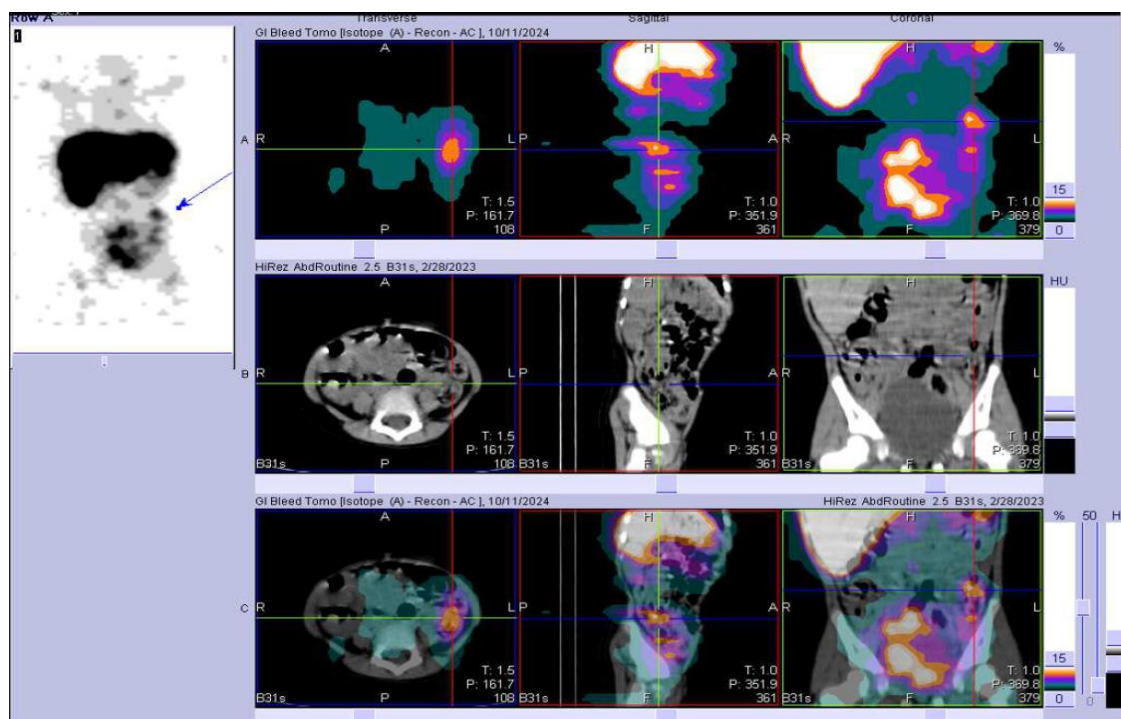


Figure 3. Single photon emission computed tomography (SPECT)/computed tomography (CT) 24-hours image provides detailed information on the location of the bleeding sites. The blue arrow, as the suspected site of bleeding, was located by the three-cross-section view of the tomography.

Diffuse radioactivity extravasation was found in the descending colon 24 hours after the injection of the radiopharmaceutical (Figure 3). The patient still had fresh bloody stool after the procedures. A week later, a colonoscopy was performed. Bleeding stigmata were found in the colon area, especially the descending colon and rectum. Colon samples were taken during the colonoscopy. The histopathological result from the biopsy confirmed the diffuse chronic colitis. These results were consistent with the cause of the active bleeding. The patient was discharged after improving.

## DISCUSSION

Anamnesis, physical examination, and diagnostics examinations are methods for diagnosing gastrointestinal bleeding that must be conducted carefully.<sup>1,7</sup> Lower gastrointestinal bleeding is a working diagnosis in this patient based on her symptoms and clinical findings. Colitis, which was suspected to be the cause of this gastrointestinal bleeding; more commonly occurs in females<sup>4,5,8</sup> and under 3 years (2-5 years)<sup>1,4,5</sup> with most common clinical symptoms are hematochezia<sup>1,4,5,7,8</sup>, and the patient's general condition is good but bleeding often occurs;<sup>7</sup> and her preceding etiology is diarrhea.<sup>1,4,5,6,8</sup> She also have signs of anemia on hematological examination, mucus on routine stool examination, and thickening of the lower right quadrant of the colon wall along with enlargement of the abdominal lymph nodes on abdominal ultrasound.

The presence of macroscopic blood symptoms that were not visible in routine stool examinations was in line with a study by Dam et al. stating that the clinical signs and symptoms as well as laboratory indicators of gastrointestinal bleeding were often unreliable and misleading. There was often a significant delay in the onset of bleeding with clinical findings. The study of gastrointestinal bleeding localization in this patient was performed before more invasive examinations, such as enteroscopy (mid-gastrointestinal), colonoscopy (lower gastrointestinal) or angiography, were conducted.<sup>6,9</sup>

The obscure chronic lower gastrointestinal bleeding in the patient was one of the primary reasons for determining the localization procedure of gastrointestinal bleeding. The <sup>99m</sup>Tc-nanocolloid was chosen as the radiopharmaceutical in her because the suspicion of real and active lower gastrointestinal bleeding, thus expecting images to be obtained within a short time frame



with a high target-to-background ratio. The conclusive results were expected from well-labelled radiopharmaceuticals (to determine diagnostic performance). In-vivo labelling techniques for  $^{99m}\text{Tc}$ -RBC only achieved a maximum labelling efficiency of 75% and were not recommended to this patient due to suboptimal performance and labelling within the body being affected by various drugs and other components. In previous references (during the early days when  $^{99m}\text{Tc}$ -RBC was proposed), comparisons with the results of  $^{99m}\text{Tc}$ -RBC studies were superior to  $^{99m}\text{Tc}$ -labeled colloids, only if  $^{99m}\text{Tc}$ -RBC was labelled in vitro.<sup>10-12</sup>

The choice of colloid-labelled radiopharmaceuticals relied more on their availability in each country rather than diagnostic performance, although the size range of each type of radiopharmaceutical varied.<sup>13</sup> The use of these radiopharmaceuticals for imaging the liver, spleen, and bone marrow was based on the fact that after intravenous administration, the radiopharmaceuticals would be cleared from circulation through a process of phagocytosis occurring in the macrophages of the lymphatic endothelial system.<sup>14</sup>

The examination procedure was performed by using a Siemens SPECT/CT camera. After the radiopharmaceutical injection, dynamic imaging was conducted for the first 2 minutes followed by serial static imaging.<sup>14</sup> The dynamic acquisition period was performed for 30 minutes, no focal radioactivity was yet visible indicating radiopharmaceutical extravasation. Therefore, serial static images were required until minute 120, but still no focal uptake was seen.

Static imaging was decided to be repeated on the next day. Haematochezia was still experienced. Planar imaging was performed exactly 24 hours after the radiopharmaceutical injection. Focal radioactivity was found on the projection of the descending colon. The SPECT/CT imaging was performed for the more precise localization of radioactivity, confirming that the descending colon as the source of the bleeding. Eventhough  $^{99m}\text{Tc}$  has a 6-hours half-life decay, the delayed-images could be obtained with a longer time of acquisitions. This delayed technique, for example, was also used in the bone scan delayed images in 24-hours after the injection to distinguish the metastatic lesion with the inflammations.

Several factors contributed to the extension of time in the localization of the gastrointestinal bleeding site in this patient including the severity and the complexity of her conditions, such as obscure chronic lower gastrointestinal bleeding that might necessitate additional time for accurate localization. Another factor including the delayed radiopharmaceutical uptake might occur, thus requiring an extended period of imaging to capture the desired information. Less than 10% of  $^{99m}\text{Tc}$ -labeled colloid remains intravascular after about 7 minutes (half-life approximately 2 minutes with normal liver function). Therefore, its extravasation ceased within less than 10 minutes after injection. However, there are no studies mentioning the duration of labelled colloid radioisotopes (as foreign bodies) remaining in extravasated body spaces, thus visualized on 24-hour images. Furthermore, individual patient factors, such as the presence of anatomical variations or physiological differences, could affect the distribution and detection of radioactivity, requiring a longer examination time for comprehensive evaluation. And last, the technical challenges, including difficulties in image acquisition or interpretation, might arise, necessitating extra time for meticulous analysis and localization.<sup>15</sup>

The  $^{99m}\text{Tc}$ -sulfur colloid is a commonly used radiopharmaceutical abroad, as well as in studies comparing its performance with  $^{99m}\text{Tc}$ -RBC. In the mentioned studies,  $^{99m}\text{Tc}$ -nanocolloid specifically has never been used for localizing gastrointestinal bleeding. Therefore, its diagnostic performance for localizing gastrointestinal bleeding still requires further studies. The  $^{99m}\text{Tc}$ -nanocolloid exits the stomach faster in gastric emptying studies compared to  $^{99m}\text{Tc}$ -sulfur colloid and  $^{99m}\text{Tc}$  tin colloid.<sup>14</sup> Some studies suggested that  $^{99m}\text{Tc}$ -nanocolloid escaped more rapidly from the initial injection site due to its smaller particle size.<sup>16-18</sup> Like other colloid-labelled radiopharmaceuticals used for gastric emptying studies, this radiopharmaceutical cannot be absorbed in the gastrointestinal tract or respiratory mucosa, has no effect on the gastrointestinal tract, and does not adhere to the gastrointestinal mucosa.<sup>19,20</sup> Therefore, what was visualized in this study was the expected extravasation of  $^{99m}\text{Tc}$ -nanocolloid.

The findings from further diagnostic tests were as follows. The first is abdominal

ultrasound, as a screening diagnostic tool before the patient underwent nuclear medicine examination, that revealed thickening of the colon wall in the right lower quadrant. Next is the colonoscopy, chosen after the bleeding sites were confirmed by nuclear medicine examination, that revealed signs of bleeding in the rectum, active bleeding in the descending colon, and bleeding in the ascending colon. Then the histopathological result from biopsy confirmed the diffuse chronic colitis.

Finally, the authors only had limited information about the examinations and treatments that had already been done before the patient came into Dr. Hasan Sadikin Central General Hospital. All the previous information was taken from several interviews and examination printouts from the previous hospitals.

## CONCLUSION

Examination of the localization of gastrointestinal bleeding using radionuclides is a non-invasive and very sensitive examination in Nuclear Medicine and Molecular Theranostics.  $^{99m}\text{Tc}$ -labeled colloid is still useful in gastrointestinal bleeding scintigraphy (GIBS), especially if the patient has symptoms of active bleeding. Bleeding status, acquisition techniques, and radiopharmaceutical are important factors to be considered to obtain conclusive and reliable information.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ACKNOWLEDGMENTS

The patient's family member had given written informed consent to implement the procedures and conduct scientific publication.

## AUTHORS CONTRIBUTION

HA mined data, processed ideas, prepared the manuscript, and explored the relevant literatures. All other authors contributed to the development of the ideas, manuscript editing and manuscript review. They also gave final approval and agreed to be accountable for all aspects of the work.

## LIST OF ABBREVIATIONS

ED: emergency department; RBC: red blood cell; SPECT: single photon emission computed tomography; CT: computed tomography, GIBS: gastrointestinal bleeding scintigraphy.

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