Thallium-201 single photon emission tomography after injecting an antimuscarinic agent compared with computed tomography for the diagnosis of recurrent colorectal cancer. Report of three cases

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Abstract

Thallium-201 chloride (^{201}TlCl) is frequently used for imaging of a variety of malignant tumors viz., thyroid, lung, brain, bone and breast, however in patients with colorectal cancer, its role is not well established. In this case report we present three patients with colorectal cancer recurrence, with inconclusive computed tomography (CT) findings while ^{201}TlCl single photon emission tomography (SPET) after injecting an anti-muscarinic agent, showed findings corroborating with the final diagnosis. Correlating CT with ^{201}TlCl-SPET findings, recurrence of the colorectal cancer was diagnosed in two cases; surgical treatment accordingly planned, confirmed the diagnosis. In the third case, CT was falsely positive while ^{201}TlCl-SPET was negative, compatible with the final diagnosis.

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Introduction

Colorectal cancer is the third most common cancer in men and women. Approximately 150,000 new cases of colorectal cancer and almost 56,000 deaths due to this malignancy occurred in the United States in the year 2005 [1]. It is the second most common cause of cancer death proceeded only by lung cancer [1,2], representing 10% of all cancer deaths in the US [2]. Early diagnosis of the primary cancer or of its local recurrence is the most important prognostic factor [1]. Routine post-treatment regular follow up includes orthoscopy, colonoscopy, computed tomography (CT), magnetic resonance imaging (MRI) and biochemical markers such as carcinoembryonic antigen (CEA). However, each one of these methods has its own limitations. Abnormally raised blood CEA levels may be present in the absence of disease recurrence, rendering the test non-specific [1]. Pelvic or abdominal CT may demonstrate a suspicious mass, but it is doubtful whether this mass represents tumor recurrence or a postoperative / post-radiation scar. According to many publications, positron emission tomography (PET) is superior to MRI for detecting recurrence, especially when only a tumor marker such as CEA is increased [1,3]. PET has also been reported to be useful in evaluating early response to treatment [4,5] but limited availability and also high cost, restrict its routine applicability. Surgical biopsy may be the final answer for the diagnosis of recurrence. A positive biopsy is highly predictive of recurrence; however, since it is impossible to sample the entire mass, a negative biopsy cannot absolutely exclude recurrence [1]. Accurate diagnosis of local recurrence of colorectal cancer is clinically very important in determining the appropriate treatment. Thallium-201 chloride (^{201}TlCl) with single photon emission tomography (SPET) has been used to detect the tumor viability in malignant diseases, including tumors of the thyroid, lung, brain, bone and breast, but in cases of colorectal cancer, the application of this technique is controversial [6,7]. Accumulation of ^{201}TlCl has been observed only in viable tumor tissue, reflecting the proliferating potential of malignant cells on the basis of Na^+- K^+ and ATPase activity [6], whereas no ^{201}TlCl uptake was seen in non-viable post-surgical or post-radiation scars [6].

In this case report we describe three cases of colorectal cancer, after the primary cancer was ablated by surgery, suspected to have recurrence. The CT findings in these patients were inconclusive, while the ^{201}TlCl-SPET study after injecting an antimuscarinic agent was consistent with histopathology findings.

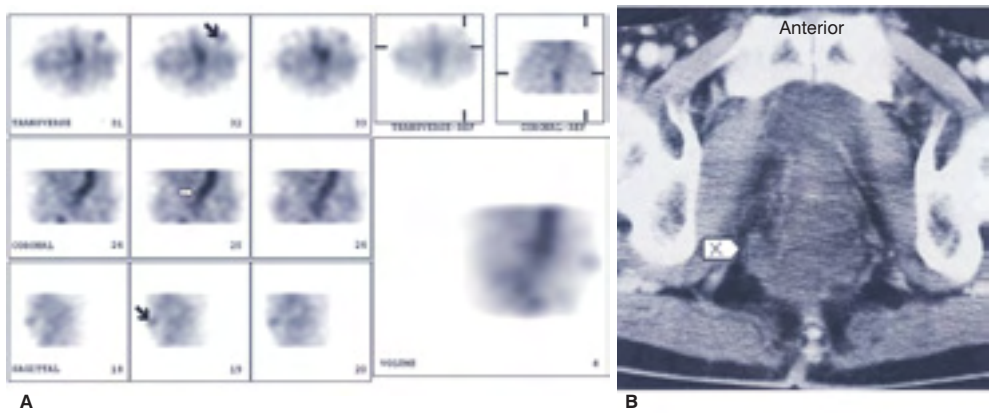

Figure 1. Inconclusive CT and highly positive ^{201}TlCl-SPET. ^{201}TlCl SPET (A) is showing a focus of activity in the left lower quadrant, corresponding to the site of colostomy (↘) and also areas of intensely increased activity along with the anatomical site of the rectum and sigmoid which are best seen in the coronal slices (➔). CT scan (B) reveals a mass lesion of undetermined origin in the anatomical site of the rectum (⌦)

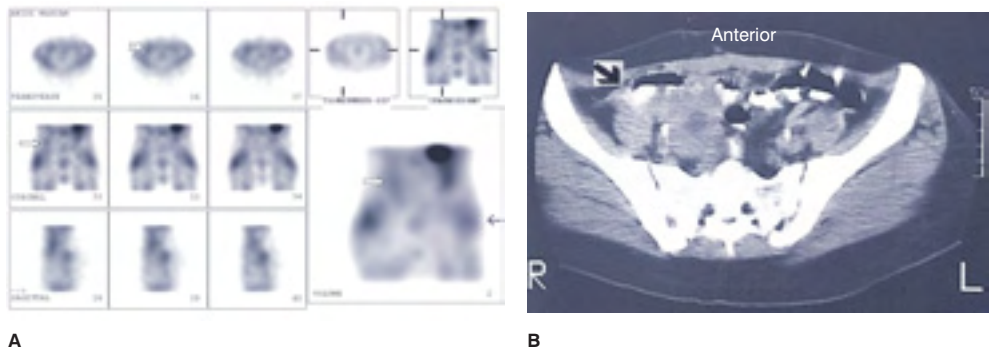

Figure 2. Inconclusive CT and faintly positive ^{201}TlCl-SPET. On the scintigraphic images (A), normal distribution of Tl-201 in the muscles of buttocks (🡐) and abdominal muscles (⇨) are seen. The faint increased radiotracer activity in the right lower quadrant is also observed in the site of previous surgery (⌦) corresponding to an irregular shaped mass delineated on the abdominal CT scan (B) but is roughly differentiated from normal uptake of the abdominal muscles

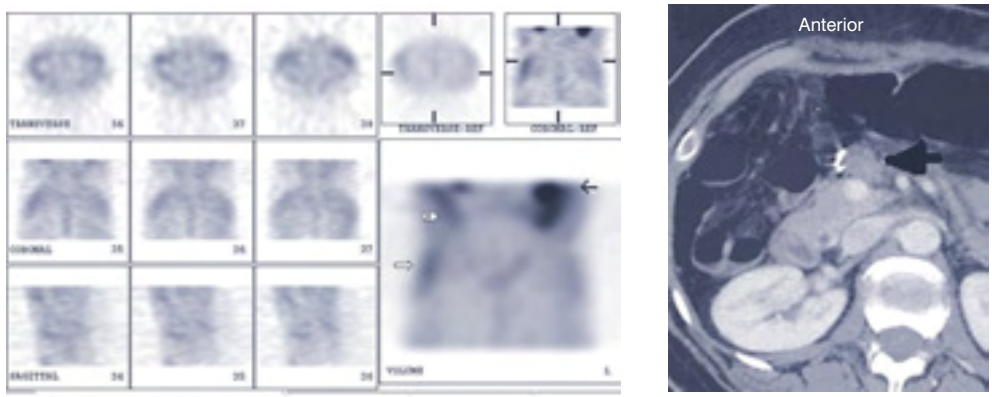

Figure 3. Inconclusive CT and negative ^{201}TlCl-SPET. Normal pattern of Tl-201 distribution in the kidneys (🡐), muscles of buttocks (⇨) and abdominal muscles (⌦) are noted. No abnormal focus of tracer activity is noted, corresponding to the mass delineated on CT images, indicating fibrosis or non-viable lesion

Description of the cases

^{201}TlCl-SPET imaging

Following an intra-muscular injection of 20 mg of hyoscine N-butyl bromide, ^{201}TlCl in a dose of 111 MBq was injected intravenously (iv) to all three patients. Imaging started 10 min later, using a dual detector system gamma camera SPET (ADAC Genesys Malpitas, CA, USA) coupled with a low energy general purpose (LEGP) collimator. Imaging was repeated 60 min after the injection. A symmetric 20% window was centered at 80 keV, and images were acquired into a 64×64 matrix through a 360° rotation with 40 sec per azimuth. Reconstruction was performed by standard back projection using Butterworth filter with a cut off: 0.35 and order: 10. Imaging was repeated 60 min after the injection. Criteria for positive findings included the presence of foci of increased tracer activity in the abdomen showing no displacement with time and also not appearing to be due to physiological excretion of the radiopharmaceutical or to vascular activity. All ^{201}TlCl-SPET images were interpreted by two experienced nuclear medicine physicians (Dr. Babak and Dr. Armaghan) who were blinded to the report of the CT images.

Patient 1 was a 64-year-old man who had undergone left colectomy seventeen months ago, for invasive poorly differentiated colorectal cancer of the rectosigmoid colon. He was referred to our Institute of Nuclear Medicine for evaluation of a mass in the rectum shown on the CT images but not differentiated from a post-operative fibrous tissue. Blood CEA levels were stable and normal during the last 12 months. ^{201}TlCl-SPET images showed a focus of moderately increased tracer uptake corresponding to the site of colostomy and another focus of intensely increased radiotracer uptake between the rectum and sigmoid (Fig. 1). Both foci showed increasing intensity from the 10th to the 60th min of the study, which was in-

terpreted as local recurrence of the disease. Despite chemotherapy, the patient died after 5 months. Recurrence of colorectal carcinoma in both the above mentioned regions was confirmed by post-mortem.

Patient 2 was a 26-year-old woman with a well-differentiated mucin-producing adenocarcinoma of the rectum and colon who had undergone multiple surgical operations ending 20 months ago in near total colectomy. CEA levels were abnormal and rising over the six months period between 18 to 12 months past. She was referred to Shariati hospital for a CT and a ^{201}TlCl-SPET scan. The CT scan showed an irregular mass-lesion of undetermined significance in the right lower quadrant of the abdomen, while the ^{201}TlCl-SPET scan revealed a mild abnormal uptake of the radiopharmaceutical at the site of the mass, which on the early views 10 min post injection, was roughly separated from the abdominal muscles. Consequently, on delayed views at 60 min post injection at the same site, mild increased uptake was noted (Fig. 2). Curative resection of the mass was performed 11 months ago and local recurrence of the tumor was histologically confirmed. Chemotherapy was also applied. Follow up studies with interval CT scanning and serial CEA measurements have shown no evidence of disease relapse in the past 11 months.

Patient 3 was a 63 year-old man who had undergone right colectomy and radiation treatment seven months prior to his referral to our Institute of Nuclear Medicine, two years ago. CT scan showed an apparent extra-luminal lesion in the right lower quadrant of the abdomen with minimal radiocontrast enhancement while ^{201}TlCl-SPET imaging showed no abnormal accumulation of the radiotracer in the abdomen even on delayed views at 60 min of the study (Fig 3). The CT finding was most likely due to post-operation/radiation fibrosis because serial CEA measurements remained normal and also no change was noted in the size and morphology of the mass on repeated radiocontrast-enhanced CT and in gadolinium-enhanced MRI during the past 20 months.

Discussion

Nowadays, PET is the modality of choice for the diagnosis and staging of colorectal cancer and for the differential diagnosis between a lesion and a scar [1]. PET is more accurate than CT and/or MRI in detecting local and distant metastasis; however it has a low specificity due to the normal excretion of radiotracer in the bowel [1], is expensive and is not available in some countries. ^{201}TlCl uptake is considered to reflect the regional perfusion and viability of the tumor cells [6]. Yukiharu et al (1998), in 22 patients have shown that ^{201}TlCl-SPET images had a sensitivity of 81.8%, a specificity of 90.9% and an accuracy of 86.4% for the diagnosis of suspected local recurrence of colorectal cancer [7]. However, ^{201}TlCl has some limitation such as low signal-to–noise ratio that can lead to low sensitivity in the diagnosis of local recurrence. Early ^{201}TlCl-SPET imaging and pre-medication with an anticholinergic agent, as used in our Institute, might decrease the excretion of ^{201}TlCl into the intestine and consequently improve the image quality [6,7]. In addition, multi-headed SPET camera systems, with higher sensitivity and better resolution can provide superior SPET images to those obtained with other systems [6,7].

In the present study postoperative fibrous tissue was the cause leading to a false positive CT scan (third case); while the ^{201}TlCl-SPET scan findings were true positive in each one of the three cases.

The cases we have presented, confirm the value of the ^{201}TlCl-SPET imaging following the injection of an anti-muscarinic agent in case of a doubtful CT scan for the diagnosis of post surgical recurrence of colorectal cancer and for decision making for a surgical or a conservative treatment, especially when PET is not available. This study is underway on more cases.

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