Comparison of gallium scan, computed tomography, and magnetic resonance in patients with mediastinal Hodgkin's disease

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Summary

Background: In patients with Hodgkin's disease, the use of gallium-67 scintigraphy (Ga-67) compared to conventional staging and restaging techniques is still controversial. In particular, in a combined modality treatment with chemotherapy and radiotherapy given in sequence, its role in detecting active disease after chemotherapy may be useful in planning the subsequent radiotherapeutic strategy.

Patients and methods: From March 1990 to September 1994, 125 patients with previously untreated histologically proven Hodgkin's disease were enrolled in two different prospective trials according to clinical stage. Staging procedures included Ga-67, chest-abdominal computed tomography (CT), and/or magnetic resonance (MR). All three tests were performed in 53 patients at staging and in 47 at restaging. Results of Ga-67 at staging were compared to conventional procedures or pathological findings. Results of Ga-67, CT scan, and MR at restaging were compared to disease outcome during the follow-up.

Results: At staging, Ga-67 showed lower sensitivity than CT and MR (90% vs. 96% and 100%, respectively) because of the number of false-negative images. Nevertheless, by using both CT and Ga-67 scan, the sensitivity is equal to that observed with MR (100%). At restaging, Ga-67 is superior to CT scan and equivalent to MR in detecting true negative patients (specificity: 98% vs. 45% vs. 92%).

Conclusions: As a single technique, Ga-67 scan cannot substitute for CT scan or MR in staging patients with Hodgkin's disease. Nevertheless, Ga-67 scan has an important role in defining complete remission after treatment and therefore in planning subsequent treatment. Considering the lower costs of CT scan plus Ga-67 ($320) versus MR alone ($810), the two tests may be considered procedures of choice in staging as well as in restaging patients with Hodgkin's disease.

Key words: computed tomography, gallium scan, magnetic resonance, mediastinal Hodgkin's disease

Introduction

The use of Ga-67 scan in detecting Hodgkin's disease has been described since 1969 [1]. Its value in documenting nodal disease above the diaphragm and its limited use in predicting abdominal disease have subsequently been confirmed [2]. Nevertheless, its role in staging and restaging patients with Hodgkin's disease compared to conventional techniques remains controversial. As a staging procedure, CT can give information about tumor size and sites of distribution [3, 4], but it does not reflect changes such as fibrosis, necrosis, and inflammation after treatment with chemotherapy and radiotherapy. A residual mediastinal abnormality on CT, for instance, does not necessarily mean persistence of active disease [5-7], therefore representing a common and difficult diagnostic problem. In this particular issue, MR is able to differentiate fibrosis from active disease in a high proportion of patients [8, 9], but the availability and cost of this technique has limited its routine use. In the present study, we evaluated the role of Ga-67 compared to conventional radiological imaging such as CT scan and MR in detecting initial disease extent as well as in the evaluation and management of mediastinal Hodgkin's disease after chemotherapy treatment. In addition, we evaluated the procedures of choice in terms of economic advantages.

Patients and methods

Patient characteristics

From March 1990 to March 1994, 125 previously untreated patients with histologically proven diagnosis of Hodgkin's disease admitted to the Istituto Nazionale Tumori of Milan, Italy, were studied before and after two different chemoradiotherapy programs delivered according to disease stage. We analyzed the results of the 53 patients with mediastinal Hodgkin's disease who underwent Ga-67, CT, and MR at staging and of the 47 patients who underwent all three procedures at the end of the chemotherapy program. The main characteristics of the patients who underwent all three techniques at staging are reported in Table 1. The treatment program consisted of four cycles of ABVD [10], followed by involved-field radiotherapy (IF) or subtotal nodal irradiation (STNI) in 77 patients with clinical stage (CS) I-IIA, whereas eight cycles of VEBEP (VP16, epirubicin, bleomycin, cytoxan, prednisolone) [11] followed by RT (IF) were given in 48 patients with CS IIIB-IV.
Table 1. Main characteristics of 53 patients in whom Ga-67, CT, and MR was performed at staging.

<table>
<thead>
<tr>
<th>No.</th>
<th>%</th>
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<tbody>
<tr>
<td>Total</td>
<td>53</td>
</tr>
<tr>
<td>Median age (yr)</td>
<td>28</td>
</tr>
<tr>
<td>CS I-II A</td>
<td>34</td>
</tr>
<tr>
<td>CS III-IV</td>
<td>19</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
</tr>
<tr>
<td>ABVD/RT</td>
<td>34</td>
</tr>
<tr>
<td>VEBEP/RT</td>
<td>19</td>
</tr>
<tr>
<td>Mediastinal disease</td>
<td>53</td>
</tr>
<tr>
<td>Bulky mediastinum</td>
<td>9</td>
</tr>
</tbody>
</table>

* VEBEP: VP16, etoposide, bleomycin, cytoxan, prednisolone.

Evaluation of Ga-67, CT scan, and MR

Before treatment, 125 Ga-67 scans, 110 chest CT scans, and 69 chest MRs were performed in 125 patients. All three tests, if initially positive, were also evaluated after the end of the chemotherapy program. To better define the role of Ga-67 compared to CT and MR in detecting mediastinal disease, we retrospectively analyzed the results of the three procedures in 53 and 47 patients who had all three tests performed before and after the chemotherapy program, respectively. At staging, to define false or true negativity of the tests, results were compared to each other and to clinical or histological findings. At restaging, a cutoff of less versus more than 12 months of complete remission was arbitrarily chosen to define false or true positive.

Ga-67 study was performed 48 hours after the intravenous injection of 185-259 MBq of 67-Ga citrate. A large-field-of-view digital SPET camera equipped with a medium energy collimator, with three energy peaks of 93, 184, and 296 keV, was used. Total-body images were supplemented, when necessary, by appropriate spot views of the mediastinum and lung region. In selected cases, a SPET study was acquired with a three-head gamma camera (120 projections per head 30 sec/step) on a matrix of 64 x 64. Images were reconstructed with the filtered back-projection method. Coronal and sagittal slices were obtained from the transaxial sections.

MR imaging was performed with a 1.5 Tesla Super Conductive Magnet (Siemens Magnetom). Spin echo sequences with cardiac gating were used in all cases. TI and T2 weighted images were acquired. TR depended on the heart frequency rate (600-900 msec for TI and 1200-2000 msec for T2 images) and TE varied from 17 to 90 msec. The area of interest was studied in axial and coronal planes with 6-8 mm thick slices and 10% of separation volume. Gadolinium injection was used only in selective cases.

CT was carried out using a Siemens Somaton 11 scanner. Ten contiguous cuts were obtained and intravenous contrast enhancement was administered in all cases.

Results

Table 2 reports the results in terms of true positivity and true negativity at staging as well as at restaging. Results for the 53 patients on whom all three tests were performed to evaluate mediastinal extent before therapy are as follows: Ga-67 was positive in 44 cases and negative in 9, while CT and MR were positive for active disease in 47 and 49 cases and negative in 6 and 4 cases, respectively. Five out of 9 negative Ga-67 scans resulted in false negatives compared to 2 out of 4 CT scans, whereas no false-negative imaging was observed with the MRs.

At restaging all three procedures were performed for 47 patients (Table 2). At the end of treatment, in 44 patients Ga-67 was negative for active disease, whereas abnormal Ga-67 uptake was observed in 3 patients. CT scan and MR were negative in 20 and 41 patients and positive in 27 and 6 cases, respectively. With a median follow-up of 42 months (range 20-72), 6 patients relapsed. At restaging, 2 patients tested positive in all three procedures, and new disease manifestations were documented after 6 and 8 months, respectively, from the end of therapy; 2 other patients had both a Ga-67 and an MR negative with a doubtful CT scan and relapsed after 10 and 2 months, respectively. Finally, 2 other patients, who were negative on all three tests, showed new lymphoma manifestations after 15 and 18 months. The Ga-67 scan was always positive at the time of relapse.

Table 3 outlines the comparison of the three techniques in terms of sensitivity, specificity, accuracy, positive (PPV) and negative (NPV) predictive values in evaluating mediastinal involvement both at staging as well as at restaging. At staging, MR alone was the most sensitive test in detecting mediastinal disease (sensitivity 100% and NPV 100%) followed by CT (96 and 67%) and Ga-67 (90 and 44%). It is important to note that when Ga-67 was combined with CT, the overall findings were superimposable on those observed with MR alone (100%). At restaging, Ga-67 proved the most accurate procedure in confirming mediastinal complete remission (specificity and PPV 98 and 67%) compared to CT (45 and 11%) and MR (91 and 33%).

To help define the procedure of choice further, we determined the cost benefit ratio of each technique. Con-
verted into US dollars, the expenses according to the Italian National Health Service for each procedure were as follows: Ga-67 scan: $164; chest CT scan $156; chest MR: $810. Therefore, the combined use of Ga-67 and CT amounted to a total of $320 and was able to achieve the 100% sensitivity of the more expensive MR.

Discussion

The ability to identify structural modifications in the body has dramatically improved in the last two decades with the development of noninvasive imaging techniques. Nevertheless, it is still difficult to discriminate between normal and disease-involved lymph nodes or between active disease and fibrosis in the presence of a residual mediastinal mass after treatment. In recent years, the use of Ga-67 scintigraphy in the management of patients with lymphomas has been the subject of controversies, mainly because of the poor predictive value of a negative finding when low doses of Ga-67 (about 111 MBq) and rectilinear scanner [12, 13] were used. However, in a retrospective study, Anderson et al. [14], reported a sensitivity of 97% and a specificity of 100% in the staging of Hodgkin's disease using high-dose Ga-67 and optimum imaging. The main clinical problem, however, is represented by the prediction of disease activity in residual mediastinal masses after therapy. In fact, although up to 64% of lymphoma patients may present a residual mass, only 18% of these patients will eventually relapse [15, 16]. This diagnostic issue has been reported since 1982 by different authors [4–6]. In particular, in planning the subsequent therapeutic strategy after first-line chemotherapy for patients with Hodgkin's disease, one important question is how to identify the procedure of choice in defining clinical complete remission. Israel in 1988 [15] comparing Ga-67 with CT scans and chest X-rays clearly demonstrated an advantage for Ga-67 scans in terms of specificity (95% vs. 57% vs. 55%). These results have also been confirmed by Karimjee et al. [17] with Ga-67 SPECT in 30 patients with mediastinal Hodgkin's disease.

More recently, MR has emerged as an accurate procedure in discriminating between active disease and necrosis or fibrosis [9] and represents a very accurate technique for restaging patients with mediastinal lymphoma. Subsequently, other authors have compared MR with Ga-67 and showed that both techniques are accurate in assessing the tumor activity in lymphoma mediastinal masses after therapy [18, 19]. At present, no findings comparing the Ga-67 scan, MR, and CT scan have been reported in homogeneously treated patients. To better define the clinical value of each procedure, we compared the Ga-67 scan, CT scan, and MR performed at staging as well as at restaging in patients with Hodgkin's disease entered in two different prospective trials. In our series, MR alone proved superior to the CT and Ga-67 scans when used alone in detecting mediastinal lymphoma at staging. Nevertheless, combining Ga-67 and CT scans, results were superimposable on those achieved with MR alone. At restaging, the Ga-67 proved as accurate as MR in confirming mediastinal complete remission, while the specificity of the CT scan was much lower.

Considering the high cost of MR, we can conclude that, as staging procedures, Ga-67 scan and chest CT scan performed concomitantly, are accurate tests to define supradiaphragmatic disease, allowing both functional and anatomic information. At restaging, in patients with a positive Ga-67 scan before treatment, the most accurate way to confirm clinical complete remission is to repeat the test after chemotherapy. In contrast, for patients with an initial negative Ga-67 scan (false negative) and a residual mediastinal mass at CT scan, an MR should also be performed to assess the persistence or the absence of active disease at the end of the planned therapy.

References


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