Evaluation of gastrointestinal involvement of Behçet’s disease by nuclear medical techniques

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To evaluate the value of nuclear medicine procedures in the diagnosis of gastrointestinal involvement of Behçet’s disease in asymptomatic patients, Tc-99m human immunoglobulin (HIG) and Tc-99m leucocyte (LC) whole body scintigraphies were performed on 30 patients with major symptoms of the disease. Comparison of the results with other diagnostic techniques showed that Tc-99m HIG whole body scanning can be a useful diagnostic aid before the disease becomes clinically active in the gastrointestinal system.

Key words: Behçet’s disease, Tc-99m human immunoglobulin, Tc-99m leukocytes

INTRODUCTION

Behçet’s syndrome is a multisystem disease which may also involve the gastrointestinal tract (GI). A fatal outcome may occur when the gastrointestinal system is involved.1

The exact cause of the disease is unclear and there is no universally accepted diagnostic test. In 1990 an international study group (ISG) agreed upon a set of criteria for the diagnosis of Behçet’s disease. According to ISG criteria, genital ulcers, eye lesions, positive pathergy test, skin lesions and oral ulcers are major symptoms of the disease; whereas subcutaneous thrombophlebitis, deep vein thrombosis, epididymitis, arterial occlusion and/or aneurysms, central nervous system involvement, arthralgia, family history, GI features and arthritis are named as minor symptoms.2

Being a systemic disease that can be seen in any organ of the body, Behçet’s disease is the concern of all specialties in medicine. Researchers give conflicting values for the involvement rate of the disease in certain organs and it also seems to be region dependent.3 Since the etiology of the disease is still unknown, clinicians rely on identification of symptoms with various techniques for diagnosis.

The use of nuclear medical techniques in Behçet’s disease is limited to only a few studies. Mudun et al.4 tried Tc-99m glucoheptonate scintigraphy in patients suffering from uveitis because of Behçet’s disease and concluded that the method was not sensitive enough for evaluating ocular involvement of the disease. Nuclear medical techniques were also used in a case of aggressive pulmonary involvement of Behçet’s disease.5 Keshavarzian et al.6 are among the first who used labeled leukocytes in Behçet’s disease and concluded that GI involvement of the disease is rare in the absence of symptoms. A case study showed the utility of In-111 leukocyte imaging for detecting active inflammatory bowel disease in a patient with documented Behçet’s vasculitis.7

Another group performed Tc-99m LC scintigraphy in patients with known Behçet’s disease to demonstrate vasculitic changes occurring in this disease. Their results showed that Tc-99m LC scintigraphy might be indicative of vascular pathology in Behçet’s disease.8 There is a combined radionuclide ventriculography and Doppler echocardiography study claiming that left ventricular function is altered in Behçet’s patients.9 All other studies related to the use of NM techniques in Behçet’s disease are about Tc-99m HMPAO brain scanning in neuro-Behçet disease.10–16

The aim of this study is to present a scanning technique for the determination of gastrointestinal involvement of...
Fig. 1  A–B. Normal appearance of Tc-99m HIG and Tc-99m LC. (4 hr)

Fig. 2  A patient with Behçet’s disease. Positive Tc-99m HIG (A) and negative Tc-99m LC (B) in GI tract (4 hr). Histopathology and immunopathology were considered to be abnormal.

Behçet’s disease in asymptomatic patients. For this purpose Tc-99m HIG and Tc-99m LC whole body scintigraphies were performed and the results were compared with those of other diagnostic techniques.

METHODS

Patients
For this study 30 patients with major symptoms of Behçet disease according to ISG criteria were chosen. They were being followed and under colchicine therapy in the Outpatient Clinic for Behçet’s disease of Ankara University Hospital. Ages ranged from 21 to 48 (mean: 38.1 ± 4.1 yrs). Sixteen were men and 14 women. The study was made 1–15 yrs (Mean 5.4 ± 1.8 yrs) after the first diagnosis of the disease. None of the patients reported flare up periods within the previous 3 months and none of them had specific gastrointestinal complaints.

Scintigraphy
A polyclonal HIG kit (Mallinckrodt Diagnostica, Petten, The Netherlands) was labeled with 740 MBq (20 mCi) Tc-99m pertechnetate in 2 ml saline. Each patient was intravenously injected with 370 MBq (10 mCi) of Tc-99m HIG. Whole body SPECT images were taken 2–4 h and 20–24 h after the injection. Abdominal spot images also were taken.

Two days later the same patients were scanned with Tc-99m hexamethylpropylene-amine oxime (HMPAO) labeled autologous leukocytes starting with 45 ml whole
Table 1  List of 13 patients showing positive Tc-99m HIG and negative Tc-99m LC scans

<table>
<thead>
<tr>
<th>Patients</th>
<th>Tc-99m HIG</th>
<th>Tc-99m LC</th>
<th>Colonoscopy</th>
<th>Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Transverse and ascending colon</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>Descendant and ascending colon</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>Multiple foci</td>
<td>–</td>
<td>–</td>
<td>+</td>
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<tr>
<td>4</td>
<td>Multiple foci</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>Multiple foci</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>Descending and transverse colon</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>Ascending colon</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>Ascending and descending colon</td>
<td>–</td>
<td>–</td>
<td>+</td>
</tr>
<tr>
<td>9</td>
<td>Multiple foci</td>
<td>–</td>
<td>–</td>
<td>+</td>
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<tr>
<td>10</td>
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<tr>
<td>11</td>
<td>Descending and ascending colon</td>
<td>–</td>
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<td>+</td>
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<td>12</td>
<td>Multiple foci</td>
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<td>+</td>
</tr>
<tr>
<td>13</td>
<td>Multiple foci</td>
<td>–</td>
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<td>+</td>
</tr>
</tbody>
</table>

RESULTS

Figures 1A and 1B show normal images of Tc-99m HIG and Tc-99m LC scintographies. Scintigrams were considered to be positive only if the early (2–4 h) image showed an area of increased accumulation in the gastrointestinal region that persisted or increased in intensity in the late (20–24 h) image either for Tc-99m HIG or for Tc-99m LC. Thirteen patients showed positive Tc-99m HIG (Fig. 2A) and negative Tc-99m LC (Fig. 2B) scans. Twelve of the 13 patients showed multiple uptake of the radiopharmaceutical, whereas one had only a single uptake (Table 1).

None of them had accumulation in the thyroid region. They all had negative colonoscopies. But histopathology and immunopathology of the biopsy specimens were considered to be abnormal. Two patients with positive Tc-99m HIG and positive Tc-99m LC scintographies had soon developed gastrointestinal symptoms. But they were not excluded from the study since they were asymptomatic when they were selected for this study (Table 2).

Percentage sensitivity compared to pathology was 15/15 (100%) with Tc-99m HIG and 2/15 (13.3%) with Tc-99m LC.

DISCUSSION

The aim of this study was to evaluate the extend of involvement of Behçet’s disease in patients who did not have any specific gastrointestinal complaints within three months before the study but had already been diagnosed with Behçet’s disease according to ISG criteria and who were under colchicine therapy.

Thirteen patients with positive Tc-99m HIG but negative Tc-99m LC and negative colonoscopy did not have any clinical GI symptoms. Diffuse cellular infiltration, capillary dilation, focal infiltration areas and active hyperemia were commonly observed in histopathological investigation of these patients’ specimens. Immunopathological investigation of the same specimens showed positive lymphocyte cell markers. Although these findings are not specific for Behçet’s disease, they may be considered as indicators of gastrointestinal abnormality and the presence of inflammation.18,19 The regions of positive Tc-99m HIG uptake in the scintographies were not all in the positions where biopsy specimens were taken. This can be explained by thinking that there is a diffuse change in the submucosal region of the gastrointestinal tract in the asymptomatic period of Behçet’s disease. This result is in agreement with the finding of Liberatore and Clemente who observed that “Tc-99m IgG accumulated in joints which were clinically uninvolved,” but the histology of these joints was not reported.21 Since the changes occurring in Behçet’s disease are usually in the submucosal region of the GI tract; it is not always possible to observe them by colonoscopy.

Abdominal activities observed in the images were not considered as free peristalsis because the in vitro quality controls showed that percentage labeling was
always above 95% and almost no radioactive accumulation was observed in the thyroid region. Since these foci of increased accumulation did not move with time and persisted until the next day, we have excluded the possibility of physiological uptake of this radiopharmaceutical.

GI symptoms can be seen at any stage of Behçet's disease but it is quite rare for it to occur before the major symptoms. Patients may complain of fever, vomiting, diarrhea or rectal bleeding, but the symptoms are usually so slight and at such long intervals (sometimes years) that the patient and the clinician may be unaware of GI involvement of the disease. It may sometimes be life threatening. The prevalence of GI Behçet's disease was reported to be very low by various investigators, but in our study group it turned out to be quite high, which may be attributed to the capability of Tc-99m HIG scintigraphy in showing involvement of the disease in the asymptomatic period.

Although the mechanism of accumulation of Tc-99m HIG is not clear, the proposed mechanisms are: exudation of plasma proteins through a leaking capillary bed, binding to bacteria, specific trapping of IgG by Fc receptors of inflammatory cells, polymerization of IgG and binding of IgG to monocytes. The reason for Tc-99m HIG uptake of involved organs in Behçet's disease may be a combination of some of these mechanisms because it is an autoimmune disease. Determination of the exact mechanism of localization for this radiopharmaceutical may contribute to discussions about the etiology of the disease.

**CONCLUSION**

It is concluded that Tc-99m HIG scanning is a useful test in determining the extent of gastrointestinal involvement of Behçet's disease in patients who have already been diagnosed with cardinal manifestations of the disease but are asymptomatic in terms of gastrointestinal symptoms.

**REFERENCES**


