CONCISE REPORT

Gallium-67 SPECT scintigraphy may be useful in diagnosis of temporal arteritis

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Background: Temporal arteritis (TA) is a common syndrome in the elderly, consisting of persistent pain in the temporal area of the skull, jaw claudication, sudden visual loss, high erythrocyte sedimentation rate, and tenderness on palpation in the temporal area. The diagnosis of this condition is relatively straightforward when the typical symptoms and a positive temporal artery biopsy are present. However, only half of the patients have a positive temporal artery biopsy. Other diagnostic procedures, such as colour Doppler sonography or superficial carotid artery angiography which have been proved to be useful for the diagnosis of TA, do not discriminate between inflammatory and non-inflammatory temporal artery disease and may be helpful only in experienced hands. Gallium-67 (^{67}Ga) planar scan was reported to be useful in the diagnosis of the disease. Quantitative ^{67}Ga single photon emission computed tomography (SPECT) may raise the accuracy of the diagnosis.

Objective: To investigate the effectiveness and usefulness of ^{67}Ga SPECT scintigraphy in the diagnosis of TA.

Methods: Nine patients (five male, four female) and six controls were included in the study. All of them received 8–10 mCi ^{67}Ga intravenously 48 hours before the scan. ^{67}Ga uptake ratios were calculated on transaxial and coronal slices.

Results: All patients showed increased uptake in the temporal area of the skull compared with controls.

Conclusion: The data suggest that ^{67}Ga skull SPECT may be useful in the diagnosis of TA, especially if the uptake ratio in the area of interest is calculated. Further studies are needed to confirm these data.

Giant cell (temporal) arteritis (TA) is vasculitis of unknown origin occurring most frequently in the elderly. It usually affects large and medium sized vessels, with a predisposition to the extracranial branches of the carotid arteries. TA is diagnosed clinically. The American College of Rheumatology requires three of the following five criteria to be met in order to establish the diagnosis: age >50 years, new onset of headache, temporal artery tenderness or decreased pulse, raised erythrocyte sedimentation rate, and histology findings.¹ Temporal artery biopsy is the “gold standard” test for the diagnosis of TA.² As the pathological lesion is segmental and localised to some fragments of the artery, the inflammatory lesion is often missed, and in some series normal biopsies have been reported in more than 40% of the patients.³ Additionally, some patients are reluctant to undergo surgical procedures.

Colour Doppler sonography and positron emission tomography (PET)^{4–5} were recently described as useful in the diagnosis of TA, but these observations have not yet been confirmed, and the high cost of a PET procedure restricts its wide use.

Gallium-67 citrate (^{67}Ga) scintigraphy is widely used in the diagnosis and follow up of infections, lymphomas, and granulomatous diseases.^{6–7}

Gallium citrate binds to the transferrin receptor expressed on the surface of activated macrophages and therefore concentrates in the areas of inflammation.⁸ Immunohistochemical analyses have shown that monocyte derived macrophages and CD4+ T lymphocytes dominate in TA lesions and express on their surface receptors to HLA-DR, transferrin, and several interleukins.⁹ Therefore, ^{67}Ga scintigraphy may be useful in the diagnosis of TA.

Genereau *et al* have recently demonstrated increased ^{67}Ga uptake in the temporal area of patients with TA by calculating the ratio between two regions of interest: the temporal region and the control zone in the parietal region.¹⁰ In their work they used a planar scan of the skull for calculation.

We present here a study whose objectives were to assess the contribution of a ^{67}Ga single photon emission computed tomography (SPECT) scan to the accuracy of diagnosis of TA by visualisation of the inflamed temporal artery.

PATIENTS AND METHODS

Patients

Nine consecutive patients with TA who were admitted to the rheumatology outpatient clinic of Barzilai Medical Centre, Ashkelon, Israel between 1999 and 2000 were included in the study. All the patients fulfilled the American College of Rheumatology criteria for TA.¹

Exclusion criteria included any other known or clinically evident inflammatory or granulomatous disease which might enhance ^{67}Ga uptake in the temporal area, or known allergic reaction to gallium citrate.

Controls

The control group comprised six patients who underwent ^{67}Ga scintigraphy in the nuclear medicine department of Barzilai Medical Centre in the same period for febrile disease.

 ^{67}Ga SPECT scan

All the patients underwent a ^{67}Ga SPECT scan, which was performed on a dual head helix gamma camera two days after intravenous injection of 8–10 mCi of gallium citrate. Data were collected on 64×64 matrices with acquisition time 20–25 sec per frame. An Mz-type filter was used for reconstruction of the acquisition data. The ^{67}Ga uptake ratio—temporal bone region/bone out of temporal area (TR/bone)—was estimated on transaxial and coronal slices after SPECT scan reconstruction. For each patient and control, calculations of both temporal areas were made.

Abbreviations: FDG, fluorodeoxy-glucose; PET, positron emission tomography; SPECT, single photon emission computed tomography; TA, temporal arteritis

Table 1 Clinical data of the patients and results of ^{67}Ga uptake ratio

Patient No	Age/sex	Clinical features	ESR (mm/1st h)	TA biopsy	Prednisone treatment	^{67}Ga uptake ratio			
						Coronary vein		Transaxial vein	
						Left	Right	Left	Right
1	54/F	Headache, both TA tenderness, shoulder pain, legs claudication	70	Yes, right TA neg	60 mg, 48 hours before ^{67}Ga scan	1.28	1.31	1.23	1.24
2	69/M	Headache, left TA tenderness, fever, jaw claudication	65	Yes, right TA pos	60 mg, 48 hours before ^{67}Ga scan	1.42	–	1.23	–
3	73/M	Headache, left TA tenderness, jaw claudication	60	Yes, left TA neg	No	1.44	1.52	1.23	1.51
4	66/F	Headache, sudden left eye blindness, left TA tenderness, fever	100	Yes, left TA neg	100 mg, 48 hours before ^{67}Ga scan	1.42	1.42	1.23	1.12
5	81/M	Headache, both TA tenderness, shoulder pain, fever, jaw claudication	68	Yes, left TA neg	40 mg, 72 hours before ^{67}Ga scan	1.88	1.76	1.40	1.29
6	87/M	Headache, both TA tenderness, shoulder pain, jaw claudication	72	Yes, right TA neg	20 mg, 24 hours before ^{67}Ga scan	1.47	1.57	1.71	1.35
7	81/M	Headache, right TA tenderness, shoulder pain, fever	80	No	60 mg, 48 hours before ^{67}Ga scan	1.41	1.45	1.27	1.25
8	70/F	Headache, left TA tenderness, shoulder pain	75	No	60 mg, 48 hours before ^{67}Ga scan	1.57	1.51	1.25	1.36
9	55/F	Headache, right TA tenderness, shoulder pain	56	No	No	1.25	1.32	1.24	1.33
Mean (SD)	70.11 (12.31)		71.8 (12.8)			1.47 (0.16)		1.31 (0.14)	

TA, temporal arteritis.

Figure 1 ^{67}Ga skull SPECT. Transaxial (A1, A2) and coronal (B1, B2) slices. In the circles can be seen temporal artery regions of right (A1, B1) and left (A2, B2) sides of the skull with increased ^{67}Ga uptake.

Statistical analysis

Results are presented as mean and SD. The mean quantitative values for the groups were compared using the two tailed Student's *t* test. A value $p < 0.01$ was considered significant.

RESULTS

Fifteen patients participated in the study—nine with TA and six controls. The patients diagnosed as TA showed typical clinical features of this disease such as new onset headache in the temporal area, temporal artery tenderness on palpation—unilateral in six and bilateral in three, and an erythrocyte sedimentation rate above 50 mm/1st h. Four patients had jaw claudication, while six were found to have polymyalgia rheumatica. One patient was admitted to the hospital with sudden blindness in one eye as the presenting symptom of TA. Six of the nine patients underwent temporal artery biopsy—five after a ^{67}Ga scan and one before. In this latter patient the ^{67}Ga uptake ratio of the biopsied side was not calculated (patient No 2) in order to avoid false results. Only one patient showed positive results on biopsy, and in the five other patients the results of biopsy were negative, probably because of prednisolone treatment which was given 4–5 days before biopsy. Prednisolone treatment was introduced before performing a ^{67}Ga scan in seven patients. Table 1 presents the clinical data of the patients.

The group of controls comprised six patients who underwent ^{67}Ga scanning because of febrile disease. The mean (SD) age of these patients was 64.4 (25.7), and their mean (SD) erythrocyte sedimentation rate was 45 (13.3) mm/1st h. None of the control patients had headache in temporal areas, none had shoulder pain.

All the nine patients showed an increased uptake in both temporal areas of the skull in comparison with control patients. The calculated ^{67}Ga uptake ratio in the patients was

Figure 2 Three dimensional volume cine pictures show increased ^{67}Ga uptake in the temporal regions (arrows).

1.47 (0.16) in the coronary view and 1.31 (0.14) in the transaxial view. In control patients the calculated ^{67}Ga uptake ratios were 1.11 (0.06) and 1.04 (0.09), respectively. The results showed a significant difference ($p < 0.001$). Figures 1 and 2 show examples of increased ^{67}Ga uptake in the temporal area.

DISCUSSION

The diagnosis of TA is mainly based on clinical criteria and although temporal artery biopsy may confirm the diagnosis, it is not instructive in many cases. There is a genuine need for a non-invasive procedure which may contribute to the diagnosis and follow up of patients with TA. Scintigraphy is a non-invasive diagnostic procedure that may eventually help the clinician to diagnose and localise the vasculitic process.

^{67}Ga is a commonly used agent for the imaging of inflammation because of its ability to accumulate non-specifically in inflamed areas as a metal-transferrin complex, followed by further binding to transferrin receptors.

^{67}Ga scintigraphy has been performed in patients with polyarteritis nodosa, Wegener's granulomatosis, and Kawasaki disease.¹¹⁻¹³ Interestingly, in Takayasu's arteritis, which is a large vessel vasculitis, ^{67}Ga scintigraphy has been widely used. Hahn *et al* reviewed 31 patients with Takayasu's arteritis over a 15 year period. A ^{67}Ga SPECT study was done in 16 of them and found positive in 12.¹⁴ Moreover, ^{67}Ga scintigraphy was a helpful tool in assessing disease activity during the treatment.¹⁵

In recent years, PET has been introduced for the imaging of vasculitic processes. Blockmans *et al* performed fluorodeoxyglucose PET (FDG-PET) in patients with polymyalgia

rheumatica/TA. They found increased FDG uptake in the tibial arteries and thoracic large vessels in 19/25 (76%) patients. However, high uptake of FDG in the brain and the relatively small diameter of temporal arteries prevented direct investigation of these arteries.⁵

We have demonstrated significantly increased ^{67}Ga uptake in the temporal area of the skull in patients with TA in comparison with control patients. Moreover, all patients showed increased ^{67}Ga uptake in both temporal areas, despite the clinical picture of unilateral process in some patients.

SPECT is a method that offers the advantage of cross sectional imaging as compared with conventional planar imaging. Further, computer aided, three dimensional reconstruction of SPECT data helps to make measurements directly in the zone of interest, to obtain a higher image contrast and a clear cut signal of the investigated area. Therefore, the anatomical description of the process is better. In our work after the performance of skull SPECT and further three dimensional reconstruction of the data, we chose for calculation the particular slice of temporal artery anatomical area. It helped us to localise the vasculitic process and contributed to the accuracy of measurements.

Despite treatment with prednisolone before ^{67}Ga scintigraphy in eight of nine patients, all our patients had positive uptake suggestive of active TA.

Therefore, we suggest that the 48 hours lag time which is needed for realisation of a gallium scan does not interfere with prednisolone treatment and if TA is strongly suspected on clinical grounds, the treatment should be started immediately.

In conclusion, ^{67}Ga skull SPECT seems to be a useful non-invasive technique in the investigation of patients with TA. We are aware of the limitations of our study, which included a small number of patients. It may be argued that the low incidence of histological findings typical of TA does not allow an appreciation of the accuracy of this method. However, this is the first study which aimed at clarifying the contribution of ^{67}Ga SPECT scan to the diagnosis of TA. These preliminary results are encouraging and suggest a role of ^{67}Ga SPECT scan in the evaluation of patients with TA.

Further studies in larger groups of patients are needed to confirm these data.

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