Absence of gallium uptake in multicentric Castleman's disease of plasma cell type

Multicentric Castleman's disease (MCD) of plasma cell type is a reactive lymphoproliferative disease. While ^{67}Ga scanning is useful in the detection of malignant lymphomas, its role in reactive lymphadenopathy is unknown. We report the absence of ^{67}Ga uptake in three patients with MCD of plasma cell type and present a review of the English literature on this condition.

Castleman's disease is an atypical lymphoid hyperplasia that can be localized or multicentric, with the latter form being much less common. Multicentric Castleman's disease (MCD) of plasma cell type is characterized by systemic upset, generalized lymphadenopathy, hepatosplenomegaly and various laboratory abnormalities.[1] MCD may be complicated by malignant lymphomas, vascular neoplasms such as Kaposi's sarcoma, follicular dendritic cell tumor and plasmacytoma.[1] Rarely, concomitant Kaposi's sarcoma and glomerulonephritis have been reported.[2] The clinical course of MCD is variable and ranges from a chronic, indolent disease to a rapidly fatal disease. The terminal events are either infections or development of malignant lymphoma.

Gallium scanning has been shown to be useful in the detection of both Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL).[3] However, there are very few data on gallium uptake in Castleman's disease. In this report, we discuss the use of ^{67}Ga scanning in MCD and present a review of the English literature from 1966 onwards.

Three patients with MCD of plasma cell type were studied (Table 1). They were not receiving steroids or iron supplementation during the study. ^{67}Ga scintigraphy was performed with a dual-head large rectangular field-of-view gamma camera (SP-6D Helix; Elscint, Haifa, Israel) equipped with a medium-energy parallel-hole collimator (HPC-5; Elscint). Multiple localized anterior and posterior views of the chest and abdomen were obtained 48-72 hours after injection of 260MBq (7 mCi) of ^{67}Ga citrate to obtain whole-body images for planar imaging studies. Further planar images of the torso were obtained up to day 7. Single photon emission computed tomography (SPECT) images of neck, thorax, abdomen and pelvis were taken 3-5 days after injection of ^{67}Ga. Tomographic images were displayed in standard transaxial, coronal and sagittal planes. ^{67}Ga scanning did not reveal abnormal uptake in any of the three patients (Figure 1: a,b,c). In comparison, a patient with *de novo* high grade NHL showed intense ^{67}Ga uptake in the corresponding sites of lymphadenopathy (Figure 1: d,e,f).

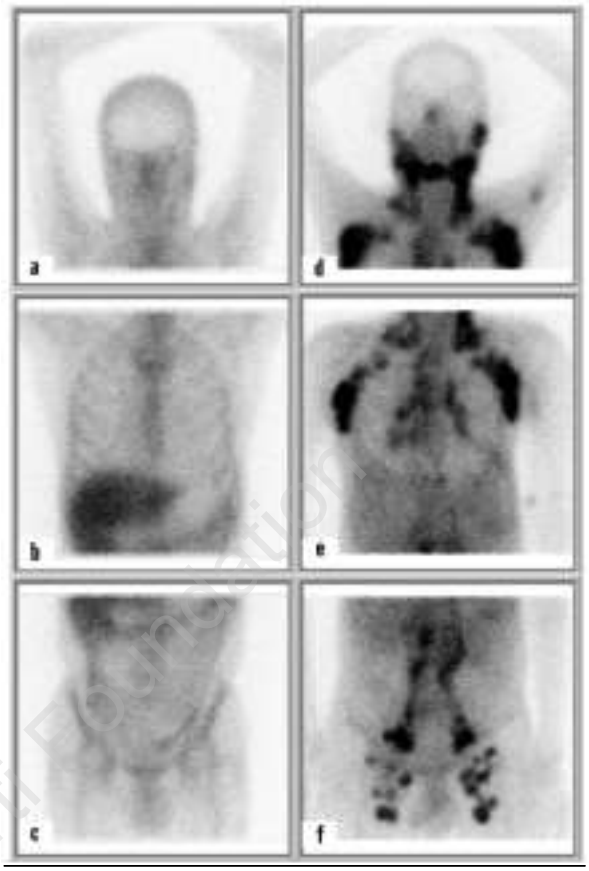

Figure 1.
a, b, c: planar imaging on day 2 after ^{67}Ga injection showing absence of abnormal ^{67}Ga uptake in a patient with multicentric Castleman's disease of plasma cell type presenting with generalized cervical, axillary and inguinal lymphadenopathy.
d, e, f: planar imaging on day 2 after ^{67}Ga injection of a patient with diffuse large B cell lymphoma presenting with cervical, submandibular, axillary, mediastinal, para-aortic and inguinal lymphadenopathy.

^{67}Ga scanning is useful for the initial staging of patients with malignant lymphomas, both HD and NHL, having a high sensitivity and specificity.[3] In our study, the sensitivity and specificity of ^{67}Ga scanning was enhanced by using a higher dose of ^{67}Ga and SPECT scanning techniques.[3,4] The relatively high sensitivity of ^{67}Ga scans in histologically aggressive (Working Formulation D to J) NHL[3] makes them potentially useful in the early detection of development of malignant lymphoma in atypical lymphoproliferative disorders, since a whole body image including all lymph node areas is included. In a study of HIV positive patients with generalized lymphadenopathy, individuals with grade 2 or 3 ^{67}Ga uptake in the lymph nodes had tuberculosis or

Table 1. Multicentric Castleman's disease.

Patient	*sex*	*age*	*clinical findings at diagnosis*	*histology*	*HIV status*	*years of diagnosis*	*complication*	*current LN status*
WF	F	54	gen LN, polyclonal HG	plasma cell	N	1994	GN, KS, LN	Cx, SCF, axilla
WKW	M	60	gen LN, polyclonal HG	plasma cell	N	1987	LN	Cx, SCF, axilla
YHP	M	60	high ESR, polyclonal HG, no LN	plasma cell	N	1991	gen LN	Cx, axilla, groin

M: male; F: female; gen: generalized (cervical, supraclavicular, axillary and groin lymphadenopathy); HG: hypergammaglobulinemia; LN: lymph node;ESR: erythrocyte sedimentation rate; GN: glomerulonephritis; KS: Kaposi's sarcoma; Cx:cervical; SCF: supraclavicular; HIV: human immunodeficiency virus serology status; N: negative; gen LN: generalized lymphadenopathy; Cx: cervical; SCF: supraclavicular; N: neg.

lymphoma transformation, while those without gallium uptake had reactive follicular hyperplasia, illustrating the specificity of ^{67}Ga uptake in lymphoma.[5]

In a review of the English literature from 1966 onwards, there have been three reports of positive ^{67}Ga uptake in Castleman's disease.[6-8] Of these, one case had MCD of plasma cell type.[6] However, biopsy of the ^{67}Ga avid pelvic mass showed necrotic tissue with multiple fibrinous adhesions throughout the abdomen. These features are atypical of Castleman's disease and indicate superimposed infection of the lymph node. The other two patients with positive ^{67}Ga uptake had hyaline vascular histology.[7,8] This suggests that different histology may cause inherent differences in ^{67}Ga uptake. Similarly, with CT imaging, contrast enhancement has been reported to occur in Castleman's disease of hyaline vascular histology but not in the plasma cell type.[9]

In the present study, none of the three cases of MCD of plasma cell type showed ^{67}Ga uptake. After being administered intravenously, ^{67}Ga is largely bound to transferrin and the transferrin receptor (CD71) appears to be the major mechanism by which tumor cells accumulate ^{67}Ga.[3] Transferrin receptor is expressed in activated or proliferating lymphocytes and thus is much more frequently expressed in high grade lymphomas than in low grade ones.[10] This may account for the higher sensitivity of ^{67}Ga imaging in high grade lymphoma and the absence of ^{67}Ga uptake in our patients who may have had a low density of activated lymphocytes.

Our preliminary data suggest that ^{67}Ga uptake does not occur in MCD of plasma cell histology. This requires further validation in larger studies including cases of both plasma cell type and hylaline vascular type. If our findings are validated, ^{67}Ga might be of value in the early detection of lymphoma complicating Castleman's disease.

Chor Sang Chim, Frankie Pak Tat Choi, Gaik Cheng Ooi,° Yok Lam Kwong*

University Departments of Medicine and Radiology,° Queen Mary Hospital, University of Hong Kong; Hong Kong and Department of Nuclear Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong*

Correspondence: James C.S. Chim, M.D., Senior Medical Officer, Department of Medicine, Queen Mary Hospital, Hong Kong. Phone: international +0852-28554776 – Fax: international +0852-29741165 - Email: jcschim@hkucc.hku.hk

Key words: ^{67}Gallium, Castleman' disease.

References

1. Herrada J, Cabanillas F, Rice L, Manning J, Pugh W. The clinical behavior of localized and multicentric Castleman's disease. Ann Intern Med 1998; 128:657-62.
2. Chim CS, Lam KY, Chan KW. Castleman's disease with Kaposi's sarcoma and glomerulonephritis. Am J Med 1999; 107:186-8.
3. Van der Wall H, McLaughlin AF, Southee AE. Gallium scintigraphy in tumor diagnosis and management. In: Murray IPC, Ell PJ. Nuclear medicine in clinical diagnosis and treatment. 2nd Ed. New York: Churchill Livingstone, 1998: 813-29.
4. Tumeh SS, Rosenthal DS, Kaplan WD, English RJ, Holman BL. Lymphoma: evaluation with Ga^{67} SPECT. Radiology 1987; 164:111-4.
5. Podzamczer D, Ricart I, Bolao F, et al. Gallium-67 scan for distinguishing follicular hyperplasia from other AIDS-associated diseases in lymph nodes. AIDS 1990; 4:683-5.
6. Stansby G, Hilson A, Hamilton G. Gallium scintigraphy in the diagnosis and management of multifocal Castleman's disease. Br J Radiol 1991; 64:165-7.
7. Wahner HW, Goellner JR, Hoagland HC. Giant lymph node hyperplasia resembling abdominal abscess on gallium scan. Clin Nucl Med 1978; 3:19-21.
8. Kinoshita T, Ishii K, Mori Y, Naganuma H. Castleman's disease in the anterior neck: the role of Ga^{67} scintigraphy. Clin Nucl Med 1996; 21:626-8.
9. Yamashita Y, Hirai T, Matsukawa T, Ogata I, Takahashi M. Radiological presentations of Castleman's disease. Comput Med Imaging Graph 1993; 17:107-17.
10. Esserman L, Takahashi S, Rojas V, Warnke R, Levy R. An epitope of the transferrin receptor is exposed on the cell surface of high-grade but not low-grade human lymphomas. Blood 1989; 74:2718-29.