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. MCD may be complicated by malignant lymphomas, vascular neoplasms such as Kaposi’s sarcoma, follicular dendritic cell tumor and plasmacytoma. Rarely, concomitant Kaposi’s sarcoma and glomerulonephritis have been reported.

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). 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).

$^{67}$Ga scanning is useful for the initial staging of patients with malignant lymphomas, both HD and NHL, having a high sensitivity and specificity. 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. The relatively high sensitivity of $^{67}$Ga scans in histologically aggressive (Working Formula-
Lymphoma transformation, while those without gallium uptake had reactive follicular hyperplasia, illustrating the specificity of 67Ga uptake in lymphoma. In a review of the English literature from 1966 onwards, there have been three reports of positive 67Ga uptake in Castleman's disease. Of these, one case had MCD of plasma cell type. However, biopsy of the 67Ga 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 67Ga uptake had hyaline vascular histology. This suggests that different histology may cause inherent differences in 67Ga 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.

In the present study, none of the three cases of MCD of plasma cell type showed 67Ga uptake. After being administered intravenously, 67Ga is largely bound to transferrin and the transferrin receptor (CD71) appears to be the major mechanism by which tumor cells accumulate 67Ga. 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. This may account for the higher sensitivity of 67Ga imaging in high grade lymphoma and the absence of 67Ga uptake in our patients who may have had a low density of activated lymphocytes.

Our preliminary data suggest that 67Ga 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 hyaline vascular type. If our findings are validated, 67Ga might be of value in the early detection of lymphoma complicating Castleman's disease.

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References