

*Case Report*

## **Pattern of Calcification on CT and FDG-PET of a Rare Perineural Mantle Cell Lymphoma: A Potential of Non-Histological Imaging Marker**

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### **ABSTRACT**

The presence of calcification in a particular FDG-avid soft tissue lesion may at times present uncertainty regarding the clinical course of the disease pathology. Calcific deposits are not specific for either benign or malignant aetiologies (Brant et al., 2010). Altered glucose metabolism with associated calcification may underpin underlying aggressive pathophysiology with necrosis as sequelae. Mantle Cell Lymphoma (MCL) is a subtype of non-Hodgkin's lymphoma. It is a rare B-cell NHL that is prevalent in men over the age of 60. The disease may be aggressive but it can also behave in a more indolent fashion in some patients. MCL comprises about 5% of all NHLs. The disease is called Mantle Cell Lymphoma because the tumour cells originally come from the 'mantle zone' of the lymph node (Zhou et al., 2004). Pretreatment Hodgkin's lymphoma with calcification may masquerade as other second primary pathologies, e.g. extrasosseous osteosarcoma or myositis ossificans (Apter et al., 2002; Korek-Amorosa et al., 1974). A calcified perineural lymphoma prior to treatment is exceedingly rare and calcification usually occurs one to five years after chemotherapy or radiation therapy with an incidence of 2% (Apter et al., 2002). This case documents how the manifestation of a rare malignant perineural mantle cell lymphoma may be indistinguishable from other pathological entities based on its pattern of distribution in a combined FDG- PET-CT study.

*Keywords:* Mantle Cell Lymphoma, PET-CT, FDG, calcification, perineural

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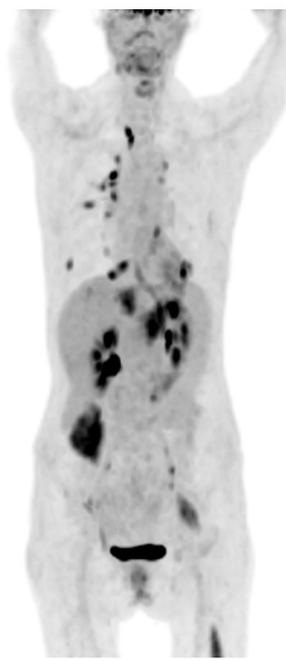
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### **CASE REPORT**

A 71-year-old female, who presented with chronic cough with associated dyspnea and constitutional symptoms, underwent 18F-FDG-PET-CT for investigation of a

suspicious pulmonary nodule found on a CT scan. Her symptoms persisted in spite of antibiotic treatment. On examination, she looked pale and had pulmonary rhonci on auscultation. Biochemical results were unremarkable. FDG-PET-CT revealed numerous FDG-avid pulmonary nodules, FDG-avid nodal disease above and below the diaphragm and extra-nodal disease in the left thigh soft tissue with suspicion of stage IV lymphoma (Figure 1). The left thigh FDG avidity (standardised uptake value: SUV of 14.5) was associated with dystrophic peripheral rim calcification (Figure 2). Biopsy of the lymph node and the left thigh lesion confirmed a diagnosis of Mantle Cell Lymphoma (MCL)

Peripheral rim calcification of an FDG-avid lesion in a florid lymphomatous disease may masquerade as other concomitant second pathologies e.g. extrasosseous sarcoma or a benign lesion e.g. myositis ossificans. There are two types of CT pattern of calcification: dystrophic and metastatic. Typically, in an aggressive tumour, associated dystrophic calcification commonly results from necrosis in an unchecked altered cellular glucose metabolism (Apter et al., 2002). Such infarction typically occurs in histologically aggressive lymphoma e.g. Mantle Cell (Korek-Amorosa et al., 1974; Ishikawa et al., 1999). This is likely to represent a dystrophic process when bulky tumours outgrow their blood supply. In this case, the untreated lymphomatous deposit in the perineural region featuring as peripheral rim calcification indicated the likelihood of a malignant feature on the CT scan (Henry, 2012). On the one hand, the dystrophic calcific deposition in MCL is peculiar to its aggressive nature as opposed to the now common calcification in post-treatment lymphoma. On the other hand, the basis of metastatic calcification manifested by a raised serum calcium level is not demonstrated in this patient (Apter et al., 2002).



*Figure 1.* Multiple image projection (MIP) PET image showing numerous FDG-avid nodal diseases above and below diaphragm with an extranodal avid disease in the left mid-thigh.



*Figure 2.* Coronal non-contrasted CT and coronal fused PET-CT images showing an elongated FDG-avid mid-thigh soft tissue lesion (SUVmax: 14.5; value>2.5 is significant) with adjoining dystrophic peripheral rim calcification (arrowed).

The dystrophic rim calcification shown on the CT scan with FDG avidity has been described in myositis ossificans, with a potential resemblance to the features shown in this case. The calcification is the result of mineralisation of the mature lamellar bone, which occurs after 4 to 6 weeks of trauma (Brant et al., 2010). Nevertheless, by virtue of the previous surgical history of non-traumatic bodily harm, potential second pathology of myositis ossificans was unlikely.

Extraskeletal osteosarcoma on the combined FDG PET-CT may also resemble the pattern of disease in this case. It is a rare malignant neoplasm that produces osteoid or unmineralised bone in soft tissues without an attachment to bone or periosteum (McAuley et al., 2012). Clinically, this patient denied any history of an enlarging soft tissue mass, which is not always accompanied by pain.

The dystrophic peripheral rim calcification of a soft tissue lesion on the FDG-PET-CT is otherwise non-specific for MCL with an aggressive malignant tendency resulting from the necrosis. The index of suspicion of MCL is rendered high when dystrophic calcification is seen with the adjoining FDG-avid masses along the nodal chain. Other diagnostic methods include CT and fine needle biopsy with a sensitivity of 37% and 63-100%, respectively (Dong et al., 2001). Multiparametric MRI exploiting diffusion-weighted sequences have been shown to improve lesion detection by 47% compared to conventional MRI sequences, which renders differentiation of benign from malignant pathology an adjunct to the FDG-PET-CT (Gu Ji

et al., 2011; McAuley et al., 2012). The cytologic features of MCL have yet to be directly correlated with the FDG-PET-CT in the altered glucose metabolism, for which the latter would potentially serve as a non-invasive imaging marker for the suspicion of the diagnosis (Fathinul et al., 2014). More correlative studies of this cell line is needed to ascertain the significant correlative pathological imaging features. Magnetic Resonance Imaging (MRI)/PET would also be important to further associate the soft tissue characterisation adjunct to the CT (Nagata, 2005).

## CONCLUSION

The recognition of the disease distribution pattern on the combined 18-FDG-PET-CT is potentially important in suspecting the likelihood of an underlying disease when a typical calcific pattern of pathology is indeterminate. This could potentially become a non-histological imaging marker for the rare perineural Mantle Cell Lymphoma.

## REFERENCES

- Apter, S., Avigdor, A., Gayer, G., Portnoy, O., Zissin, R., & Hertz, M. (2002). Calcification in lymphoma occurring before therapy: CT features and clinical correlation. *American Journal of Roentgenology*, *178*(4), 935-938.
- Brant, W., & Helms, C. (2010). Skeletal “don’t touch” lesions. *Fundamentals of Diagnostic Radiology* (4th ed.). p. 1078. Philadelphia: Lippincott Williams & Wilkins.
- Dong, H. Y., Harris, N. L., Preffer, F. I., & Pitman, M. B. (2001). Fine-needle aspiration biopsy in the diagnosis and classification of primary and recurrent lymphoma: a retrospective analysis of the utility of cytomorphology and flow cytometry. *Modern Pathology*, *14*(5), 472-481.
- Fathinul Fikri, Nordin, A. J., & Lau, E. F. (2014). 18[F] FDG-PET/CT is a useful molecular marker in evaluating tumour aggressiveness: A revised understanding of an in-vivo FDGPET imaging that alludes the alteration of cancer biology. *Cell Biochemistry and Biophysic*, *55*(5), 631-640.
- Gu, J., Chan, T., Zhang, J., Leung, A. Y., Kwong, Y. L., & Khong, P. L. (2011). Whole-body diffusion-weighted imaging: the added value to whole-body MRI at initial diagnosis of lymphoma. *American Journal of Roentgenology*, *197*(3), W384-W391.
- Henry, G., Camila, M., & Andrei, I. (2012). Demonstration of peripheral nerve root involvement by non-Hodgkin’s lymphoma on 18F-FDG PET/CT. *European Journal of Nuclear Medicine and Molecular Imaging*, *39*(4), 729-730.
- Hutchings, M., Loft, A., Hansen, M., Pedersen, L. M., Berthelsen, A. K., Keiding, S., ... & Specht, L. (2006). Position emission tomography with or without computed tomography in the primary staging of Hodgkin’s lymphoma. *Haematologica*, *91*(4), 482-489.
- Ishikawa, T., Kobayashi, Y., Omoto, A., Adachi, Y., Nakagawa, S., Kaneko, T., ... & Kondo, M. (1999). Calcification in untreated non-Hodgkin’s lymphoma of the jejunum. *Acta haematologica*, *102*(4), 185-189.
- Korek-Amorosa, J., Scheinman, H. Z., Clemett, A. R., Amorosa, L. F., & McKenna, P. J. (1974). Hypercalcaemia and extensive lymph-node calcification in a patient with Hodgkin’s disease prior to therapy. *The British Journal of Radiology*, *47*(564), 905-907.

- Mc Auley, G., Jagannathan, J., O'Regan, K., Krajewski, K. M., Hornick, J. L., Butrynski, J., & Ramaiya, N. (2012). Extraskkeletal osteosarcoma: spectrum of imaging findings. *American Journal of Roentgenology*, *198*(1), W31-W37.
- Nagata, S., Nishimura, H., Uchida, M., & Hayabuchi, N. (2005). Usefulness of diffusion-weighted MRI in differentiating benign from malignant musculoskeletal tumors. *Nihon Igaku Hoshasen Gakkai zasshi. Nippon Acta Radiologica*, *65*(1), 30-36.
- Zhou, Y., Wang, H., Fang, W., Romaguer, J. E., Zhang, Y., Delasalle, K. B., ... & Wang, M. (2008). Incidence trends of mantle cell lymphoma in the United States between 1992 and 2004. *Cancer*, *113*(4), 791-798.

