Title: Intense focal pituitary FDG uptake due to Intravascular Large B-Cell Lymphoma in Pyrexia of Unknown Origin.

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DIAGNOSTIC IMAGING IN HEMATOLOGY:

Intravascular Large B-Cell Lymphoma (IVLBCL) is a rare extranodal lymphoma characterised by the presence of neoplastic lymphocytes in the lumina of small vessels[1]. Diagnostic delay (often made post-mortem) is at least in part responsible for its poor prognosis. We present two cases with pyrexia of unknown origin (PUO) despite exhaustive prior investigation (repeated radiologic, serological and bone marrow biopsy) and prolonged inpatient admission referred for ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) / computed tomography (CT). Intense pituitary uptake (SUVmax=9.9) without abnormality on co-registered CT was the dominant finding in Case 1 (Image 1A), a 58-year-old man with nine-month history of fevers, 20kg weight loss, raised inflammatory markers and pancytopaenia. Magnetic resonance imaging (MRI) excluded pituitary macroadenoma and transphenoidal-surgical biopsy was diagnostic for IVLBCL with CD20+ve staining in small arterioles (Image 1B) but complicated by panhypopituitarism. Case 2 is a 63-year-old man hospitalised with a six-week history of fever, weight loss, raised inflammatory markers, anaemia and thrombocytopaenia. A similar finding of focal pituitary FDG uptake (SUVmax=7.1, image 1C), raised suspicion of IVLBCL that was subsequently confirmed by CD20+ve staining of bone marrow biopsy (Image 1D). MRI pituitary was unremarkable and repeat FDG PET/CT after 5 cycles of R-CHOP demonstrated complete resolution of previously intense pituitary uptake. Both patients remain in complete remission at 68 months and 31 months following diagnosis, respectively.

IVLBCL demonstrates highly varied clinical presentation and end-organ involvement with FDG uptake abnormalities described in bone (focal or diffuse), kidneys, spleen, liver, meninges or stomach[2,3]; however isolated focal pituitary uptake has not been reported. It is critical that referring clinicians and reporting nuclear medicine physician recognises the significance of intense pituitary FDG uptake in this context, as the diagnosis of IVLBCL may be confirmed by identification of CD20+ve cells on random skin biopsy[4], avoiding the risk of potentially unnecessary pituitary surgery. The intravascular disease process rarely results in macroscopic parenchymal involvement or lymphadenopathy and thus limits the role of conventional morphologic imaging in the diagnosis of IVLBCL, however functional imaging with FDG PET/CT is useful to identify sites of hypermetabolic disease. FDG PET/CT has also been shown to be a sensitive[5] and cost-effective[6] test to localise the source of PUO, and we recommend early use of FDG PET/CT in this setting to avoid diagnostic delay.

379 words

Image 1. A & C: Sagittal fused FDG PET/CT and FDG PET images demonstrate focal intense pituitary uptake. B: Transphenoidal pituitary biopsy, with CD20+ve immunohistochemical staining of small vessels. D: Bone marrow trephine, CD20+ve immunohistochemical staining associated with small vessels.

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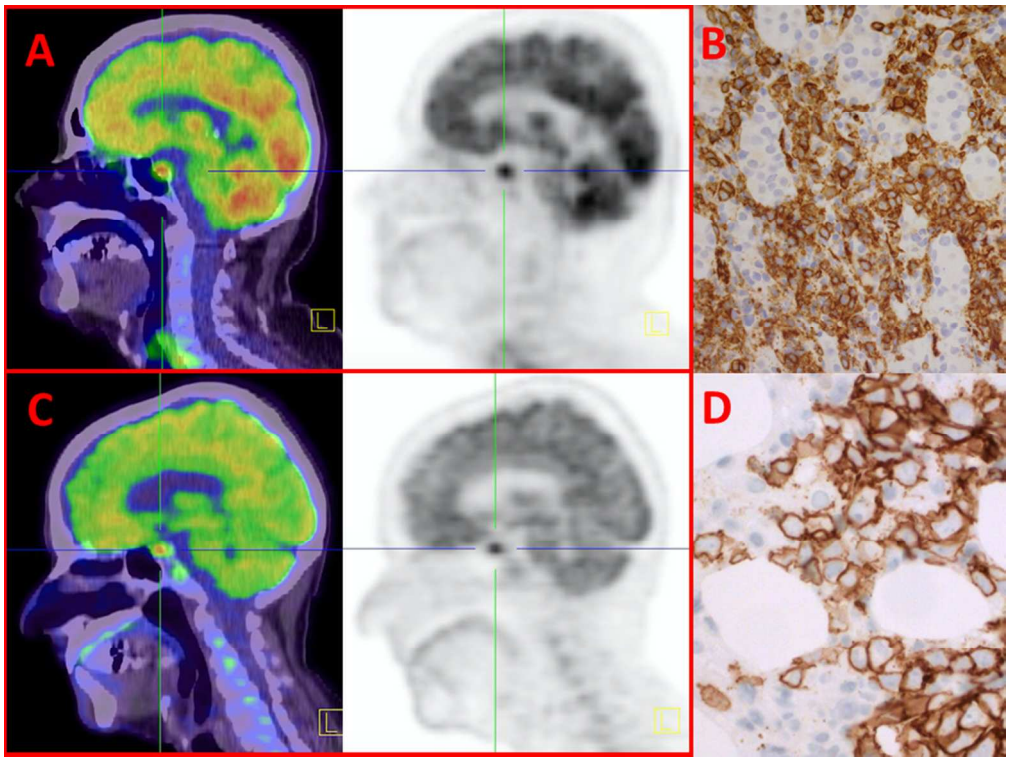

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