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## CASE REPORT

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# Epstein-Barr Virus Infection Mimics Malignancy in an Elderly Patient: Appearance on 18F-fluorodeoxyglucose Positron Emission Tomography-Computed Tomography

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### ABSTRACT

*Epstein-Barr virus infection commonly affects adolescents and young adults. We present such an infection in a 72-year-old woman, who presented with weight loss for investigation. 18F-fluorodeoxyglucose positron emission tomography-computed tomography demonstrated multiple 18F-fluorodeoxyglucose-avid lymph nodes and spleen. The initial clinical diagnosis was lymphoma, but subsequent biopsy of the lymph nodes as well as a bone marrow trephine revealed these changes to be due to Epstein-Barr virus infection. The patient was given symptomatic treatment, and follow-up 18F-fluorodeoxyglucose positron emission tomography-computed tomography revealed complete resolution of these 18F-fluorodeoxyglucose-avid lymph nodes and spleen. Our case highlights the fact that in an elderly patient, Epstein-Barr virus infection can mimic malignancy both clinically and radiologically; a biopsy and histopathological confirmation of the diagnosis should be undertaken. If the diagnosis is in doubt, follow-up 18F-fluorodeoxyglucose positron emission tomography-computed tomography should be performed.*

**Key Words:** Epstein-Barr virus infections; Fluorodeoxyglucose F18; Lymphoma; Positron-emission tomography; Tomography, X-ray computed

## 中文摘要

### 一名年老病人出現擬似惡性腫瘤的EB病毒感染：在18F-脫氧葡萄糖正子攝影電腦斷層攝影上的影像

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Epstein-Barr病毒（EB病毒）感染多發生在青少年或年青的成年人身上。本文報告一名受EB病毒感染的72歲女性，她病發時體重下降。18F-脫氧葡萄糖正子攝影電腦斷層攝影（18F-FDG - PET/CT）顯示患者在淋巴結和脾臟出現多個18F-FDG放射性增高灶，初步診斷為淋巴瘤，但其後淋巴結及骨髓切片活檢均顯示患者感染EB病毒。病人接受對症治療後，18F-FDG - PET/CT顯示在淋巴結和脾臟的18F-FDG放射性增高灶完全消失。本病例證明受EB病毒感染的年老患者，可能在臨床及放射影像方面，出現與惡性腫瘤極為相似的特徵。所以應為病人進行活檢，並以組織病理學結果為病人確診。如有懷疑，也應用18F-FDG - PET/CT為病人跟進。

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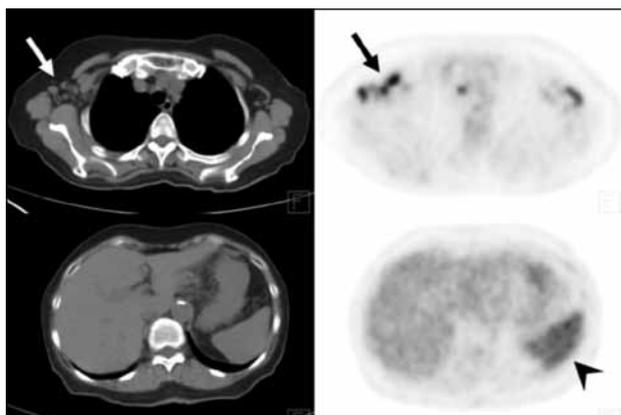
## CASE REPORT

### Clinical Presentation

A 72-year-old woman, without any pre-existing medical problems, presented to our institution in June 2008 for investigation of weight loss over several months. She was unable to quantify the extent of the weight loss. She had no other constitutional symptoms such as fever, no loss of appetite, and no particular localising symptoms or physical findings on examination. Initial blood investigations showed raised inflammatory markers (C-reactive protein of 27.5 [normal range, 0.2-8.8] mg/l) and erythrocyte sedimentation rate (34 [3-20] mm/h) and nil abnormal in her full blood count, serum electrolytes, liver function test, and lactate dehydrogenase test results. Given the age of the patient, the differential diagnoses entertained were malignancy, granulomatous infection (tuberculosis), endocrine disorder (hyperthyroidism and diabetes mellitus) or a cardiac or pulmonary disorder; malignancy was a prime consideration owing to her age.

### Imaging Findings

<sup>18</sup>F-fluorodeoxyglucose positron emission tomography-computed tomography (FDG PET/CT) [GE Discovery LS; Milwaukee, Wisconsin, USA] was performed with images acquired 79 minutes after intravenous administration of 315 MBq (8.5 mCi) of FDG (Figure 1). FDG PET/CT demonstrated multiple FDG-avid cervical, axillary, subpectoral, mediastinal, para-aortic



**Figure 1.** An <sup>18</sup>F-fluorodeoxyglucose (FDG) positron emission tomography-computed tomography demonstrates multiple FDG-avid lymph nodes above and below the diaphragm. There are metabolically active cervical, axillary (arrows), subpectoral, mediastinal, para-aortic and iliac lymph nodes, with the most prominent node in the right external iliac region measuring 2.2 x 1.2 cm (maximum standard uptake value [SUVmax] 12.2) [not shown]. There is also diffusely increased FDG uptake in the spleen (SUVmax 6.6) [arrowhead].

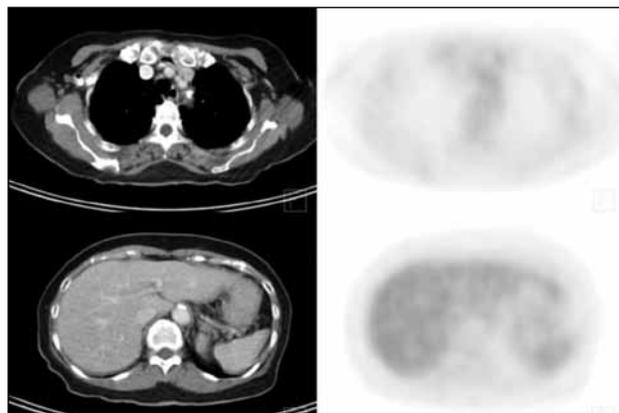
and iliac lymph nodes, the most prominent being in the right external iliac region measuring 2.2 x 1.2 cm (maximum standard uptake value [SUVmax], 12.2). In addition there was a diffusely increased FDG uptake in the spleen (SUVmax 6.6). The metabolic activity of the liver was considered normal, with an SUVmax of 3.5. Hence the patient had lymphadenopathy for investigation, and with non-specific blood investigations results, the differential diagnosis list was extensive (Table).

### Management

Excision biopsy of a right axillary lymph node revealed reactive follicular hyperplasia with evidence of Epstein-Barr virus (EBV) infection and no evidence of malignancy. Bone marrow trephine biopsy showed normocellular marrow with trilineage haematopoiesis

**Table.** Causes of lymphadenopathy

1. Inflammatory disorders like lupus erythematosus, serum sickness, drug reactions such as to phenytoin, Castleman's disease, sinus histiocytosis with massive lymphadenopathy, Langerhans cell histiocytosis, Kawasaki syndrome, Kimura's disease
2. Malignant disorders of the immune system (e.g. chronic and acute myeloid and lymphoid leukaemia, non-Hodgkin's lymphoma, Hodgkin's disease, angioimmunoblastic-like T-cell lymphoma, Waldenström's macroglobulinemia, multiple myeloma with amyloidosis, malignant histiocytosis)
3. Other malignancies (e.g. breast carcinoma, lung carcinoma, melanoma, head and neck cancer, gastrointestinal malignancies, germ cell tumors, Kaposi's sarcoma)
4. Storage diseases (e.g. Gaucher's disease, Niemann-Pick disease)
5. Endocrinopathies (e.g. hyperthyroidism, adrenal insufficiency, thyroiditis)
6. Miscellaneous (e.g. sarcoidosis, amyloidosis, dermatopathic lymphadenitis)



**Figure 2.** A follow-up <sup>18</sup>F-fluorodeoxyglucose (FDG) positron emission tomography-computed tomography performed 3 months later. There is complete metabolic resolution of all the FDG-avid lymph nodes and abnormal splenic uptake.

and no malignant infiltrate. Hence the diagnosis arrived at was EBV infection with reactive changes in the lymph nodes and spleen.

### Follow-up Imaging

The patient was treated symptomatically and follow-up FDG PET/CT (Siemens Biograph LSO; Erlangen, Bavaria, Germany) was performed 3 months later, and demonstrated complete metabolic resolution of all the FDG-avid lymph nodes and abnormal splenic uptake (Figure 2). The SUVmax of the spleen was 2.4. As reference, the SUVmax of the liver was similar to the one noted previously (SUVmax, 3.0), the inflammatory markers had also normalised.

### DISCUSSION

The most common manifestation of EBV infection in adolescents and adults is infectious mononucleosis; over 50% of patients present with the clinical triad of fever, lymphadenopathy and pharyngitis, and often they have splenomegaly and palatal petechiae. Less-common presentations include haemolytic anaemia, thrombocytopenia, aplastic anaemia, myocarditis, genital ulcers and rash.<sup>1</sup> Our patient was an elderly woman with unexplained weight loss, which was an unusual clinical presentation for EBV infection and mimicked malignancy. Blood investigations in patients with infectious mononucleosis are usually abnormal; there being an increase in the number of peripheral mononuclear cells, elevated aminotransferase levels and the presence of atypical lymphocytes.<sup>1</sup> Apart from raised inflammatory markers, the blood counts and liver function tests of our patient were unremarkable. Her biochemical and haematological manifestations were also unusual for EBV infection. FDG PET/CT revealed multiple widespread FDG-avid lymph nodes and increased splenic uptake. The clinical and imaging findings were therefore suggestive of lymphoma.

However, excision lymph node biopsy and bone marrow trephine confirmed a benign cause of EBV infection with no evidence of malignancy.

Lustberg et al<sup>2</sup> reported EBV infection in a middle-aged man with FDG PET/CT showing avid FDG uptake in the abdominopelvic lymph nodes, liver, spleen and marrow, all suspicious of lymphoma, but pelvic lymph node biopsy and bone marrow biopsy indicated EBV infection. Follow-up FDG PET/CT after two months revealed marked improvement of the previous findings. Thomas et al<sup>3</sup> presented EBV infection in a 17-year-old girl with avid FDG uptake in the adenoids, cervical lymph nodes, abdominal lymph nodes and spleen, also suspicious of lymphoma, but cervical lymph node biopsy was consistent with EBV infection.

EBV infection can mimic lymphoma in all age-groups, including the elderly as our patient. Clinical and imaging findings of EBV infection can be non-specific and can also mimic malignancy.

### CONCLUSION

EBV infection should always be considered in patients with hypermetabolic lymphadenopathy and spleen, for which histopathological correlation becomes necessary. If the diagnosis of EBV infection remains doubtful, follow-up FDG PET/CT after three months would be expected to show metabolic resolution at the corresponding sites.

### REFERENCES

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