



A case of headache in a liver transplant recipient

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A 51 year old man presents with increasing headache and confusion over one week. Fourteen months ago he had a liver transplant for primary sclerosing cholangitis and was treated with immunosuppressive drugs (cyclosporine). Computerised tomography (CT) scan of the brain showed hypodense areas in both frontal lobes. MRI of the brain was performed for further assessment.

Figures 1, 2 show postcontrast T1-weighted images.

Question 1

Which is the most likely diagnosis?

- A. intracranial haemorrhage
- B. meningioma
- C. cerebral infarction
- D. lymphoma.

Question 2

Regarding primary central nervous system lymphoma, which of the following is false?

- A. it occurs most commonly in the general population
- B. it occurs most commonly in immunocompromised patients
- C. the majority of lymphomas are non-Hodgkin's B-cell type
- D. it usually occurs within 7-33 months post-transplant.

Question 3

Which of the following viruses is thought to be a significant cofactor in the development of lymphoma in transplant recipients?

- A. cytomegalovirus
- B. human papilloma virus
- C. Epstein-Barr virus
- D. herpes simplex virus.

Question 4

Regarding types of neoplasms that develop in chronically immunocompromised patients, which of the following is false?

- A. lip and skin carcinoma
- B. Kaposi's sarcoma
- C. lymphoma
- D. transitional cell carcinoma.

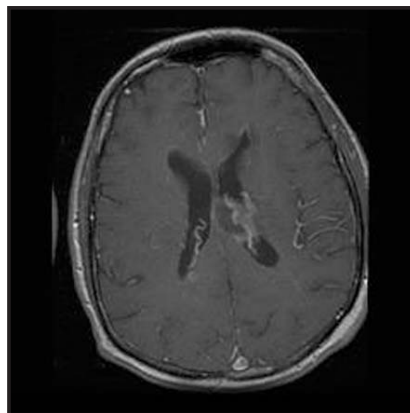


Figure 1

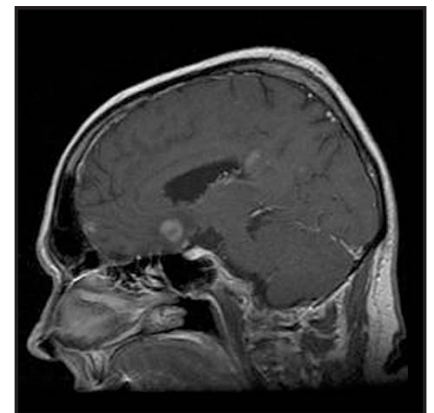


Figure 2

Answers

1. Answer D

Magnetic resonance imaging (MRI) appearances of lymphoma include ring or solid enhancing mass or masses. Mass effect and oedema tend to be less prominent than for the masses of similar size of other aetiology. It is not unusual for the tumour to become multicentric and subependymal spread is frequent. In this case MRI demonstrate multiple ring enhancing lesions with leptomeningeal and subependymal disease and vasogenic oedema. Contrast enhanced axial (Figure 1) and sagittal (Figure 2) T1-weighted MRI demonstrate ring enhancing lesions in anteromesial frontal lobes and subependymal enhancement of lateral ventricles. In this clinical context these appearances are highly suggestive of lymphoma, with differential diagnosis being opportunistic infection such as toxoplasmosis, cryptococcosis or tuberculosis. Of note, toxoplasmosis is less common in transplant patients than in AIDS patients. Primary glioma was thought to be less likely in this particular case. Biopsy of the lesions showed

primary non-Hodgkin's B-cell type lymphoma.

MRI appearances of intracranial haemorrhage depend on magnetic properties of blood products and compartmentalisation. A week old haemorrhage (late subacute) would be hyperintense on both T1W and T2W MRI. Meningiomas are extraaxial tumours typically isointense with grey matter with strong homogeneous enhancement and dural tail. Cerebral infarction respects distribution of the affected vascular territory, this is not present in this case.

2. Answer A

A number of cancers that are rather unusual in the general population occur more often in transplant recipients. While only 1% of the non-Hodgkin's lymphoma in the general population involves the central nervous system (CNS), in transplant recipients this figure rises to 28%. Approximately 2% of transplant recipients develop primary CNS lymphoma, which in turn represents 21% of all cancers occurring in this population.

Unlike systemic involvement of the CNS by lymphoma, transplant related lymphoma often involve the brain only. The majority of lymphomas are non-Hodgkin's B-cell type, arising within 7-33 months post-transplant.

3. Answer C

The increased incidence of neoplasia in chronically immunocompromised patients is related to an inability of the immune system to combat neoplastic cellular activity. The majority of transplant recipients and AIDS patients who develop lymphoma are infected with Epstein-Barr virus, which is the causative agent responsible for infectious mononucleosis and is thought to be a significant cofactor in the development of Burkitt's lymphoma. Epstein-Barr virus directly infects B-lymphocytes and induces a diffuse polyclonal B-lymphocyte proliferation. In infectious mononucleosis the proliferation is moderate and ultimately reversed by an intact host immune system. In transplant and AIDS patients,

T-cell function is weakened or suppressed, which leads to unbridled B-cell proliferation resulting in a spectrum of diseases ranging from mild diffuse polyclonal adenopathy to malignant monoclonal lymphoma. This spectrum is most evident in transplant patients in whom it is referred to as post-transplant lymphoproliferative disorders.

Cytomegalovirus and herpes simplex viruses may cause opportunistic infections in immunocompromised patients, including meningoencephalitis. Human papilloma virus is associated with cervical carcinoma.

4. Answer D

All chronically immunocompromised patients exhibit a marked increased incidence of malignant neoplasms. The types of neoplasms differ from those frequently seen in the general population, with the most common being skin, lip, cervical, rectal and perineal neoplasms, Kaposi's sarcoma and lymphoma. Of these tumours, lymphoma is of particular interest because, in transplant and AIDS

patients, it exhibits aggressive and atypical features not commonly seen in lymphomas occurring in the general population. Furthermore, lymphoma in transplant patients is unique because, if detected early and treated by reduction of the patient's immunosuppressive agents, the majority of cases completely resolve. Unfortunately, the clinical presentation of lymphoma in these patients is often ambiguous, resulting in delayed diagnosis. If untreated these lymphomas are almost universally fatal. Therefore, an awareness of the imaging appearance of these lymphomas may directly affect clinical care by allowing for timely diagnosis and intervention.

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