Teaching Point
(Section Editor: Professor K. Kühn)

Multiple hepatic masses in a 38-year-old male 10 years after renal transplantation

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Introduction

Increased risk of haematolymphoid and epithelial neoplasms is well recognized in the post-transplant population. The clonal Epstein–Barr virus (EBV) genome is causative in many of these neoplasms in this clinical setting. The present case illustrates a less frequently encountered post-transplant complication which presents management challenges to the nephrologist.

Case

The patient is a 38-year-old male, diagnosed with IgA nephropathy at age 24, who underwent renal allograft transplantation 10 years ago. He presented with complaints of fever and non-productive cough. Clinical examination was notable for a low grade temperature (99.5°F), bibasilar crackles and a distended abdomen with overlying varices. Laboratory studies showed anaemia of chronic disease and normal liver function tests, except for a mildly depressed serum albumin level. Serum creatinine was elevated from his baseline of 2.5 mg/dl to 4.2 mg/dl. Additional past medical history includes former heavy use of alcohol, with none following his transplant. A right sided pulmonary infiltrate was detected on chest X-ray. Following antibiotic therapy for presumed pneumonia, his clinical symptoms resolved and his creatinine reverted to baseline level.

An out-patient computed tomography (CT) scan was performed to evaluate the abdominal findings. Massive liver nodules in the lobes were present, replacing the hepatic parenchyma. The largest measured 13.5 cm in the left lobe, with a separate 12.5 cm mass in the right lobe (Figure 1). Radiologically, the lesions were perplexing, with a broad differential diagnosis including abscesses, haemangiomas, benign cystic lesions, metastases or hepatocellular carcinoma. Percutaneous core needle biopsy yielded a moderately cellular spindle cell neoplasm with minimal cellular pleomorphism and no mitotic activity (Figure 2). The spindle cells contained elongated, blunt-ended nuclei with finely stippled chromatin. Immunohistochemistry by the standard avidin–biotin–peroxidase complex method demonstrated myogenic differentiation of the tumour cells, which were immunoreactive to smooth muscle actin. In situ hybridization for EBV virus was strongly positive in >90% of the spindle cell nuclei (Figure 3). These findings are indicative of an EBV-associated myogenic tumour.

A reduction of the immunosuppressive agents was recommended to the patient, who declined for fear of impending rejection. Currently he is being followed, with slow expansion in the size of the liver nodules. Six months following diagnosis of the liver lesions, a palpable 4 cm nodule in the right gluteal region developed. Additional smaller nodules in the same region were noted by imaging studies. Percutaneous needle core biopsy illustrated a histologically identical EBV-associated myogenic tumour.

Discussion

EBV-related myogenic tumours represent an infrequent complication of long-term renal transplantation. Our understanding of the nature of these unusual lesions is largely derived from individual case reports. EBV-associated smooth muscle tumours have been described in individuals immunosuppressed due to solid organ transplantation [1–6], bone marrow transplantation [7],
AIDS [8,9] and common variable immunodeficiency syndrome [10]. A viral aetiology is strongly supported by the consistent finding of clonal EBV virus in myogenic tumours arising in immunosuppressed individuals, but not in sporadic smooth muscle tumors [8].

The evolution of EBV-associated neoplasms in renal transplant patients arises out of an altered immune surveillance milieu in which EBV-infected cells escape immunoregulation and proliferate without challenge. These tumours are more frequently reported in the paediatric population, probably due to infection of EBV-negative recipients transplanted from EBV-positive donors. The liver is the most common site of involvement in both the paediatric and the adult population. Other sites involved include lungs, lymph nodes, adrenal gland, spleen, heart, kidney and, less often, the central nervous system [1,10]. Multicentric involvement of the bone has been documented [11]. EBV-associated smooth muscle tumours may arise in the allograft kidney, allograft liver or allograft lung [4,11], and show donor or recipient genotype [3,11].

EBV-associated myogenic tumours in immunocompromised individuals show a highly varied histological spectrum. The lesions can be broadly classified into those with overt malignant features of leiomyosarcoma, and ‘borderline’ cases with minimal pleomorphism, cellular crowding and mitotic activity. Histological features may be deceiving, in that myogenic tumors which fall into this latter category may still behave in a clinically aggressive manner. As such, until we acquire reliable indicators of behaviour, the most appropriate classification of EBV-associated myogenic tumours without clear-cut sarcomatous features remains ‘uncertain biological potential’, rather than benign.

Surgical excision with negative margins remains the mainstay of treatment. A theoretical argument can be made for immunoreduction as a means to control lesional growth, in cases in which surgical therapy is not possible. The continued expression of specific immunogenic antigens in EBV-myogenic tumours suggests that reduction in immunosuppressive treatment may allow for the proliferation of EBV-specific cytotoxic T-cell responses. In particular, two ‘Achilles heel’ immunogenic EBV proteins are expressed in EBV-myogenic tumours—EBNA-2 and the initial EBNA-1 promoter [2,4,5]. The efficacy of antiviral therapy and chemotherapy has not been proven.

**Teaching points**

1. EBV-related myogenic tumours retain expression of immunogenic EBV-related antigens, providing a theoretical justification for a trial of immunoreduction in complicated cases.
2. Tumours with histologically ‘benign’ features may recur or metastasize; as such, any EBV-related myogenic tumour lacking overt sarcomatous features should be regarded as having ‘uncertain biological behaviour’.

3. Complete surgical excision is recommended when clinically feasible, with the role of adjunctive chemotherapy, antiviral agents and radiotherapy uncertain.

Conflict of interest statement. None declared.

References


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