Compromised immunosurveillance of the host is increasingly recognized as a risk factor for the development of a primary neoplasm and for virus-associated neoplasms. Neoplastic disease, especially malignant lymphoma and Kaposi’s sarcoma (KS), is an increasing problem in adults with acquired immunodeficiency syndrome (AIDS) [1–3]. Although smooth-muscle tumors are relatively rare, there is a growing awareness of the tendency for smooth-muscle tumors to develop in patients with AIDS, particularly children [4–6]. These tumors probably arise from smooth muscle of the vessels or biliary tree. In addition to the well-known role of Epstein Barr virus (EBV) in malignant lymphoma, histologic evidence of EBV infection has been demonstrated in these smooth-muscle tumors in children with AIDS [6]. In this report, we describe a 32-year-old heterosexual man with a 4-year history of AIDS, who developed a hepatic leiomyomatous neoplasm associated with EBV infection.

In 1991, this young heterosexual man was found to be seropositive for human immunodeficiency virus-1 (HIV-1) by enzyme-linked immunosorbent assay (ELISA). He developed AIDS in 1994, with subsequent opportunistic infections such as cutaneous herpes zoster along the T2–3 dermatome distribution, oropharyngeal candidiasis, and pulmonary miliary tuberculosis (TB). He had been taking anti-TB medications, which he obtained in Thailand, since February 1996 but came to our hospital because of inadequate response. When he was first admitted in April 1996, infiltrative lung disease with pleural effusion and abnormal liver function were found. Abdominal sonography revealed no focal lesion in the liver except for mild hepatosplenomegaly, and echoguided liver biopsy showed granulomatous hepatitis. He was treated for disseminated TB with anti-TB medications, and a good response was obtained. Panendoscopy was performed to investigate the possible cause of the abdominal pain, but revealed only gastritis. Acute pancreatitis was noted and might have accounted for his abdominal pain.

However, fever recurred in April 1998 and a computed tomography (CT) scan of the abdomen revealed a 3-cm adrenal mass at the right suprarenal region without focal hepatic lesion. Adrenal tumor or tuberculoma was suspected and the patient was empirically treated for disseminated TB again.

His fever and abdominal pain improved after anti-TB medications. However, fever recurred in June 1999 and a
small tumor in the left lobe of the liver was incidentally detected on a CT scan of the abdomen. Under the impression of tuberculoma of the liver, we performed echo-guided liver biopsy of the 1.8-cm nodule.

Histopathologic study of the biopsy specimen showed it to be a leiomyomatous neoplasm. Microscopically, it was composed of interlacing spindle cells with abundant eosinophilic cytoplasm (Fig. 1). Immunohistochemical study showed these spindle cells to be positive for smooth-muscle-specific actin (1:50 monoclonal mouse; Dako, Denmark) and negative for CD21 and CD68, which are used to investigate the possibility of histiocytic tumor or inflammatory pseudotumor. In situ hybridization for EBV-encoded small RNAs (EBER) showed positive nuclear staining in these spindle cells (Fig. 2). There was no signal in the nuclei of blood vessel smooth-muscle cells or hepatocytes.

Fever fluctuated during anti-TB therapy and a follow-up panendoscopy in September 1999 revealed a 2.0-cm protruding submucosal tumor with small ulcerative patches at the gastric greater curvature side of the middle body. Repeated endoscopic forceps biopsies were performed but histopathology revealed only ulceration with gastritis. At this time, the CD4 lymphocyte count was 43/µL and the patient continued anti-TB medications. Regular follow-up and abdominal sonography in January 2000 revealed that the hypoechoic nodule in the left lobe of the liver had increased to 2.3 cm in diameter, but no additional focal hepatic lesion was found.

Discussion

Smooth-muscle tumors are rare in immunocompetent children, but there is an increasingly high incidence in children with AIDS [5]. There is no clear-cut distinction between benign and malignant smooth-muscle tumors. Changes considered useful in diagnosing malignant smooth-muscle tumors include dense cellularity, nuclear pleomorphism, degenerative changes, and large tumor size [7]. Increased frequency of mitosis to more than 10 mitotic figures per 10 high-power fields has been a reliable variable for the diagnosis of uterine leiomyosarcoma, but is not applicable to gastrointestinal smooth-muscle tumors [8, 9].

Our patient developed a hepatic tumor with the classic morphologic features of a leiomyoma, including a well-circumscribed nodule, a diameter of less than 3 cm, and no necrosis. Histologic examination of the biopsy specimen showed regular spindle-shaped cells, no atypical nuclei, less than one mitotic figure/10 high-power fields, and strong immunopositivity with anti-α specific smooth-muscle actin antibody. Clinically, this tumor enlarged slowly, although no other focal lesion was found on the CT scan of the liver 6 months later. Furthermore, a gastric submucosal tumor was found that was considered to be of myogenic origin, although biopsy could not establish myogenicity. Hepatic leiomyomatous neoplasm that appears benign should be carefully followed up for possible progression to leiomyosarcoma or metastasis to adrenal glands or the stomach.

Although smooth-muscle tumors associated with HIV infection were first reported in children [5], the vast majority of patients with HIV infection are adults and the prevalence of AIDS-related lymphoma and KS is far greater in adults than in children [10]. Both KS and smooth-muscle tumors might arise from a common stem cell under the influence of some unknown factor produced during HIV infection [5]. Wittek et al published data indicating a relationship between cultured KS cells and leiomyoblasts [11]. Whether the spindle cell origin of leiomyomatous tumors bears an etiologic relationship to that of KS remains unclear.

Super- or co-infecting viral and nonviral microorganisms might be a possible promoting factor in the development of smooth-muscle tumors. EBV has been associated with nasopharyngeal carcinoma, Burkitt’s lymphoma, and virus-induced B-cell polymorphic lymphoproliferations. Lee et al detected EBER in the nuclei of neoplastic smooth-muscle cells in three cases of post-transplant spindle cell tumor [12].
Van Hoeven et al detected EBER with in situ hybridization in a child with AIDS who had an intrahepatic myogenic tumor [4]. McClain et al used in situ hybridization and quantitative polymerase chain reaction to show that EBV could infect smooth-muscle cells and contribute to the pathogenesis of leiomyomas or leiomyosarcomas in children with AIDS [6]. Prevot et al first detected EBER in an HIV-infected adult patient using in situ hybridization in smooth-muscle neoplastic cells [13]. In patients with both HIV and EBV involvement, a cocktail of antiretroviral therapy might reduce the genesis and growth of smooth-muscle tumors.

References