Virchows Arch (2000) 436:138–139

ORIGINAL ARTICLE

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Splenic smooth-muscle tumors in children with acquired immunodeficiency syndrome: report of two cases of this unusual location with evidence of an association with Epstein-Barr virus

Received: 27 January 1999 / Accepted: 23 August 1999

Abstract Smooth-muscle neoplasms are rarely located in the spleen. They have been previously reported in five cases of children with human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS). Two cases of children with HIV infection/AIDS with autopsy and surgical pathology evidence of multiple smooth-muscle neoplasms with splenic involvement are presented. DNA was extracted from histology slides in both cases for analysis for Epstein Barr (EB) virus. In both cases, the presence of EB virus was confirmed. This paper documents two additional cases of the unusual phenomenon of splenic involvement by smooth-muscle neoplasms in the setting of AIDS in childhood and further supports the role of EB virus in the development of these neoplasms.

Key words Smooth-muscle tumors · AIDS · Epstein-Barr virus

Introduction

Smooth-muscle neoplasms occur with increased frequency in immunodeficient children[2, 5]. Recent findings associate these tumors with Epstein-Barr (EB) virus [5]. Among children infected with human immunodeficiency virus (HIV), smooth-muscle neoplasms most commonly arise in the lungs, liver, and gastrointestinal tract [2]. To our knowledge, only five cases of splenic smooth-muscle neoplasms in children with HIV infection/acquired immunodeficiency syndrome (AIDS) have been reported [2, 3, 4]. We encountered two additional such children and provide further evidence of an association with EB virus.

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Clinical histories

Case 1

Case 1 involved a 4-year-old African-American male with perinatally acquired HIV infection. His terminal hospitalization was prompted by catheter-associated sepsis complicated by disseminated *Mycobacterium avium* complex (MAC), and *Clostridium difficile*-associated enterocolitis, and he succumbed to refractory respiratory failure.

Case 2

The second patient was an African-American female with perinatally acquired HIV infection diagnosed at 18 months of age. She began to experience severe and recurrent abdominal pain. A computed tomography (CT) scan of the abdomen performed at the age of 6.75 years revealed a 2-cm hypodense lesion in the spleen. A splenectomy was performed. Three months after the splenectomy, she was hospitalized with respiratory failure and diagnosed with *Pneumocystis carinii* pneumonia. She subsequently developed *Streptococcus pneumoniae* sepsis and expired.

Materials and methods

DNA was extracted from paraffin-embedded tumor scraped off histology slides from both cases. A pulmonary nodule from case 1 and the ileal nodule from case 2 were analyzed. DNA was extracted in both cases using the QI Amp Tissue DNA isolation kit (Qiagen). Primers W-1 (5' GTTCGCGTTGCTAGGCCACC3') and W-2b (5'TGGCGCTCTGATGCGACCAG3'), which amplify the 140-bp portion of the *Bam*HI fragment of EB virus were utilized. An EB virus-positive cell line (Raji) was used as a positive control.

Pathological findings

Post-mortem examination of the first case confirmed the presence of widespread MAC infection. The affected or-

gans showed multiple, well-formed, non-necrotizing granulomata, measuring up to 0.4 cm and containing numerous acid-fast bacilli. In addition, three small clinically unsuspected neoplastic nodules were found. Two were located within the bronchial walls, in the upper and lower lobes of the right lung, and measured 0.5 cm and 1 cm in diameter, respectively. The third, 0.6 cm in diameter, was found in the spleen. Grossly, the nodules appeared well circumscribed, round, firm, and white–gray. Histologically, each nodule was well circumscribed and composed of interlacing bundles of plump, mildly pleomorphic spindle cells. Neither mitotic figures nor necrosis were seen. The spindle cells were strongly reactive to antibody directed against smooth muscle actin. Acid-fast stains showed no mycobacteria within the neoplastic nodules.

In the second case, pathologic evaluation of the splenectomy revealed a leiomyosarcoma of the spleen based on atypia, cellularity, and mitotic activity. The tumor stained for smooth muscle actin, muscle-specific actin, and desmin. Autopsy in this case confirmed the presence of *Pneumocystis carinii* pneumonia. In addition, an incidental leiomyoma measuring 1.2×1.0×0.6 cm was identified in the distal ileum.

Polymerase chain reaction (PCR) analysis yielded identical results, amplification of EB virus, in both the lung from case 1 and the ileum from case 2.

Discussion

The finding of a splenic smooth-muscle neoplasm in an immunocompetent host would be exceptional. Previously, smooth muscle tumors in AIDS patients have been shown to contain the EB virus genome, as determined by the in situ hybridization technique [2]. EB virus infection of smooth-muscle tumors was demonstrated by McClain et al. [5] in immunocompromised patients. In their study, they showed the presence of clonal EB virus genomes using Southern-blot analysis in smooth-muscle tumors of HIV-infected children, thus providing further evidence of a possible role of EB virus in the tumorigenesis of these neoplasms.

It is important to distinguish true smooth-muscle neoplasms from their histological mimics, reactive spindle-cell pseudotumors caused by nontuberculous mycobacteria [1]. The pseudotumors resemble smooth-muscle tumors and occasionally show immunoreactivity to desmin [1], but not to smooth-muscle actin. In all reported cases, special stains demonstrated numerous acid-fast bacilli within the pseudotumors.

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