Telangiectatic Focal Nodular Hyperplasia of the Liver: A Case Detected at Birth

A case of telangiectatic focal nodular hyperplasia (FNH) was detected at birth and was surgically removed. Grossly, the lesion was a solitary nodule and showed vague nodularity, appearing as an adenoma-like mass with fine fibrous septa, but having no macroscopic scar. On microscopic scale, the mass typically had neither fibrous central scar nor hyperplastic nodules different from the usual FNHs. The hepatic plates were separated by sinusoidal dilatation, sometimes alternating with areas of marked ectasia. Instead of large fibrous scar, thin fibrous septa were often found, and contained abnormal tortuous large arteries. These high-pressure vessels were connected directly into the adjacent sinusoids and made marked dilation of sinusoids. Bile ductular proliferation was also noted in the thin fibrous septa. To our knowledge, this is considered to be the first reported case of telangiectatic FNH detected at birth.

Key Words: Telangiectasia; Focal Nodular Hyperplasia; Infant, Newborn; Liver

INTRODUCTION

Focal nodular hyperplasia (FNH) of the liver is a non-neoplastic regenerative lesion characterized by a stellate central scar and hyperplastic nodules (1). FNH develops as a solitary or multifocal lesion, and is usually supplied by abnormally enlarged feeding arteries. It is now generally hypothesized that FNH represents a hyperplastic response of liver parenchyma to local hemodynamic disturbance, induced by malformed arteries (2, 3).

Typical category of FNH is composed of the two classical features, nodular architecture and malformed vessels, and it always presents bile ductular proliferation. However, a number of recent studies have proposed the non-classical categories of FNH (4-7). According to these articles, non-classical FNHs are subdivided into three histologic forms: the telangiectatic form (7), the mixed hyperplastic and adenomatous form, and a third variant with cytologic atypia (4).

We describe a case of FNH, discovered at birth, and is considered as a telangiectatic variant. We also discuss its morphological characteristics for comparison with a classical form and liver nodules in similar morphology.

CASE REPORT

Clinical History

An eleven-month-old boy was admitted to Seoul National University Children’s Hospital, complaining of an abdominal mass, which had been detected at his birth by his family. The patient had been delivered normally at full term with a birth-weight of 3.2 kg. No significant information was available about his past medical history. Physical examination was normal, except for the abdominal mass. The mass was palpable on the whole abdomen, extending to 13 cm below the xyphoid process. It was freely movable, firm, and non-tender. No icterus was found. No significant finding was noted during laboratory examination. Alpha-fetoprotein was 13 ng/dL, and serum HBsAb was positive. On abdominal CT, a 16 × 12 cm homogeneously enhanced mass replaced the right lobe of the liver completely and compressed the remainder of the left lobe (Fig. 1). Radiological and clinical impressions were hepatoblastoma. The liver needle biopsy was performed, and the diagnosis was “consistent with hepatoblastoma, fetal type”. The boy was treated through several cycles of chemotherapeutic regimens. After chemotherapy, however, there was no change in size and shape of the mass on radiological studies. Then, the mass excision was performed. On laparotomy, there was much bleeding from the cut surface of the mass. The mass...
could not completely be removed, because a part of the tumor encircled the inferior vena cava. The postoperative course was unremarkable. The patient had been followed up with no sign of recurrence for two years.

Materials and Methods

The surgically resected tumor was fixed in 10% neutral formalin, and was embedded in paraffin blocks. Hematoxylin and eosin, PAS, D-PAS, reticulin, and Masson trichrome stains were performed. Immunohistochemical study was performed. Serial sections (3 μm-thick) were cut from paraffin blocks, and were deparaffinized in xylene. For antigen retrieval, sample slides were heated for 5 min in a microwave oven, and then were incubated in 0.3% hydrogen peroxide for 30 min to block endogenous peroxidase activity. The primary antibodies used were anti-CK19, CD34 and factor VIII-related antigen (DAKO, U.S.A.). Slides were incubated with the primary antibodies overnight at 4 °C and washed in PBS, and then incubated with biotinylated goat anti-rabbit, anti-mouse immunoglobulin at room temperature for 20 min and washed again, prior to treatment with avidin-complex peroxidase. Slides were developed with 3,3′-diaminobenzidine tetrahydrochloride for 4 min, and finally, sections were counterstained with Harris hematoxylin. Buffer was substituted for the primary negative controls.

Pathologic Findings

On macroscopic examination, the lesion was a solitary mass. The specimens measured 16 × 10 × 5 cm and weighed 380 g.
were easily found. On low power microscopic examination, there was neither a central scar nor hyperplastic nodular appearance. Instead, thin and short fibrous septa were found throughout the tumor. The septa contained abnormally enlarged tortuous arteries with hypertrophied muscular media, but without intimal proliferation. These abnormal arteries drained directly into the adjacent sinusoids, and made sinusoidal dilatation (Fig. 3). The sinusoids were congested with red blood cells, which made characteristic 'telangiectatic' appearance (Fig. 4A). Also, thin branching fibrous stroma contains proliferating small bile ductules (Fig. 4A inlet).

Hepatic plates showed generally one cell thickness, while hypertrophic hepatic cords revealed two to three cells' width occasionally. Sometimes microvesicular fatty changes are noted in hepatocytes. However, neither necrosis nor mitosis was seen. The hepatic plates were separated by dilated sinusoids, which sometimes alternated with peliotic areas of marked ectasia. The sinusoids were always lined by flat endothelial cells and were filled with pools of red blood cells. Also, Kupffer cells and extramedullary hematopoiesis were noted in the sinusoids. Moderate amount of lymphocytic infiltration was noted in the parenchyma. The endothelial cells lining dilated sinusoids were strongly positive for CD34 staining, and weakly reactive for factor VIII-related antigen. Bile ductular proliferation was easily noted with CK19 immunohistochemistry (Fig. 4B).

**DISCUSSION**

Focal nodular hyperplasia of the liver in the pediatric patient is a rare benign lesion that usually presents as an asymptomatic abdominal mass, and must be diagnosed differentially from other common benign or malignant lesions. One large series have reported 72 cases from birth to 20 yr and only three cases from birth to 2 yr during 30 yr (8). Sixteen cases of FNH including our case have been reported in Republic of Korea (9-19). They ranged in age from 1 to 75 yr, of which seven were children (11 months and 15 yr). The male to female ratio was 1:1. Our case was discovered at birth by the parents. Unusual feature of lesions in the radiological studies and biopsy findings may mislead us to erroneous initial diagnosis. No radiological change was noted in the contour or the size of the mass even after several cycles of chemotherapy. Surgical exploration proved the lesion is a benign lesion associated with vascular abnormality.

Telangiectatic variant of FNH was described first by Wanless et al. (7). In their series, telangiectatic FNHs were usually associated with multiple FNH syndromes. In a recent study, a total of 47 FNHs of the telangiectatic type were identified in 16 patients (15.4% of their series) (4). This form presented as a solitary tumor in 10 patients. In the other six patients, it was the only histologic type identified (20 of 20 lesions of the same patient) or one of the morphologic variants among other types of FNH (1 of 2, 1 of 4, 1 of 15, 13 of 15, and 1 of 30 lesions from five patients). Therefore, the telangiectatic type seems to be more prevalent in multiple FNH cases than in solitary cases, although some previous reports and our case were solitary lesions (5, 6).

On the macroscopic scale, the aspects of telangiectatic FNH are dissimilar to a classical form with its less prominent lobulation and no macroscopic central scar. The remaining lesions
showed a homogeneous parenchyma resembling adenoma. In terms of size, telangiectatic FNH seems variable from less than 2 cm to 19 cm (4). In a manner similar to these studies, our case was ill defined and non-encapsulated, and had a vaguely lobular architecture on cut surfaces. It measured 16 cm in diameter.

Microscopically, telangiectatic FNH differs from the typical form by the absence of nodular architecture and by its mild architectural distortion. The lobulated appearance found in gross examination could result from the alternating of solid and ectatic areas. The hepatic cords generally consist of single or two cells in width and almost regular. However, they are separated by characteristically dilated sinusoids, which are irrigated directly by high-pressure arterial blood from adjacent abnormal arteries. These vessels are generally located in short and slender fibrous stroma. The arteries have a moderately thickened muscular wall. However, the intimal proliferation is not easily seen, while the latter features a usual characteristic of classical FNH. The very helpful feature in the diagnosis of FNH is the presence of areas of bile ductular proliferation because liver cell adenoma usually lacks bile ducts (20). Mild to marked degree of cholangiolar proliferation was found in 100% of telangiectaticFNHs, including our case (4).

Telangiectatic FNH must be differentiated from other hepatic nodules showing vague nodularity and prominent vascular pattern. Hepatic adenoma is a rarely occurring benign tumor of the liver reported primarily in teenage girls taking oral contraceptives. It is usually a solitary nodular lesion, often with large blood vessels over its surface (21). Microscopically the tumor is composed of sheets of neoplastic cells in two-cell thickness, separated by compressed sinusoidal spaces lined by endothelial cells and some Kupffer cells. Areas of necrosis and hemorrhage may be present, and foci of dilated sinusoids may impart a "pelioid" appearance. However, hepatic adenoma has neither bile ductular element in the tumor parenchyma, as well as diffuse sinusoidal dilatation, compared to telangiectatic FNH. Infantile hemangioendothelioma (IHE) is the most common liver tumor in the first year of life. IHE may be single or multicentric, and is composed of thin vascular channels. Microscopically, IHE lesion is composed of vascular channels lined by a single continuous layer of plump endothelial cells in a supporting fibrous stroma (type 1 IHE). In about 20% of cases, large pleomorphic and hyperchromatic cells are present along poorly formed vascular spaces, often displaying tufting or branching (type 2 IHE) (22). In contrast to telangiectatic FNH, IHE consists of pure vascular channels having fibrous stroma devoid of hepatocytes and bile ducts. Hepatic cords and cholangioles are found only in the periphery of IHE. Also, endothelial cells of IHE are plump and pleomorphic, especially in type 2 lesion, in comparison with flat and bland looking endothelial cells of telangiectatic FNH. Hepatoblastoma is the most common malignant liver tumor under 2 yr of age. A variety of histologic patterns are noted, which consisted of epithelial and mixed mesenchymal components (22). The fetal pattern is composed of small, round, uniform cells with abundant cytoplasm and distinct cytoplasmic membranes. The cells are arranged into thin trabeculae, usually two- or three-cell thickness, with alternating light and dark areas. The embryonal pattern shows sheets of irregular, angulated cells with a high nucleocytoplasmic ratio, increased nuclear chromatin, and indistinct cytoplasmic membranes. Pseudorosette, ribbon and acinar formation are common features. The mixed epithelial and mesenchymal type of tumor contains varying amounts of fetal and embryonal type cells admixed with primitive mesenchyme, consisted of spindle cells, and osteoid and cartilaginous tissue. The small-cell undifferentiated or anaplastic pattern is composed of small round cells that have a scanty cytoplasm and hyperchromatic nuclei. Telangiectatic FNH does not show characteristic neoplastic proliferation of hepatoblastoma, such like 'light and dark' pattern, tubular or rosette-like arrangement, and mesenchymal components.

However, in the biopsy specimen, it does not seem easy to discriminate the telangiectatic FNH from other hepatic nodules, due to unusual radiological and histological findings and the rarity of the lesion. Telangiectatic FNH should be considered as a differential diagnosis in the biopsy diagnosis of solid hepatic nodules, which show bland-looking hepatic cord with marked sinusoidal dilatation and mild bile ductular proliferation.

In conclusion, telangiectatic FNH is a benign hyperplastic parenchymal lesion of the liver associated with malformed arteries. Although precise pathogenesis should be elucidated by further studies, the direct connection between this high-pressure large vessels and sinusoids is considered to be a underlying pathology that produces the unique telangiectatic appearance of this lesion. To our knowledge, our case is considered to be the first reported telangiectatic FNH of congenital origin.

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