

A case of dyskeratosis congenita with portal hypertension associated with jugular venous anomaly

Jugular ven anomalisinin eşlik ettiği portal hipertansiyonlu bir diskeratozis konjenita olgusu

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Dyskeratosis congenita is an unusual inherited disease characterized by the triad of abnormal skin pigmentation, nail dystrophy and mucosal leukoplakia. Bone marrow failure and various abnormalities including genitourinary, pulmonary, skeletal, neurological, ophthalmic, dental and gastrointestinal have been reported. Portal hypertension is an extremely rare manifestation. Although arterio-venous fistulas in the lungs have been reported, gross peripheral vascular abnormality associated with the disease has not been published until now. We describe a case of dyskeratosis congenita with portal hypertension and associated coagulopathy in whom transjugular liver biopsy could not be performed because of a vascular anomaly at the bifurcation of the internal jugular and subclavian veins.

Key words: Dyskeratosis congenita, portal hypertension, vascular anomaly

Diskratozis konjenita anormal deri pigmentasyonu, tırnak değişiklikleri ve mukozal lökoplaki üçlüsü ile karakterize az rastlanan kalıtsal bir hastalıktır. En önemli sorunu olan kemik iliği yetmezliği yanında genitoüriner, solunum, iskelet, nörolojik, oftalmik, dental ve gastroentestinal sistem gibi birçok sistemin tutulumu bildirilmektedir. Portal hipertansiyon oldukça nadir rastlanan bir bulgudur. Akciğerlerde arterio-venöz şantlar rapor edilmekle birlikte, bugüne kadar hastalıkla ilgili periferik büyük damar tutulumu bildirilmemiştir. Bu olgu raporunda internal jugular ven ve subklavian venin bifurkasyonunda rastlanan vasküler anormali nedeni ile transvenöz karaciğer biyopsisi yapılamayan, portal hipertansiyonuna koagulopatinin eşlik ettiği bir diskeratozis konjenita olgusu sunulmaktadır.

Anahtar kelimeler: Diskratozis konjenita, portal hipertansiyon, vasküler anormali

INTRODUCTION

Classic dyskeratosis congenita (DC) is an unusual inherited disease characterized by the triad of abnormal skin pigmentation, nail dystrophy and mucosal leukoplakia (1). Bone marrow failure, which occurs in approximately 50% of cases, and predisposition to malignancy are principal causes of early mortality (2, 3, 4). The X-linked recessive, autosomal recessive and autosomal dominant forms of the disease are recognized (5), along with genitourinary, pulmonary, skeletal, neurological, ophthalmic, dental and gastrointestinal abnormalities (2, 4, 6, 7). Gastrointestinal findings, such as esophageal strictures, hepatomegaly or cirrhosis, are seen in 10% of cases (8). A possible association with noncirrhotic portal hypertension has also been suggested (8, 9). No gross peripheral vascular abnormality has been reported until now.

Transvenous liver biopsy, which is usually used in disorders associated with coagulopathies, is a safe method, with a mortality rate of 0.0% to 0.5% (10).

Here, we present a case of DC with portal hypertension. We could not perform transjugular liver biopsy because of a vascular anomaly at the bifurcation of the internal jugular and subclavian veins.

CASE REPORT

A 20-year-old man was admitted to the hospital because of malaise, headache, epistaxis, syncope and dyspnea. Epistaxis had been intermittent since his first decade. Skin pigmentation on his chest and forearms started to appear at six years of age. There was no family history of skin or hematologi-

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Manuscript received: 28.06.2005 **Accepted:** 08.12.2005

cal disorders. Two years before admission, during an evaluation in a peripheral hospital for his malaise, weakness and dyspnea, diagnosis of DC was made by characteristic dermatologic features and extracutaneous manifestations.

Dermatologic findings were reticulated skin pigmentation affecting the face, chest and arms. Dystrophic nail changes were longitudinal striations, with some brittleness, and slight deformity (Figure 1). Loss of fingerprints was striking. Leukoplakia on the tip of the tongue was conspicuous. Histopathologic evaluation of the biopsy of the tongue was reported as irregular keratosis in the squamous epithelium, pallor in the spinal cells, dyskeratosis, telangiectasia and inflammatory reaction in the subepidermal area, all of which are consistent with the diagnosis of DC. Physical examination was normal except for splenomegaly. Routine biochemistry was normal except for mild hypoalbuminemia (3.3 g/dl). Complete blood count revealed pancytopenia with white blood cell count 1,600, platelet count 15,000 and hemoglobin 10 g/dl. Prothrombin time and aPTT were 16 and 35.5 seconds, respectively. Echocardiography measurements indicated pulmonary hypertension with minimal dilations in the right atrium and ventricle. Pulmonary function tests showed restrictive changes. Bone marrow biopsy was reported as normocellularity and erythroid hyperplasia, which suggested that pancytopenia might have been due to a hemolytic process, possibly hypersplenism. Abdominal computerized tomography revealed sple-

nomegaly, splenorenal venous shunts, and dilations in portal and splenic veins. Doppler ultrasonographic findings were consistent with portal hypertension. Upper gastrointestinal endoscopy showed grade II esophageal varices. A percutaneous liver biopsy was avoided because of marked thrombocytopenia. He was discharged from the hospital with the diagnosis of DC.

On admission to our hospital, physical examination, dermatologic signs, laboratory findings and upper endoscopic evaluation were similar. Additionally, he underwent magnetic resonance angiography to re-evaluate portal venous system, which similarly revealed perisplenic collateral veins and an increase in the diameters of portal and splenic veins. A mildly low level of albumin (3.1 g/dl) and mild prolongation of prothrombin time (17.3 seconds) suggesting chronic liver disease led us to attempt liver biopsy to determine the cause of portal hypertension. Because of marked thrombocytopenia (16,000) and mildly abnormal prothrombin time, transvenous liver biopsy was attempted via internal jugular vein. As it was not possible to pass the guidewire through the internal jugular vein to the subclavian vein, the antecubital approach was attempted to explore for any vascular anomaly, which revealed a tortuous and stenotic segment of the distal jugular vein at the junction where it drains to the subclavian vein (Figure 2). This anomaly prevented the procedure from being successfully completed.



Figure 1. Dystrophic nail changes



Figure 2. Venography by antecubital approach showing tortuous and stenotic segment of distal jugular vein at the junction where it drains to the subclavian vein

DISCUSSION

Dyskeratosis congenita is a rare multisystemic disorder with variable modes of inheritance, including a predominant X-linked form (1, 4). Initial clinical manifestations are abnormalities in skin pigmentation and nail growth that become apparent by the age of 10, as in our case (6). During the second decade of life, hematologic alterations are observed in approximately 50% and malignancies in about 10% of patients. The mean age of diagnosis is approximately 20 years of age (11).

The pathogenesis of DC is still unclear. The gene for the X-linked form of DC has been identified on Xq28 and designated as DKC1. The corresponding protein, dyskerin, which contains 514 amino acids, seems to have a functional role in many cells, especially keratinocytes, mucosal epithelium and bone marrow (1, 5). Three main systems were affected in our patient, including the skin, liver and lung.

Many noncutaneous abnormalities have been reported. Eye abnormalities are epiphora, conjunctivitis, blepharitis, loss of eyelashes, strabismus, cataracts and optic atrophy (12). Teeth abnormalities such as dental decay and early loss of teeth are common (6). Genito-urinary abnormalities are urethral stenosis, hypogonadism, hypospadias, phymosis and horseshoe kidney (6). Skeletal abnormalities such as osteoporosis, abnormal bone trabeculation, avascular necrosis, scoliosis and mandibular hypoplasia are seen in 20% of cases (13, 14). A subset of patients develops pulmonary complications, including reduced diffusion capacity and/or restrictive defect (7, 15). Vascular abnormalities such as arterio-venous fistulas in solid organs like lung have been reported (15). Our case had restrictive changes in pulmonary function tests but there were no eye, teeth, genitourinary or skeletal abnormalities.

Gastrointestinal findings such as esophageal strictures, hepatomegaly or cirrhosis are seen in 10%

of cases. Anal strictures, esophageal diverticula, gastroduodenitis, duodenal ulcers, and chronic diarrhea have also been described (16). Portal hypertension is very rarely associated with DC, either due to cirrhotic or noncirrhotic mechanisms. Kawaguchi *et al.* reported an autopsy case complicated by noncirrhotic portal hypertension, signet ring carcinoma of the rectum and Pneumocystis carinii pneumonia (9). Brown *et al.* suggested a possible association with noncirrhotic portal hypertension in their article reviewing the literature concerning gastrointestinal involvement in DC (8). Mildly abnormal albumin level and prothrombin time in our case with portal hypertension might indicate cirrhosis, but noncirrhotic portal hypertension should also be taken into consideration. Liver biopsy, preferably via transvenous route, should be convenient for discriminating cirrhotic from noncirrhotic portal hypertension.

Transvenous liver biopsy is a method that has generally been used in high-risk patients, including those with coagulopathy or ascites, or those unable to cooperate during percutaneous biopsy. The procedure has been shown to be safe, with a mortality rate of 0.0 to 0.5% and a bleeding rate of 0.0 to 0.1%, despite its usage in patients at high risk for bleeding (10). A liver biopsy via transjugular route was attempted in our case due to severe thrombocytopenia precluding percutaneous approach. The procedure could not be completed because of the stenotic vascular anomaly of the distal jugular vein. No vascular anomalies have been reported in DC to date.

CONCLUSION

Although it may merely be a coincidence, a vascular anomaly in the jugular vein should be taken into consideration in patients with DC in whom transvenous liver biopsy is planned.

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