Concomitance of idiopathic myelofibrosis and amyloidosis

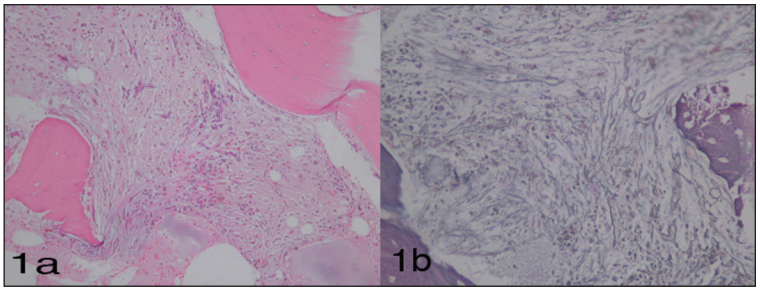

Figure 1a. Bone marrow biopsy and **(1b)** Retuciline dye showing hypocellularity and increased reticulin fibers (Hematoxylin and eosin ×100 and ×retuciline 200).

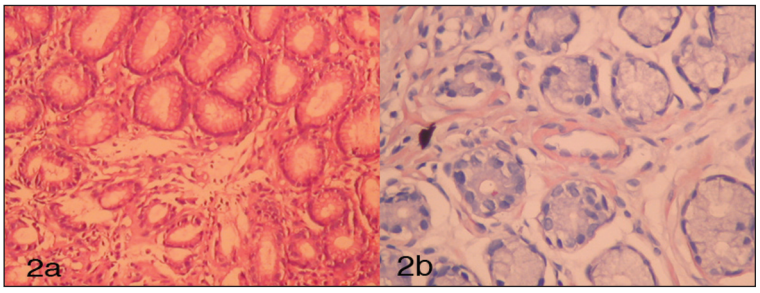

Figure 2. Renal biopsy specimen showing amyloid deposition. (Hematoxylin and eosin ×100 and Congo Red ×400)

To the Editor: Idiopathic myelofibrosis (IMF) is characterized by fibrosis of the bone marrow, extramedullary hematopoiesis primarily in the liver and spleen, splenomegaly and an increase of hematopoietic precursors in the peripheral blood. Immature granulocytes, erythroblasts and teardrop cells are observed in the peripheral blood. Although it is a disease of the elderly, it has even been reported in the neonatal period.[1] Amyloidosis is the extracellular accumulation of abnormal fibrillary protein, consequently leading to organ dysfunction.[2] Although amyloidosis is observed secondarily to some diseases, this case is of interest since development of amyloidosis secondary to idiopathic myelofibrosis is rare.

A 10-year-old male who had complaints of fatigue and foot and lumbar back pain was referred to our department after administration of multiple transfusions. At presentation, pancytopenia was detected with WBC 3200/mm^3, hemoglobin 7 g/dL and a platelet count of 32000/mm^3. A peripheral smear evaluation revealed a leucoerythroblastic reaction. Routinely, bone marrow aspiration fails because of the lack of the bone marrow medullary elements. A bone marrow biopsy performed detected a hypocellular bone marrow and a grade 3 increase in reticulin (Figure 1a and 1b). Response to corticosteroid therapy was inadequate; on-demand transfusions together with other supportive therapies and chelating therapy were carried out. Upon development of marked splenomegaly within the previous one year, etiological investigations were planned. Due to the increased requirement of transfusion, a liver biopsy and splenectomy was performed. Amyloidosis in the spleen and hemosiderin in the liver were detected. Since the patient was observed to have abdominal pain and fever episodes like those observed in Familial Mediterranean Fever (FMF) and amyloid in the spleen, fibrinogen values were investigated. FMF mutation analysis and sequential MEFV gene exon 2 and 10 region series analysis performed after detecting high fibrinogen levels revealed no FMF mutation. A renal biopsy was performed because of proteinuria. Endoscopic biopsy (**Figure 2a and 2b**) was also performed because of gastrointestinal hemorrhage revealed amyloidosis in both renal and gastric biopsies. Despite the partial improvement observed in hematological values after splenectomy, occasional erythrocyte transfusion was required. High-dose corticosteroid treatment was started (20 mg/kg) again and hematological response was achieved. After 4 years of follow up, the patient died at the age of 17 following a sepsis attack with widespread bone pain and overall status deterioration.

IMF is characterized by clonal proliferation of a single hematopoietic multipotent cell by cytokines released from abnormal megakaryocytes resulting in increased reticulin fibers in the bone marrow. As a result of these pathophysiological events, hematological clinical findings specific to disease occur.[3] Nevertheless, systemic amyloidosis could be observed mostly secondary to multiple myeloma, but rarely secondary to some other conditions such as chronic inflammation in some rheumatological and neoplastic diseases. Its association with IMF is rare and several cases were published. One of them, from Turkey, was an adult case with myelofibrosis and who was evaluated for proteinuria and recurrent diarrhea and also diagnosed as having systemic amyloidosis.[4] In three other reports, myelofibrosis with amyloidosis detected at autopsy findings.[5] In this case, renal biopsy, spleen material after splenec-

tomy and gastrointestinal endoscopic biopsy were all revealed amyloid depositions in the specimens. Bone marrow aspirations were dry tap and an increase in the reticulin fibers were presented in the bone marrow biopsy material.

Recently two children with the diagnosis of myelodysplastic syndrome has been reported as having renal amyloidosis after the proteinuria begun as other adult cases and this finding is similar to our case because of the clonal origin of both diseases.[6] Another recent report in the literature presented an adult case with the diagnosis of myelofibrosis, whose renal biopsy, performed for proteinuria, revealed amyloidosis.[7]

Although the pathophysiological mechanism(s) of amyloidosis is not known exactly, we believe that it is attributable to chronic inflammation and cytokines observed in other clonal disorders such as myelodysplastic syndrome, chronic myelomonocytic leukemia. As amyloidosis may occur secondarily to some diseases such as IMF as well. The potential for such concomitance should be kept in mind in patients with IMF or while investigating the cause of amyloidosis.

Göksel Leblebisatan,[a] Ilgen Sasmaz,[b] Bulent Antmen,[b] Melek Ergin,[b] Yurdanur Kılınç[b]

From the [a]Gaziantep Children Hospital and [b]Çukurova University, Gaziantep, Turkey

Correspondence:
Göksel Leblebisatan, MD
Pediatric Hematology
Gaziantep Children Hospital
Gaziantep 27270, Turkey
gokselleb@yahoo.com

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Cytokeratin expressing epithelioid cells in ovarian sclerosing stromal tumor: A potential diagnostic pitfall that may be mistaken for metastatic carcinoma

To the Editor: Sclerosing stromal tumor (SST) is a distinctive uncommon benign neoplasm of the ovary that mostly affects young women.[1-3] It is of unknown pathogenesis and etiology.[1] However, it is accepted that SST is part of the spectrum of sex cord-stromal tumors and several studies have supported the notion that SST belongs to the ovarian sex-cord stromal tumors category.[1,2,4,5] It is also accepted that SST may originate from the ovarian cortical stromal cells or from the perifollicular myoid stromal cells.[1,2,4]

We discovered a case of ovarian sclerosing stromal tumor with unusual immunohistochemical expression of cytokeratin (CK) that could impose an interpretation pitfall for the novice. Microscopically, SST has a heterogeneous appearance with cellular nodules that are usually separated by zones of edema or hypocellular fibrous hyalinizing stroma.[2] The vasculature is prominent with hemangiopericytoma-like staghorn blood vessels.[2] The heterogeneous cellular components include the spindle fibroblasts, the plump myoid cells, the polygonal thecalike cells, the endothelial cells of the blood vessels and primitive mesenchymal cells.[2,4] Immunostains for vimentin, inhibin, calretinin, melan-A and CD99 are usually positive, but their intensity varies.[1,3,6] The myoid cells are positive for smooth muscle actin (SMA) and sometimes for muscle specific actin (MSA) and desmin.[1,4] Positivity for estrogen and progesterone receptors has been reported.[1] The cells are usually negative for cytokeratins and epithelial membrane antigen (EMA).[1,6]

In our case, a 26-year-old woman presented with abdominal discomfort for three months. Radiology showed a right ovarian mass. The mass was resected and showed a well-defined lobulated solid tumor (**Figure 1**). Microscopically, the mass had characteristic solid cellular nodules surrounded and separated by zones of edematous and hypocellular fibrous stromal tissue with prominent vascular proliferation (**Figure 2**). The cellular nodules showed large vacuolated cells with large nuclei and prominent nucleoli (**Figure 3**). Frequent cells showed moderate atypia some of which were signet ring-like cells. Mucin stains (Alcian blue and mucicarmine) were negative. These epithelioid cells were individually wrapped by reticulin fibers.

Immunohistochemistry showed that the spindle and plump oval