Case Report

Wandering Spleen, Splenic Mesothelial Cyst and Angiomyolipoma: A New Syndrome or Coinciding Distinct Entities Reactive to Estrogen?

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Abstract

Wandering spleen is the consequence of excessive splenic mobility due to ineffective peritoneal attachment, rarely associated to splenic cysts. In cases previously reported, splenic cysts are mostly pseudocystic formations from trauma, infarction or parasitic disease. True cysts, epithelial or mesothelial lined, which are considered dysontogenetic formations, are usually not associated to wandering spleen. Angiomyolipoma is a benign triphasic tumor, usually renal. Few cases of wandering spleen associated with mesothelial cyst or angiomyolipoma are described. We present the first case to our knowledge of these three entities together; isolated evidence, once compiled, may lead to the influence of estrogen as a common factor in pathogenesis. Even though a punctual intervention in a benign panorama, we question whether these lesions act as distinct, partially associated or as the manifestation of an underlying silent syndromic disease that could harbor future outcomes to similar patients.

Keywords: wandering spleen; dermoid cyst; hormone-dependent neoplasms; angiomyolipoma; pregnancy; estrogen

Introduction

Abdominal enlargement may become a diagnostic challenge to the internal practitioner. Splenomegaly may not be a prompt differential diagnosis, especially if presented as a wandering spleen (WS), a condition in which anatomical contours are transgressed due to ineffective peritoneal attachment and, consequently, the spleen is displaced from the upper abdomen to pelvis.[1] Although mostly benign in origin, WS may lead to life-threatening complications, as splenic torsion, ischemia and rupture.[2,3] Other splenic diseases may coexist along with WS: cysts, which may behave as pseudocysts, usually secondary to trauma, infarction and parasitic disease, or; true cysts, epithelial or mesothelial-lined dysontogenetic formations.[4]

We have observed an unusual association between WS, mesothelial cyst (MC) and splenic angiomyolipoma (AML). MC is a benign mesothelium-derived lining epithelial embryological remnant[4–6] and AML is a triphasic benign tumor.[7] Our scope in this report is to discuss this unusual association, its diagnostic challenge and the role played by estrogenic influence over this triad of benign lesions that lead to an estrogenic-responsive splenoma (ERS).

Clinical Summary

A 17-year-old woman presented with an

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enlarged abdominal mass associated with postprandial discomfort six months after labor. Six months prior to her admission, a palpable abdominal mass associated with thrombocytopenia led to a bone marrow biopsy, which only displayed decreased iron reserves. No past illness, trauma and familial cancer history were present. Laboratory data were normal, except for slightly elevated CA-125 levels (37.3 U/mL; normal: 0-21 U/mL). Physical examination revealed a mass in the lower abdomen that on computed tomographic (CT) scan resembled splenic contours, notwithstanding its transgressed anatomical placement (Figure 1A) depicted by disrespected abdominopelvic boundaries protruding below the inferior iliac crest. Signs of pulpar congestion, reflected by parenchymal enlargement, were the only characteristic findings. Splenectomy was performed and after one year of follow-up, the patient was well, without signs of further disease.

Pathological Findings

Gross anatomy revealed a 1.475 kg spleen with 18 x 14 x 12 cm of dimension. Below the internal capsule, an intra-pulpar thin-walled cyst of 15 x 14 x 12 cm filled with clear fluid content, was seen (Figure 1B). Adjacent to the cyst, a gray-white well-circumscribed tumor, measuring 1.5 cm of diameter, was also observed. Microscopically, the cyst showed a single layer of cuboidal mesothelial cells without cytologic atypia (Figure 1C), positive for cytokeratin and calretinin, but negative for carcinoembryonic antigen [8] (Figures 1D, 1E and 1F, respectively). Immunohistochemistry study for estrogen and progesterone receptors (ER and PR, respectively) was performed, with exclusive immunolabelling to ER (Figures 1G and 1H, respectively). The other lesion consisted of a triphasic benign neoplasm composed of myoid spindle cells, islands of mature lipid cells and thick walled vessels. The case was diagnosed as wandering spleen associated with mesothelial cyst and angiomyolipoma.

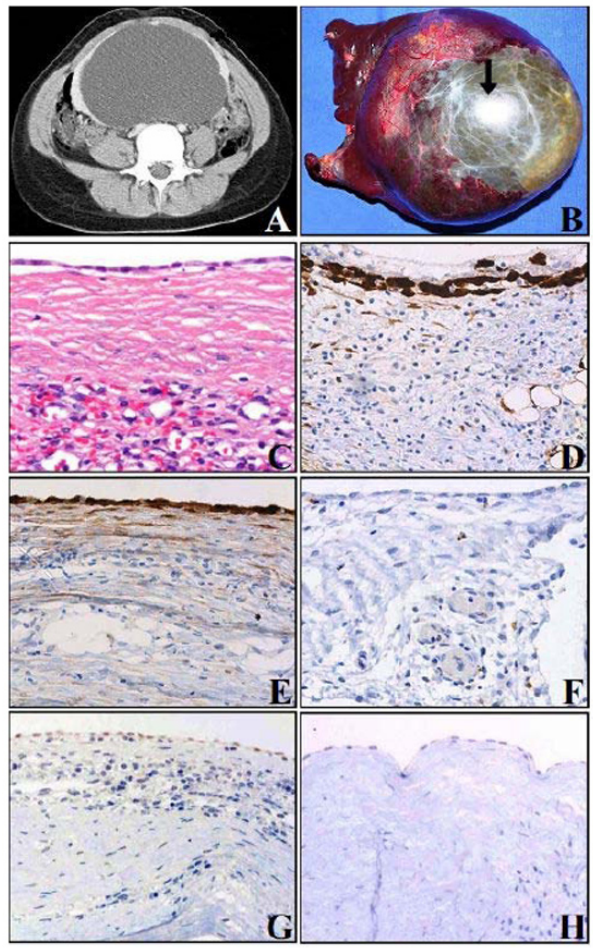

Figure 1- (A) A large intra-abdominal mass not respecting abdominopelvic boundaries is observed in this CT scan. Parenchyma is augmented, resembling spleenig pulpar congestion. (B) Gross anatomy revealed an enlarged spleen containing a thin-walled cyst with clear fluid content (arrow). (C) The cystic lesion shows a single layer of flattened mesothelial cells, without cytologic atypia (HE X 40). The cystic lesion displayed positive immunolabelling to cytokeratin (D) and calretinin (E), but negative for carcinoembryonic antigen (F) (immunohistochemistry X40). The cystic lesion was labelled by estrogen receptor (G), but not by progesterone receptor (H) (immunohistochemistry X40).

Discussion

Wandering spleen is a low-incidence disease, as evidenced by being the cause of approximately 0.20% of splenectomies.[2,3] In a classical series from 40 years of experience at Mayo Clinic, only two of 1003 splenectomies were due to WS.[5] Females have historically been a risk group for WS development, with seven times greater incidence than males after age 10 (1:7).[1] Recent reports have associated the effect of estrogen exposure in pregnancy to an increased laxity and decreased ligament stability.[6,7,9,10]

Splenic cysts also present a low incidence profile. Around one thousand cases are reported in the literature;[11] the overall incidence on general population is estimated at approximately 1%,[12] with a female

predominance of almost 2:1 (female:male) in some series.[13] Additionally, splenic cysts have been historically grouped into two categories: parasitic and nonparasitic, based on etiology and into true or false (pseudo), based on histology, according to the cells lining of its walls. [4] Much has been questioned over classifications.[4,13] In this report, we adopt the classification proposed by Mirilas et al. [3] that regards MC as a true nonparasitic congenital cyst, which represents less than 10% of splenic cysts, an especially uncommon entity.[14] Histopathogenesis is unclear once these cysts, also known as serous cysts, are lined by mesothelium-derived cells[11] that may have been originated from developmental misplacement of mesothelial-epithelial structures of the primitive spleen.[15] Investigators have observed migration of these primitive cells from the coelomic to cystic surface.[16] Also, splenic capsule and other abdominal viscera have been associated to this developmental pattern.[15]

Differential diagnosis to malignant mesothelioma is obtained by histological exam, once malignancy resembles adenocarcinomas and other epithelial tumors; [17] malignant disease is not associated to the expression of estrogenic receptors,[17] as observed in some mesenchymal tumors, as in hepatobiliary cystadenoma[18] and in myolipoma of the broad ligament,[19] in which migration of mesenchymal tissue during embryogenesis is also hypothesized to play a key pathogenic role.

AML are benign tumors composed of triphasic elements that usually behave in a benign and asymptomatic manner.[20] Although originally regarded as hamatomatous tumors,[21] AML have actually been defined as a benign clonal mesenchymal neoplasm, included in the family of perivascular cell derived tumors. [22] There are two main forms of this disease, a sporadic form, which accounts for approximately 70-80% [23] and a tuberous sclerosis complex associated form, caused by dominant mutation on genes located on chromosomes 9q and 16p (TSC1 and TSC2, encoders hamartin and tuberin, respectively).[23,24] The triphasic composition varies among diverse presentations, from the combination of varying amounts of thick-walled dysplastic or dysmorphic vascular elements, spindled or epithelioid differentiated smooth muscle elements and mature adipose tissue.[22] Mainly renal in origin, it may display scattered distribution throughout the body. [25] Primary splenic AML has been reported only once, [25] while splenic and renal concomitant lesions were reported by three investigators.[26-28]

Its etiology is poorly comprehended, although epidemiological data may abate hormonal influence, once a female predominance (4:1 female to male rate) is observed in sporadic forms.[22] Additional evidence to this hypothesis is presented by isolated reports of tumor progression during hormone replacement therapy [29] and pregnancy.[30] Boorijan et al.[24] have shown that renal AML arising in female patients expressed ubiquitously estrogen receptors (ER) while nearly 80% expressed aromatase (AR). ER, progesterone receptors and AR were inversely correlated with age. Investigators have also hypothesized the estrogenic expression as consequence of metaplastic response in extra-renal AML and MC.[31]

Recently, isolated reports have fostered evidence to estrogenic responsive elements linked to the conditions we report: on WS, as evidenced during increased ligament laxity during pregnancy;[9] on AML; [7] and on mesothelium-derived epithelia in some cystic tumors.[10] This report presents further evidence, once immunohistochemical labeling to ER in splenic tissue was observed after prolonged estrogenic exposure by pregnancy.

Some have questioned the antagonism of estrogenic receptors as a manner of halting progression of disease on prone individuals (those displaying ER positive tumors), as has been reported on a case of liver hamartoma.[10] Although evidence is still rudimentary, further observational studies may shed some light into the efficiency of estrogenic antagonism in these patients.

Both WS and MC are benign conditions subject to complications that may lead to fatal disclosure.[7,32] Each harbor the stigma of "rare diseases" due to low incidences, commonly being diagnosed as incidental imaging findings on asymptomatic patients or during acute abdominal pain. English language literature contemplates twelve cases reported of this association. However, WS, MC and primary AML has not been described before.

In this report, besides describing this association, we propose a pathophysiological explanation that abridges all the phenomena into an estrogen related disease, which we denote estrogenic-responsive splenoma (ERS). This uncommon association might shed some light over the role played by hormones on neoplastic development and the broad application of hormone antagonists.

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