Primary Splenic Epithelioid Angiosarcoma – Case Report

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Abstract

Primary splenic angiosarcomas are extremely rare malignant tumors of mesenchymal origin. This tumor has very high rate of metastasis and generally associated with poor prognosis. We describe a case of 79-year-old patient with non-specific clinical presentation.

Introduction

Primary spleen neoplasms, with an exception of lymphoma, are uncommon. Splenic angiosarcoma, although the most common primary non-lymphoid neoplasm of the spleen is overall extremely rare mesenchymal malignant tumor of vascular endothelial origin with annual incidence of 0.14 to 0.25 cases per million, generally being amongst rarest types of neoplasms.

Case Presentation

A 79-year-old woman was brought to the emergency department with complaints of abdominal pain for several months. On physical examination ascites is confirmed. In our ER, patient underwent blood examination, which showed normocytic anemia (RBC 4.10 × 10¹²/L; HCT 35.9%), mild elevation of D-dimers (18.68 mg/L FEU), hepatic markers (Total bilirubin 25 μmol/L; Direct bilirubin 6 μmol/L; Indirect bilirubin 19 μmol/L; AST 43 U/L) and C-reactive protein (14.95 mg/L). Coagulation tests without abnormalities. Additionally, abdomen and lesser pelvis Computer Tomography (CT) scans with contrast medium Visipaque 320 were performed, which revealed enlarged spleen (14.0 cm × 5.5 cm) with hypodense poorly demarcated mass (6.0 cm × 9.0 cm) with heterogenous contrast medium enhancement in the superior pole. From portal vein up to middle third on level of corpus pancreaticus, v. splenica with thrombotic masses (prominent contrast medium demarcation in both venous and arterial phase) which extend into segmentary branches. CT findings indicative of tumorous thrombotic masses. Another finding included hypovascular node (up to 2.0 cm in diameter) in III segment of the left hepatic lobe. Radiological conclusion of malignant splenic neoplasia with v. splenica thrombosis and liver metastases (Figures 1-3). Tumor marker lab tests were performed – CEA and α-fetoprotein were within normal range, but there was marked mild increase in CA 19-9 (141.9 U/mL) and CA 125-2 (189.0 U/mL). Due to bleeding risk ultrasound guided hepatic biopsy was unfeasible. Further therapy tactic involved spleen embolization. In adjunct, liver nodule excision was performed intraoperatively. Surgery resulted in ~90% devascularization of splenic parenchyma. Afterwards, patients’ condition deteriorated; spleen infarction with abscess formation was radiologically confirmed. Laparoscopic splenectomy was indicated with no absolute contraindications. Laparotomy was performed; on inspection hemoperitoneum (in lesser pelvis), grossly splenic neoplastic process. Splenectomy was performed with linear cutting stapler. Liver biopsy material was also retrieved during the surgery. After the surgery, the patient was observed and subsequently discharged with optimal general condition. In postoperative period, patient received gynecological consultation under ultrasound-based suspicion of endometrial hyperplasia. Endometrial cytology examination was performed; prismatic epithelium with no cell atypia was found (A1).

Histopathological Findings

Spleen weighed 460 g and measured 17 cm × 10 cm × 6 cm with one nodule with 10 cm diameter in one pole and 1.7 cm diameter in spleen hiatal fat tissue. All nodules were soft grayish, whitish color with multiple hemorrhages. Histopathological examination revealed tissues containing tumor nodules composed of vascular spaces lined by epithelioid, multilayering atypical cells mostly arranged in solid areas (Figure 4). These areas exhibited high mitotic activity (35 to 50 mitotic figures in 10 consecutive High-Power Fields (HPF)). Tumor cells demonstrated moderate nuclear pleomorphism with size, shape, and staining heterogeneity. Peritumoral area contained
mild lymphoplasmacytic infiltration and mild stromal desmoplasia. Additionally, two sarcoma nodules (interpreted as distant metastasis) were evacuated from the liver with negative resection lines (Figure 5). Diagnosis of epithelioid angiosarcoma grade 3 was set based on WHO 2020 and FNCLCC diagnostic criteria. Tumor staging in accordance with AJCC 8th Ed. Guidelines (2020 revision). Tumor stage according to TNM classification - pT4aN0M1 L+V+R0.

On the resection line of v. splenica sarcoma complexes were found. Macroscopically, nodes in v. splenica, which are formed of splenic blood vessels with sarcoma complexes with lumina invasion. Spleen capsule was intact. Resection lines without tumor cells. In splenic hiatal area one lymph node with reactive changes 0.9 cm in diameter was detected. Immunohistochemically, tumor cells both in the spleen and liver samples expressed CD31+, EMA+, and CK+. Both samples were CD8-, CD68-, and CD34- negative. High proliferation fraction with Ki-67 >80% (Figure 6 and 7). IHC supported the impression of the diagnosis.

Discussion

Primary spleen neoplasms, with an exception of lymphoma, are uncommon. Splenic angiosarcoma, although the most common primary non-lymphoid neoplasm of the spleen is overall extremely rare mesenchymal malignant tumor of vascular endothelial origin.
with annual incidence of 0.14 to 0.25 cases per million, generally being amongst rarest types of neoplasms [1,2]. In literature, it has been reported under variety of designations, such as, hemangiosarcoma, malignant hemangiendothelioma, and endothelial sarcoma, with some cases being falsely attributed the diagnosis of angiosarcoma. Currently, etiopathogenesis of splenic angiosarcoma is unknown [3], while some cases show association to prior chemotherapy for lymphoma and exposure to ionizing radiation; in some cases, hemangiomas and hemangiendotheliomas being reported as precursor lesions for splenic angiosarcoma [2]. Development of angiosarcoma is possible at any age, with median age of 50 to 60 to 65 years [4,5]; incidence in pediatric population is very low [2,6,7]. There seems to be no gender predominance, with some studies showing slight male predominance [8] clinical presentation upon admission is often diagnostically ambiguous. Non-specific symptoms, such as, abdominal pain (75% to 83%), splenomegaly (71% to 100%) weakness/fatigue (5% to 39%), fever (10% to 21%), and weight loss (10% to 40%), have been consistently reported in numerous case reports and systemic reviews [4,5,7,8], where pain and/or tenderness in the left upper abdominal quadrant is the most common [7,5]. In fewer cases following symptoms have been reported - chest pain (10%) [4], severe lower back pain with bilateral weakness in legs, ascites, bleeding gums [6,7]. The duration of symptoms is variable, in one review being reported lasting from 1 to 7 months, with an average of approximately 2 months [4]. The most common sites for early metastases include liver (89%), lung (78%), lymph nodes (56%), and bone marrow (22%) [9]. Follow-up blood works show anemia (46% to 75% to 81% [1,7]) and thrombocytopenia (14%, 55% [8]) in the hemogram, with anemia being the most common finding. Additionally, elevated tumor serum markers may be identified, albeit may not be diagnostically valuable in case of angiosarcoma. While tumor markers CA 19-9 and CA 125-2 are primarily associated with pancreatic and gynecological tumors, respectively, they have been rarely reported in cases of angiosarcomas, with at least one case report showing elevation of both markers [10]. Increase of these tumor markers may not be clinically important for the diagnosis of splenic angiosarcoma, as the elevation of CA 125-5 may be attributed to ascites (both in our and aforementioned case) [10-12]. Increase of CA 19-9 has been shown to be elevated in both benign and various malignant conditions [13-15]. CT scan findings indicative of splenic tumor include splenomegaly with large mass or masses with or without metastases (liver or spine) variably described as hypodense, in-homogenous, heterogenous, with liver metastases being more common. In majority of cases (83%), primary splenic neoplastic process could be suggested based on radiographic findings alone, with angiosarcoma being high on the list of differential diagnoses [4,16]. Microscopic findings of spleen angiosarcoma are identical to angiosarcoma of soft tissues, while varying amongst cases. Degree of differentiation, typical growth patterns as well as cell populations may vary within the tumor. Degree of differentiation may differ in different areas, but significant nuclear pleomorphism is at least focally present. Presence of malignant vasiformative (anastomosing vascular channels lined by atypical endothelial cells) component is, in general, more frequent than solid mass, though spindle cell fascicles and papillary formations are also possible [1,4,5]. Immunohistochemical findings show positive expression of at least 1-2 endothelial markers (vWFAg+, CD31+, and CD34+) with CD31+ being considered highly specific, as it is positive in approximately 90% of angiosarcomas of all types [4,8]. Significant histological prognostic factor includes mitotic counts; other histologic factors were not significant for survival [17]. Splenectomy remains preferred treatment in case of splenic angiosarcoma. Other possible treatments include chemotherapy and radiotherapy, but without existing guidelines and evidence-based recommendations, efficacy of these treatments may not be properly assessed. Findings in our patient are consistent with findings in various systemic reviews and case reports.

**Conclusion**

We describe a case of primary epithelioid splenic angiosarcoma. In our case, initial presentation of patient with symptoms of low diagnostic value, opens the possibility to plethora of differential diagnoses. While radiological findings give impression of neoplastic process, histological microscopic and immunochemical findings give better understanding of tumor nature. Definitive diagnosis prior surgery remains challenging, therefore characteristic radiological findings and patient history must be combined and evaluated to suggest splenic angiosarcoma.

**References**

