Case Report

rare tumors

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Primary leiomyosarcoma of the colon with synchronous liver metastasis

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Introduction

Leiomyosarcomas (LMS) are mesenchymal tumors of smooth muscle origin. Approximately 20% of leiomyosarcomas are found in the GI tract, and account for 1–2% of GI malignancies.[1] Within the gastrointestinal tract, the small intestine is the most common site of presentation followed by the colon.[2] They are often diagnosed incidentally during abdominal pain investigation, and they usually present in the fifth decade of life. In the past, the diagnostic differentiation between leiomyosarcomas of gastrointestinal tract and gastrointestinal stromal tumors (GISTs) was very challenging as they share common microscopic appearance.[3] Nowadays, these tumors are diagnosed by immunohistochemical methods as they are positive for smooth muscle markers actin (SMA) and desmin, negative for GIST markers such as receptor tyrosine kinase (KIT), CD34, DOG1, and negative for the schwannoma marker S100 protein.[4,5] In the current literature, most cases of intestinal leiomyosarcomas are localized in the small intestine, and there are no reports of synchronous liver metastases at the time of presentation of the primary tumor. Herein, we present a patient who was admitted in our department, with the diagnosis of primary leiomyosarcoma of the colon and synchronous liver metastasis.

Case report

A 74-year-old female patient with a history of hyperthyroidism was referred to our hospital for investigation of atypical epigastric pain. The physical examination was unremarkable. After thorough investigation, a liver tumor was diagnosed by an ultrasound in the segments V and VI. An MRI scan confirmed the diagnosis of a tumor in the right lobe of the liver with dimensions of 6.7×8×7 cm (Figure 1(a), (b), (c), (d)) and a mass of the descending colon was also described (Figure 1(e), (f), (g)). Blood tests were normal regarding liver biochemistry and serum tumor markers were within normal range. Serology testing was negative for viral hepatic disease. An upper GI endoscopy was performed with no pathological findings. A colonoscopy followed, and a mass in the descending colon was revealed that occluded ¾ of the intestinal canal (Figure 2). Biopsy specimens reported multiple cells with atypia, while immunochemistry was negative for S100, CD117, and CD34. The patient was presented at the multidisciplinary team (MDT) meeting of our hospital and a surgical approach was suggested as the appropriate treatment. During an exploratory laparotomy, left colectomy and segmental hepatectomy was performed removing segments V and VI of the liver. The pathology report of the surgical specimens reported the mass of the colon as a leiomyosarcoma, and the liver specimen as metastatic focus from the colonic leiomyosarcoma. Microscopically, the leiomyosarcoma of the colon had a maximal size of 4 cm in continuity with the muscularis propria, and it was composed of spindle cells with high grade nuclear atypia (Figure 3(a)). The mitotic

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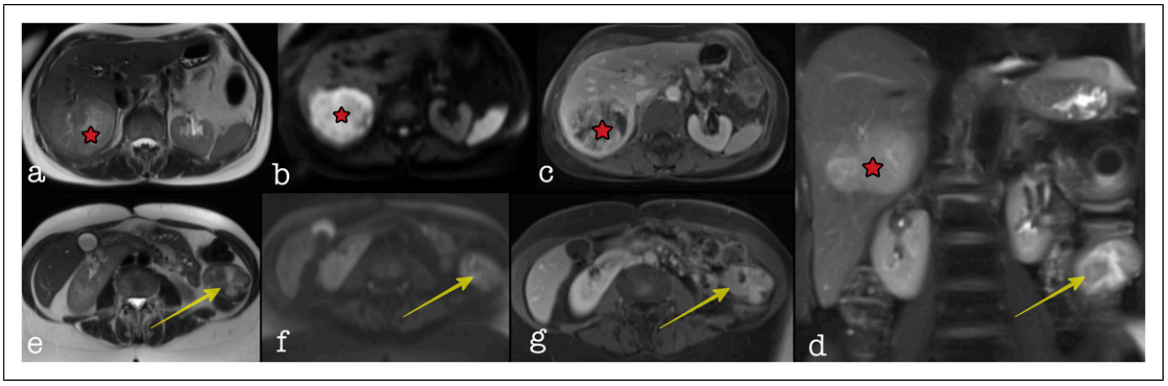

Figure 1. MRI: (a) Axial T2W, (b) axial DWI, (c) axial contrast-enhanced T1W, (d) coronal T2, (e) axial T2, (f) axial DWI, (g) axial contrast-enhanced T1. Right liver lobe mass in liver segments VII/VI (red star) with inhomogeneous high T2 signal, intense diffusion restriction (b) and inhomogeneous intense contrast enhancement (c). Pedunculated polypoid mass (yellow star), in transverse colon protruding in descending colon with high inhomogeneous T2 signal, diffusion restriction and intense contrast enhancement.

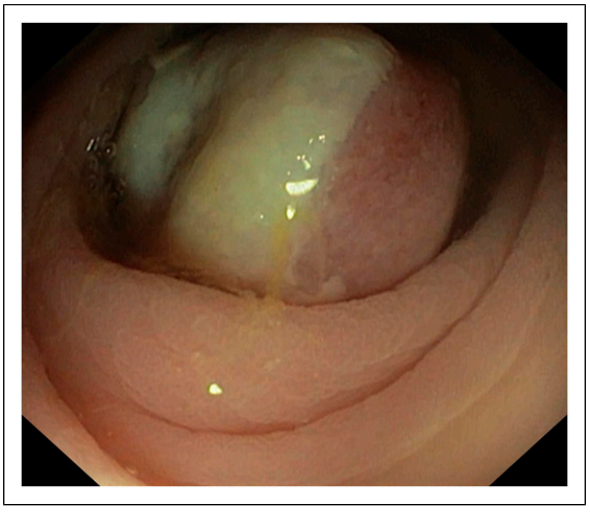

Figure 2. Endoscopic image of colonic mass in the descending colon obstructing the intestinal canal.

activity was high with ki-67 index of 40% (Figure3(b)). Additionally, several lymph nodes were present in the specimen with one paracolic lymph node positive with metastasis (Figure 3(e)). Immunohistochemically, the tumor cells were positive in vimentin, aSMA, desmin, and caldesmon (Figure 3(c) and (d)), whereas MDM2, CD34, S100, CD117, and DOG1 markers were negative. The liver specimen was a high-grade metastatic neoplasm with a maximal volume of 13 cm. The immunohistochemical characteristics were similar to those of the primary tumor in the colon (Figure 3(f)). The patient had an uncomplicated postoperative course and was discharged on the seventh post-operative day. During the follow-up, the patient received no chemotherapy. The patient deceased after 10 months due to multiple lung metastases.

Discussion

Leiomyosarcomas (LMS) of the gastrointestinal tract, and more specifically of the colon, are a very rare entity of primary tumors in the GI tract. Previously, these tumors were classified as GI leiomyomas, leiomyosarcomas, or schwannomas on the basis of histologic findings and the fact that these tumors apparently originate in the muscularis propria layer of the intestinal wall. In 1998, Hirota et al. reported the oncogenic role of KIT in GISTs making the differentiation of these tumors possible.[6] With the advent of immunohistochemical staining techniques and ultrastructural evaluation, GISTs now are recognized as a distinct group of mesenchymal tumors. According to the present classification, GISTs account for approximately 80% of mesenchymal tumors.[7,8,9] As a result, many tumors that were previously characterized as leiomyosarcomas are now characterized as GIST due to their different histopathological characteristics. Leiomyosarcomas of the gastrointestinal tract are aggressive neoplasms and have a poorer prognoses than adenocarcinomas or GISTs.[10] Additionally, they have such a low prevalence that there are no demographic or clinical data of the disease. Consequently, it is important to differentiate the diagnosis of LMSs from other mesenchymal tumors, particularly GISTs, as those two have different strategies in therapy and different prognoses.[11] Firstly, the cellular origin of GISTs is the interstitial cells of Cajal in the muscularis propria, while the proposed cellular origin of smooth muscle tumors is the fibers of the muscularis mucosae and muscularis propria. Furthermore, GISTs occur most commonly in the stomach (60–70%) followed by the small intestine (20–25%), rectum and anus (4%), and colon (1%). In contrast, leiomyosarcomas occur preferentially in the small intestine (45%), colon (38%), and are extremely rare in stomach and esophagus.[12,13] Finally, the hallmark histochemical stain that differentiates LMS

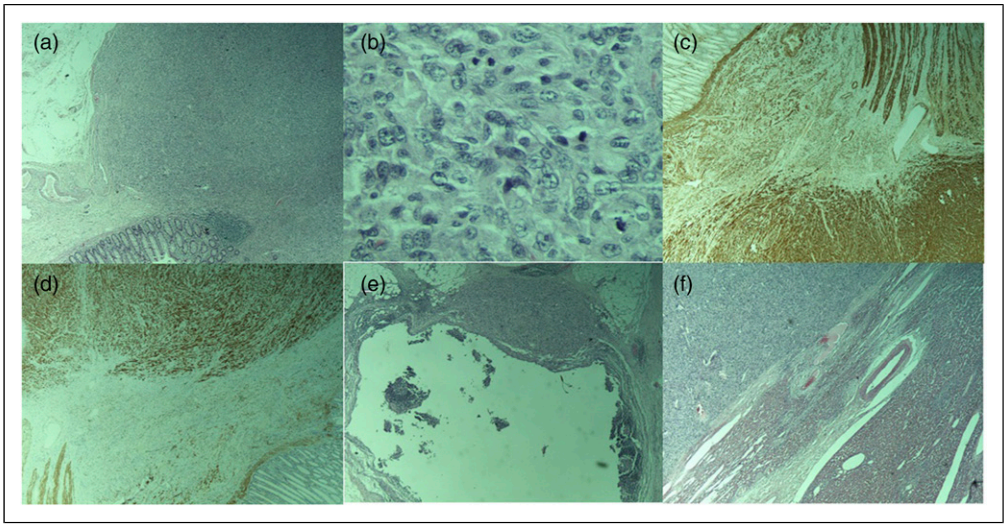

Figure 3. (a) The bulk of the tumor occupies the muscularis propria of the colonic wall. The neoplasm is growing circumferentially as well as transmurally, replacing the colonic submucosa and mucosa (hematoxylin-eosin staining original magnification ×20). (b) The tumor is composed of spindle-like and elongated cells with round nuclei and coarsened chromatin, displaying moderate to severe atypia. At least mitoses can be identified in this high power field (hematoxylin-eosin staining original magnification ×400). (c and d) Immunohistochemically, the neoplastic cells were strongly and diffusely positive for smooth muscle cell markers (c): h caldesmon x20, d:desmin ×20). (e) Paracolic lymph node with metastasis from the malignant mesenchymal neoplasm of the colon (hematoxylin-eosin staining original magnification ×20). (f) The tumor of the liver showed the same morphological and immunohistochemical characteristics with the colonic tumor and was considered metastatic (hematoxylin-eosin staining, original magnification ×20).

from GIST is KIT, which is uniformly positive in GIST, but is generally negative in LMS. LMS will stain positive for smooth muscle markers actin and desmin, and will have negative CD117, CD34, and DOG1 stains, which are positive in GIST.[14]

The typical presentation of leiomyosarcomas of the gastrointestinal tract is in middle-aged patients with a mean age of diagnosis of 50 years of age. Initial symptoms include abdominal pain, rectal bleeding, weight loss, or even constipation. LMS of the colon was found to be more aggressive compared to other colonic tumors and has a high local recurrence rate and significant hematogenous spread and rare lymph node involvement.[15,16] When present, metastases most commonly occur in the lungs and peritoneum but can occur in the liver as well. The most common cause of death in these patients is metastatic spread to either the liver or the lungs, as in our case.[14]

The best treatment plan for patients presenting with a leiomyosarcoma is surgical resection although that many of them recur even after adequate resection. Chemotherapy and radiation have shown limited benefit in these patients. Conventional chemotherapy for soft-tissue sarcomas based on anthracyclines is the first-line treatment for these patients. In addition, doxorubicin plus dacarbazine is another option as multi-agent first-line chemotherapy.[17] However leiomyosarcomas are relative resistant to chemotherapy.[12]

Conclusion

Leiomyosarcomas of the colon are a rare entity of gastrointestinal tumors and have highly aggressive characteristics. They often metastasize in the lung and rarely in the liver. These neoplasms are usually characterized as GISTs in the primary investigation due to the similarities that share radiologically and clinically. However, the correct differentiation for the diagnosis is crucial as different treatment plans are offered to the patients. The suggested treatment plan for leiomyosarcomas of the colon is surgical excision, as they are usually resistant to chemoradiotherapy.

(1) Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series

(2) Informed consent

Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

Declaration of conflicting interests

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Ethical approval

Reporting of individual rare cases does not require Ethical Committee approval at our institute—University of Athens, Aretaieion Hospital.

Informed consent

Informed consent was taken from patient.

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