

Intraabdominal Schwannomas

Single-center experience



Ann Ital Chir, 2021 92, 2: 172-179
pii: S0003469X21031067
Online ahead of print 2020 - Oct. 14
free reading: www.annitalchir.com

Ahmet Gökhan Sarıtaş*, Uğur Topal*, Abdullah Ülkü*, İsmail Cem Eray*, Burak Yavuz*, Tolga Akçam*, Figen Doran**

*Department of General Surgery, Cukurova University Faculty of Medicine, Cukurova/Adana, Turkey

**Department of Pathology, Cukurova University Faculty of Medicine, Cukurova/Adana, Turkey

Intraabdominal Schwannomas: single-center experience

OBJECTIVE: Intraabdominal schwannomas are rare benign tumors. In this study, we aimed to present our clinical experience in patients with intrabdominally located Schwannoma.

MATERIAL-METHOD: Patients who received the diagnosis of intrabdominal schwannoma between 2011-2019 were retrospectively examined. Demographic and clinical characteristics, treatment methods, short- and long-term results and immunohistochemical characteristics of the patients were analyzed.

RESULTS: A total of 7 patients were included in the study. Four patients were female and three were male. The mean age was 51.5 (31-63) years. The most common clinical presentation was abdominal pain (57.1%). Tumor location was stomach (n=2), pelvic region (n=2), rectum (n=1), retropancreas (n=1), and left juxtadrenal space (n=1). Postoperative wound infection developed in one patient and pancreatic fistula complication was seen in one patient. Re-admissions to the hospital were due to anemia and pleural effusion in two patients. The mean tumor diameter was 6 cm (0.3-13 cm). All patients were S 100 strongly positive Mitoses / 50 HPFs (high power field), <2 Ki67 <3%. The mean follow-up period was 60 months. Currently, 5 patients are being followed without disease, 1 patient survives despite recurrence and 1 patient has died due to non-cancer reasons.

CONCLUSION: Intrabdominal schwannomas are rare tumors which most commonly exhibit gastrointestinal involvement. Since these tumors are mostly benign, the long-term prognosis of patients is good. Schwannoma should be kept in mind in the differential diagnosis of intrabdominal masses. Radical resections with high morbidity and mortality should be avoided if preoperative diagnosis is made.

KEY WORDS: Abdominal tumor, Mesenchymal tumor, Nerve sheath tumor, Schwannoma.

Introduction

Schwannoma is a benign tumor originating from Schwann cells in the peripheral nerve sheath ¹.

Schwannoma is a homogenous tumor and can occur in any tissue of the body. Although the most common localization is the head and neck region, it is rarely seen in

the intraabdominal region. In the intraabdominal region, it is mostly seen in the gastrointestinal tract 1) GIS (Gastrointestinal System) schwannomas were first reported by Daimaru et al. in 1988 ². Gastrointestinal schwannomas are most commonly seen in the stomach (83%), small intestine (12%) and rarely localized in the colon and rectum. However, intraabdominal, pancreatic and retroperitoneal schwannomas are extremely rare ³⁻⁵.

Gastrointestinal schwannomas are equally common in both sexes. It is most common between the ages of 50-60 and has the highest incidence in the sixth decade of life ^{6,7}. Although most of the Schwannoma cases are benign and asymptomatic, there is a potential for malignant transformation and this is related to the size of the tumor ⁶.

Pervenuto in Redazione Giugno 2019. Accettato per la pubblicazione Settembre 2019.

Correspondence to: Uğur Topal M.D, Department of General Surgery, Cukurova University Faculty of Medicine, 01100 Sarıçam/Adana Turkey (E-mail: sutopal2000@hotmail.com)

Pancreatic schwannoma is a slowly growing, encapsulated, benign neoplasm, typically presenting in the peripheral epineurium of the sympathetic or parasympathetic autonomic fibers of the pancreas or branches of the Vagus nerve ⁷.

Schwannomas in the adrenal medulla are very rare. Retroperitoneal localized schwannomas occur especially in the juxta-adrenal space and differential diagnosis should be made with adrenal masses. It has been shown in the literature that approximately 0.5% to 5% of schwannomas are retroperitoneal ⁸.

Preoperative diagnosis of soft tissue schwannomas is difficult ⁹. Complete resection with negative surgical margin should be performed for definitive treatment ¹⁰.

A limited number of series have been reported in the literature on intrabdominal schwannoma ^{3,9,11}. Our knowledge of these rare tumors is often based on case reports.

In this study, we aimed to present our clinical experience in patients operated on with the diagnosis of intraabdominal schwannoma in a tertiary referral center.

Material-Method

Patients with a diagnosis of schwannoma with intrabdominal localization, who were diagnosed between January 2011 and January 2019 in the General Surgery Clinic of Çukurova University Medical Faculty based on the combination of histological and immunohistochemical features, were included. Approval was obtained from

the Local Ethics Committee 89/1numbered and 14.06.2019 dated. Patient files and hospital information system records were examined and a database was created. The cases were analyzed retrospectively. Follow-up data were supported by telephone interviews with patients. Patients under 18 years of age and patients whose records could not be reached were excluded from the study.

Patients' demographic characteristics, Body Mass Index (BMI), American Society of Anesthesiologists (ASA) score, presenting symptoms, tumor localization, histopathological and immunohistochemical features of the tumor, treatment procedures, intraoperative complications, postoperative complications, postoperative hospital stay, unplanned re-operation, postoperative 90-day mortality, 90-day unplanned re-admission, mean follow-up times and current clinical status were analyzed.

Anastomotic leakage was defined as the deterioration of anastomotic integrity detected by clinical and radiological imaging methods.

Wound infection was defined as superficial or deep surgical site infection in the incision according to the definition of Centers for Disease Control and Prevention (CDC) ¹².

Unscheduled re-operation was accepted as a surgical intervention under general, spinal or epidural anesthesia within 30 days after primary surgery, according to the definition of the National College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) ¹³. Data were analyzed using IBM SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, N.Y., USA).

TABLE I - *Demographics and Clinical Characteristics of patients*

Case no.	Age/Sex	BMI	ASA	Clinical presentation	Tumor location
1	31/F	17,5	1	Abdominal pain	Left juxtadrenal space
2	63/F	22,9	2	Constipation	Pelvic
3	49/F	28,1	3	Abdominal pain, Dyspepsia	Stomach small curvature
4	55/F	24,5	2	Intrabdominal mass	Pelvic
5	59/M	24,2	1	Abdominal pain, Dyspepsia	Stomach small curvature
6	46/M	25,9	1	Abdominal pain	Retropancreas
7	58/M	26	1	Constipation	Rectum

TABLE II - *Operative procedures, surgical morbidity*

Case no	Surgical approach	Intraoperative complications	Postoperative complications	Postoperative Length of Hospital stay(day)
1	Partial Pancreatectomy+R-Y Pancreatojejunostomy	-	Pancreatic Fistula	32
2	Mass excision	Sudden hypotension	-	13
3	Proximal Gastrectomy +Esophagogastrostomy	-	-	9
4	Cytoreductive Surgery + HIPEC	-	Wound infection	11
5	Wedge Resection	-	-	75
6	Debulking	-	-	-
7	Transanal Excision	-	-	1

Categorical measurements were summarized as numbers and percentages, and continuous measurements were summarized as mean and standard deviation (median and minimum-maximum where necessary).

Results

Seven patients, 4 female and 3 male, were included in the study. The mean age of the patients was 51.5 ± 10.7 (31-63) and the body mass index was 24.1 ± 3.4 (17.5-28.1). The most common clinical presentation was abdominal pain (57.1%). The tumor was mostly located in the stomach (28%) and the pelvic region localization was 28%. Demographic and clinical characteristics of the patients are shown in Table I.

Six patients underwent laparotomy and resection of tumor. One patient underwent transanal resection of rectal schwannoma. Intraoperative sudden hypotension developed in one patient and the operation was continued after treatment. One patient developed pancreatic fistula and one patient developed wound infection. The mean length of hospital stay was 11 ± 10 (1-32) days. Operative procedures and surgical morbidity of the patients are shown in Table II

None of the patients required reoperation or developed postoperative mortality. One patient had an unplanned re-admission due to pleural effusion and one patient due to anemia. Mean follow up was $60 \pm 23,7$ (37-98) months. Five patients were followed-up without disease and one patient was still alive despite recurrence. One patient died of unrelated causes. Clinical outcomes of the patients are shown in Table III.

Mean tumor diameter was $6 \pm 4,5$ (0.3-13) cm. Mitoses/50 (HPFs), <2 Ki67 $<3\%$ in all patients. The histopathological and immunohistochemical properties of

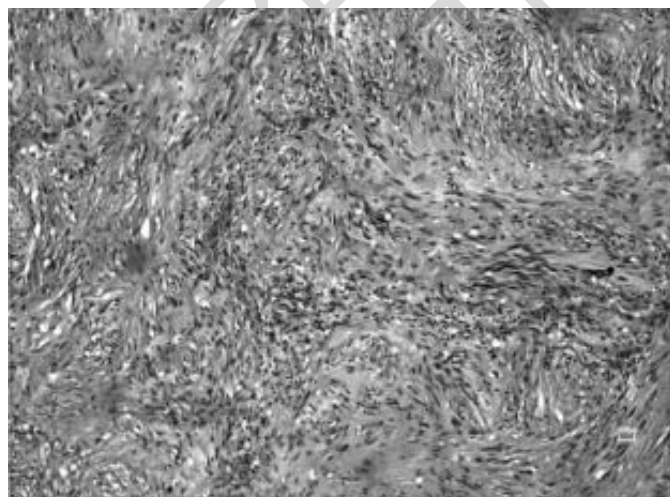


Fig. 1: H&E X200 Schwannoma in the stomach. The cytoplasmic boundaries of spindle cells are not apparent. Cell-rich and cell-poor areas coexist.

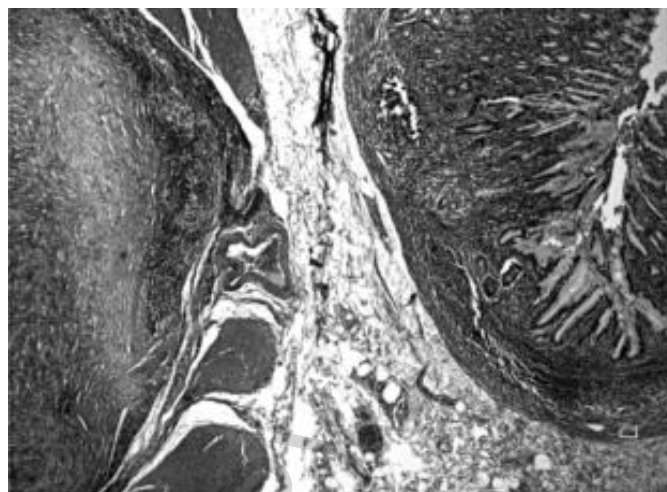


Fig. 2: Schwannoma in the submucosa of the stomach. Lymphocytic infiltration is observed around the well-defined lesion.

the patients are shown in Table IV. Pathological examination of the stomach schwannomas is shown in Figs. 1, 2.

Discussion

Schwannomas are slow-growing encapsulated tumors originating from Schwann cells in the collagen matrix¹⁴. Schwannoma was first reported by Verocay in 1910, and in 1935 Stout described its clinical and pathological features in detail¹⁵. In 1988, Daimaru et al. first described the concept of gastrointestinal benign schwannoma and demonstrated its clinical, morphological and phenotypic features². Intraabdominal schwannomas are rare tumors and constitute 2.9% to 5.6% of mesenchymal tumors^{9,11}. Since intraabdominal schwannomas outside the gastrointestinal tract are rare, this study mainly focuses on the clinicopathological features of GIS schwannomas. Gastrointestinal schwannomas are most commonly seen in the stomach (83%), small intestine (12%) and rarely in the colon and rectum³⁻⁵. According to the World Health Organization (WHO) classification of digestive system tumors, intestinal schwannoma belongs to the class of gastrointestinal mesenchymal tumors (GISTs). Some authors have classified intestinal schwannoma as a category of gastrointestinal autonomic neurogenic tumors (GANT)^{16,17}.

Gastrointestinal Schwannomas are more common in the sixth decade. Although some series in the literature indicate that incidence in both sexes are equal, there are also series in which female gender is more dominant^{6,7,18}. The mean age of our series was lower than the average age in the literature and female gender was dominant. Schwannomas are generally asymptomatic and the symptoms are not diagnostic. Mekras et al. found most of the cases in their series incidentally^{18,19}. As in the case

TABLE III - Clinical outcomes

Case no	Reoperation	Postoperative 90-day mortality	90-day readmission	Mean follow up (month)	Current Status
1	-	-	Pleural effusion	98	DUC
2	-	-	-	88	DF
3	-	-	-	58	DF
4	-	-	-	53	AWD
5	-	-	Anemia	47	DF
6	-	-	-	40	DF
7	-	-	-	37	DF

DUC, died of unrelated causes; DF=disease free; AWD Alive with disease

TABLE IV - Histopathological and immunohistochemical characteristics

Case no.	Diameter(cm)	Mitoses/50 HPFs	Immunohistochemistry
1	5	2	S100(+),Ki67<%1,SMA(-),DESM N(-),CD34(-),CD117(-)
2	10	0	S100(+),Ki67 %2
3	7	0	S100(+),Ki67 %2, SMA(-),DESM N(-),CD34(-),CD117(-),Dog1(-),EMA(-),NFP(-)
4	13,3	2	S100(+),Ki67%2,SMA(-),Vimentin(+),NSE(+),GFAP(+),CD34(-),CD117(-),Dog1(-)
5	3	1	S100(+),Ki67%2,SMA(+),DESM N(-),CD34(-),CD117(-),Dog1(-)
6	3,3	0	S100(+),Ki67 %3
7	0,3	0	S100(+),Ki 67 %1 DESM N(-),CD117(-)

reported by Antonio et al., Schwannoma cases can be incidentally detected during radiological imaging conducted for other diseases ²⁰.

However, when symptomatic, it causes non-specific clinical symptoms. Bruneton et al. reported in their series that the most common symptoms were bleeding and abdominal pain ²¹. Shu, Zhenbo et al reported that small bowel-derived Schwannomas presented with melena ²². In our series, the most common presenting symptoms of the patients were nonspecific symptoms such as abdominal pain, dyspepsia and constipation. The patient who had a mass of 13 cm presented with swelling in the right lower quadrant and had a palpable mass. Goh, Brian KP et al. reported in their series that intrabdominal Schwannomas most commonly had gastric origin, and less frequently colon, rectum and small intestine origin ¹¹. Retroperitoneal and pancreatic cases have also rarely been reported in the literature ^{4,5}. In our series, intrabdominal schwannomas were located in the small curvature of the stomach in 2 patients, rectum in 1 patient, pelvic in 2 patients, retropancreatic in 1 patient and left juxtadrenal region in 1 patient Radiological image of retropancreatic tumor is shown in Fig. 3.

Preoperative diagnosis of GIS schwannomas is often difficult because there is no specific clinical symptom of the tumor, and there are no diagnostic methods show any pathognomonic features ¹⁸. In computed tomography (CT) examination, these tumors are often detected as homogenous exophytic masses; cystic changes, cavity formation, necrosis or calcification are rare. In endoscopy, gastric schwannomas are seen as large as high submu-



Fig. 3: Paraaortic mass with celiac root at the anterior diaphragmatic crus medial to the left adrenal gland.

cosal lesions and ulcers may be seen due to ischemic changes in the mucosa ^{23,24}.

Increased incidence of malignant nerve sheath tumors has been reported in Von Recklinghausen disease or other neurofibromatosis syndromes ¹⁰. None of the patients in our study had a history of syndromic disease.

Currently, surgical resection is the recommended treatment for intestinal schwannomas. Complete surgical

resection with negative margins is the standard treatment for benign schwannomas. Radical surgery and extended resection are not recommended^{3,22}. The surgical method may vary depending on the location and size of the tumor and minimally invasive procedures are recommended for surgical treatment. When the tumor is small, endoscopic resection can be performed and transanal tumor resection can be considered for rectal tumors. There is a reported risk of recurrence after complete resection of benign schwannomas. Radical surgery is recommended for malignant schwannomas^{3,22}. Particularly for asymptomatic patients, some controversy remains as to whether tumors should be removed. Resection is necessary in cases where definitive diagnosis cannot be made preoperatively, even if asymptomatic²². Schwannomas are usually less than 2 cm in diameter and most of these patients have no significant symptoms. Gastrointestinal Stromal Tumors (GIST) are borderline tumors with a relatively high risk of malignant transformation. According to the National Comprehensive Cancer Network (NCCN) guidelines, surgical resection of GISTs with a diameter of less than 2 cm is not recommended if there are no high-risk EUS features (irregular borders, cystic spaces, ulcers, ulceration, echogenic foci). Periodic endoscopic or radiographic surveillance should be considered in determining treatment modality²⁵. Since the risk of malignant transformation of intestinal schwannoma is lower than that of GISTs, it is thought that these tumors can be followed. Resection should be prioritized when differential diagnosis of Schwannomas is difficult with GISTs, GANTs and malignant peripheral schwannomas^{22,26,27}.

Surgical treatment is applied in our clinical practice for the treatment of schwannoma cases. In our series, wedge resection and proximal gastrectomy were performed in one of the gastric origin schwannoma patients. Debulking was performed in the retropancreatic localized schwannoma case. Partial pancreatectomy r-y pancreatojejunostomy was performed in the case of schwannoma originating from the pancreas in the left juxtadrenal space. Resection was performed in one of the pelvic Schwannoma cases and cytoreductive surgery + Hyperthermic Intraperitoneal Chemotherapy (HIPEC) was performed in the other one because of peritoneal carcinomatosis. The patient who underwent pelvic mass excision as an intraoperative complication developed sudden hypotension. Hypotension was considered as an anesthesia-related complication in the patient who did not have hemorrhage and the operation was continued. Postoperative pancreatic fistula developed in the patient who underwent partial pancreatectomy. The fistula completely resolved with Somatostatin 3.5 mcg/kg/hour IV infusion therapy and parenteral nutrition. Cytoreductive surgery + HIPEC patient developed wound infection and was controlled with regular dressing without surgical intervention. The mean length of hospital stay was 11 days and the patient with the longest hospitalization was

followed up for pancreatic fistula. None of the patients required re-operation. There was no postoperative 90-day mortality. After discharge, the patient who developed pancreatic fistula was re-hospitalized because of pleural effusion and thoracentesis was performed. The effusion fluid was transudate and when investigated for the presence of intrabdominal collection, no collection was detected in the operation site. The patient who had undergone cytoreductive surgery was admitted for anemia and underwent blood transfusion.

Gastrointestinal schwannomas are usually submucosal and hypervascular. The lesions typically protrude into the lumen. Endoscopic examination shows small mucosal erosions. Schwannomas are submucosal and may not be diagnosed by superficial biopsies. It is usually clinically silent and may be discovered incidentally during upper gastrointestinal endoscopy, eroding the mucosa, causing gastrointestinal bleeding. It may present with luminal obstruction and bleeding as a result of mass growth^{7,9,28,29}.

Wedge resection, subtotal gastrectomy or total gastrectomy are the preferred treatment methods in gastric Schwannoma cases. The most important point in surgical treatment is complete resection of the tumor with a negative surgical margin. Gastric schwannomas rarely metastasize to lymph nodes like other soft tissue sarcomas and therefore surgical lymphadenectomy is not routinely recommended in gastric schwannomas¹⁴. In our series, gastric schwannoma patients presented with non-specific symptoms such as abdominal pain and dyspepsia. Patients with a non-diagnostic biopsy result underwent surgery with a preliminary diagnosis of stromal tumor and wedge resection was performed in one patient and proximal gastrectomy was performed in the other patient. Both patients are followed with disease-free survival.

Pancreatic schwannomas are most commonly localized to the head of the pancreas (40%), followed by the trunk (21%), neck (6%), tail (15%) and uncinata process (13%), respectively. Pancreatic schwannoma patients are usually asymptomatic or have nonspecific symptoms such as abdominal pain, nausea and vomiting^{7,30,31}. Complete, but conservative resection is the treatment of choice for pancreatic Schwannomas. Peripancreatic schwannomas originating from pancreatic nerve plexuses can be confused with pancreatic tumor and preoperative diagnosis in these patients may prevent unnecessary pancreatectomy^{7,32}. Retroperitoneal schwannomas may be malignant and potentially fatal. Therefore, it is important to completely remove the retroperitoneal tumors. Local recurrence has been reported in 5-10% of retroperitoneal schwannomas^{7,33}. In our series, one patient had schwannoma located in the tail of the pancreas and partial pancreatectomy was performed. The other patient had retropancreatic region localization and in this patient the pancreas was preserved and mass excision with negative surgical margin was performed.

Colorectal schwannomas are less common than other GI schwannomas. In the literature, it was reported that colorectal schwannoma was more common in the female gender (59%) and the mean age at presentation was 61.5³. More than 98% of colorectal schwannomas are benign and have a low mitosis rate and a low Ki-67 proliferation index. The best treatment option is complete surgical resection with negative margins. Radical surgery is not usually necessary^{3,34}.

In our study, one patient had schwannoma located in the rectum and transanal excision was performed. Mitotic activity was not observed in the tumor and Ki-67 proliferation index was 1%. At 37 months postoperatively, the patient continues to be monitored without any disease.

The rate of diagnosis of intestinal schwannoma in the preoperative period is relatively low. Inagawa et al. showed that preoperative diagnosis rate was only 15.2%³⁵. Diagnosis is mainly based on postoperative pathology specimen examination and immunohistochemistry studies²². Immunohistochemical examinations are necessary to differentiate between different spindle cell tumor types. Desmin and SMA positivity showed smooth muscle lesions such as leiomyoma or leiomyosarcoma; CD34 and CD117 positivity indicate GIST. S100 strongly positive staining supports the diagnosis of schwannoma^{10,36}.

Immunohistochemical examination of tumors was strongly positive for S100 in our patients and CD117, CD34, SMA and Desmin were negative, which confirmed our diagnosis of schwannoma. There is no clear standard of malignancy for Schwannoma biological behavior. Current indicators include Ki-67 proliferation index (MIB-1), nuclear atypia, mitotic activity rate, and tumor size²². GIST malignancy grades are based on tumor size and rate of mitotic activity²⁵. Ki-67 proliferative index is an indicator of malignancy and Ki-67 proliferation index above 5% is associated with high invasive potential of tumor, while Ki-67 proliferation index higher than 10% is indicative of malignancy³⁷. Mitotic activity ratio of >5/HPF and tumor size >5 cm is associated with high risk of metastasis and recurrence³⁸. Tumors with low mitotic activity and no nuclear atypia are often benign³⁷. In their intestinal Schwannoma series, Shu, et al. found Ki-67 proliferative index to be less than 3% and tumor diameter less than 5 cm²². In their series, Voltaggio et al found a mean tumor diameter of 4.5 cm and mitotic count 2/50 HPFs³⁹. In our series, the mean tumor diameter was 6 cm and the largest tumor diameter was 13 cm. Mitosis rate in two patients Mitoses / 50 HPFs:2 and it was Mitoses/50 HPFs:1 in one patient, the other patients did not show mitotic activity and Ki-67 proliferation index was <3% in our patients. During the mean follow-up period of 60 months, 5 patients are followed without disease. The patient who had peritoneal carcinomatosis at the time of diagnosis and underwent surgery had recurrence and was followed up with survival.

Gastrointestinal Stromal Tumor is one of the diseases that should be considered in the differential diagnosis of Schwannoma. GISTs are the most common mesenchymal tumor in the gastrointestinal tract and is of subepithelial origin. Schwannoma is a well-differentiated, slowly growing tumor with good prognosis after resection. GISTs are malignant tumors that may have recurrence after excision^{19,20}. While the clinical symptoms are nonspecific in both diseases and similar to each other; GIST cases may rarely present with an acute abdominal clinic due to perforation, as in the case reported by Versaci et al.⁴⁰. As reported by Troupis et al., differential diagnosis of GISTs and Schwannoma can be made by immunohistochemical and molecular analysis of the lesion^{36,41}.

In conclusion, schwannomas are rare and usually asymptomatic tumors that can be diagnosed by histopathological and immunohistochemical examination.

Schwannoma should be kept in mind in the differential diagnosis of gastrointestinal system localized masses, thus avoiding extensive resection. Negative surgical margins and surgical resection are the gold standard in the treatment of schwannomas, and these lesions are usually benign and have a favorable prognosis. Prospective studies with large case series are needed.

Riassunto

Gli schwannomi intraaddominali sono tumori benigni rari. In questo studio, intendiamo presentare la nostra esperienza clinica di pazienti con Schwannoma intra-addominale localizzato.

Sono stati esaminati retrospettivamente i pazienti in cui è stato diagnosticato uno schwannoma intra-addominale tra il 2011-2019, analizzando le caratteristiche demografiche e cliniche, i metodi di trattamento, i risultati a breve e lungo termine e le caratteristiche immunoistochimiche dei pazienti.

Nello studio sono stati inclusi 7 pazienti: quattro donne e tre uomini. L'età media era di 51,5 (31-63) anni. La presentazione clinica più comune è stata il dolore addominale (57,1%). La posizione del tumore era stomaco (n = 2), regione pelvica (n = 2), retto (n = 1), retropancreas (n = 1) e spazio iuxtadrenale sinistro (n = 1).

In un paziente si è avuta l'infezione della ferita postoperatoria, e in uno la complicazione di una fistola pancreatica. I ricoveri in ospedale erano dovuti all'anemia e al versamento pleurico in due pazienti. Il diametro medio del tumore era di 6 cm (0,3-13 cm). Tutti i pazienti erano S 100 Mitosi fortemente positive / 50 HPF (campo ad alta potenza), <2 Ki67 <3%. Il periodo medio di follow-up è stato di 60 mesi. Attualmente, 5 pazienti vengono seguiti senza malattia, 1 paziente sopravvive nonostante la recidiva e 1 paziente è deceduto per motivi non cancerosi.

Conclusione: gli schwannomi intra-addominali sono

tumori rari che presentano più comunemente un coinvolgimento gastrointestinale. Poiché questi tumori sono per lo più benigni, la prognosi a lungo termine dei pazienti è buona. Lo Schwannoma dovrebbe essere tenuto presente nella diagnosi differenziale delle masse intra-addominali. Le resezioni radicali con elevata morbilità e mortalità dovrebbero essere evitate se viene fatta una diagnosi preoperatoria.

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