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Case Report
Olgu Sunumu

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An Unusual Case; Extragastrointestinal Stromal Tumor of Rectovaginal Septum with Literature Review

Literatür Derlemesi ile birlikte Nadir bir Olgu Sunumu; Rektovaginal Septum Yerleşimli bir Ekstragastrointestinal Stromal Tümör Olgusu

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Abstract: Extragastrointestinal stromal tumors (EGISTs) are tumors that show features of gastrointestinal stromal tumors (GISTs) and are very rare. Extragastrointestinal stromal tumors that originated from female genital tract are more rare. In this case report, we will discuss a case of gastrointestinal stromal tumor originating from the rectovaginal septum. The tumor was surgicaly exised and It was positive for CD117, CD34 and DOG1, immunohistochemicaly. The tumor size was 5.5 cm and the mitotic rate was 20 mitoses per 50 high power field (HPF) and histologic examination revealed focal necrosis . After the surgery, the patient began imatinib 400 mg as adjuvant therapy and still ongoing the therapy. The patient is now healtly without evidence of recurrence 19 months after surgery. Immunohystochemistry and cytogenetics seem to be the most important methods to diagnose EGISTs. After complete surgical resection of the tumour, follow-up with adjuvant imatinib therapy is recommended in high risk disease.

Keywords: Extragastrointestinal stromal tumors, Rectovaginal septum, Genital tract

Özet: Ekstragastroentestinal Stromal Tümörler(EGİST) gastrointestinal stromal tümörlerin özelliklerini gösteren ve çok nadir görülen tümörlerdir. Kadın genital sisteminden kaynaklanan Ekstragastrointestinal Stromal Tümörler daha nadirdir. Bu olgu sunumunda, rektovaginal septumdan köken alan bir gastrointestinal stromal tümör olgusu tartışılacaktır. Tümör cerrahi olarak eksize edildi ve immünhistokimyasal olarak CD117, CD34, DOG1 pozitifti. Tümör boyutu 5,5 cm'di. Mitotik oranı 50 Büyük Büyütme Alanında(HPF) 20 mitoz olarak saptandı ve histolojik incelemede fokal nekroz saptandı. Operasyon sonrası hastaya adjuvan tedavi olarak İmatinib 400 mg başlandı ve halen tedavi devam etmektedir. Hasta ameliyattan 35 ay sonra nüks bulgusu olmaksızın halen takip edilmektedir. İmmunhistokimya ve sitogenetik EGİST'lerin tanısında en önemli yöntemlerdir. Tümörün tam cerrahi rezeksiyonundan sonra, yüksek riskli hastalıkta adjuvan imatinib tedavisi ile takip önerilmektedir.

Anahtar Kelimeler: Ekstragastrointestinal stromal tümörler, Rektovaginal septum, Genital tract

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1. Introduction

GISTs are rare mesenchymal neoplazms of gastrointestinal tract, arising from the intestinal wall (1-5). GISTs originating from atypical sites are definied as extragastrointestinal stromal tumors. GISTs have been reported in the omentum, mesentery, prostate, bladder and female reproductive organs outside the gastrointestinal tract (6, 7). The occurance of GISTs in the female genital tract is rare and has been reported in limited number of cases report and reviews in the literature. According to a literature search we have done, we revealed nineteen previosuly well-reported EGISTs as a vaginal or rectovaginal septum mass. The majority of GISTs originating from the female genital tract were reported as rectovaginal GISTs. However, tumor origin sites are controversial. There is no method to distinguish whether GISTs originate from the rectum, rectovaginal septum or vagina (8). İn this article, we aimed to present a case of EGIST originating from the female genital system and to discuss this case comperatively with the literature.

2. Case Report

70 year old woman presented with a posterior vaginal mass. In November 2021, the patient underwent diagnostic laparotomy and vaginal tumor debulking and vagen posterior wall repair operation for the mass infiltrating a five centimeter region in the retrovaginal septum. The excision pathology of this mass was reported as extraintestinal gastrointestinal stromal tumor. The tumor consisted of spindle cells that did not exhibit significant nuclear atypia histopathologically (Figure 1A). In immunohistochemical staining, CD117 (Figure 1B), DOG1 (Figure 1C), CD34 were strongly positive and Caldesmon focal positive stained in neoplastic cells. Pancytokeratin, CK7, S100, desmin, STAT6, EMA were negative. P16 was positive. There was no observed loss of SDHB immunohistochemically. Ki-67 proliferation index was 2-3%. Up to 20 mitotic counts per 50 high power fields (HPF) were counted. The mass material was submitted in a damaged form. Therefore no comments could be made on tumor size and surgical margins. There was no residual tissue and distant metastases on postoperative imaging. Oral imatinib 400 mg/day was started for 3 years as adjuvant therapy in January 2022. Local recurrence and metastasis did not develop in the patient's follow-up so far, and the follow-up continues in remission for 35 months.

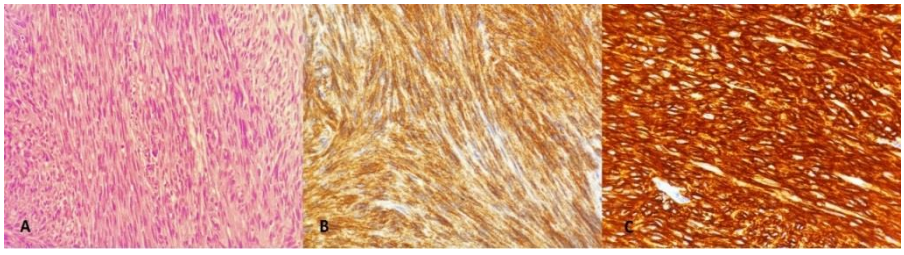

Figure 1. Spindle cell mesenchymal neoplastic infiltration arranged in elongated fascicles, displaying mild nuclear atypia, hematoxylin and eosin staining (A), CD117 (B) and DOG1 (C) expressions, immunohistochemical stainin

Table 1. Cases originated from recovaginal septum and vagina which well-repoted in the literatüre since 2004

Case	Patient no	Age	Location	Tumor size(cm)	KIT mutation	Mitotic activity	IHC(Positive)	Follow up	Management
Katherine et al. [10] (2004)	1	75	Vagina	4.5	Unknown	12-15/50 HPF	CD117, Vimentin, CD34 Caldesmon	No recurrence at 10 months	Surgery
Nasu et al. [12] (2004)	1	54	Recto vaginal septum	8	Unknown	1-2/10 HPF	Vimentin, CD34, CD117, Desmin,SMA.	No recurrence at 13 months	Surgery
Weppler et al. [13]	1	66	Rectovaginal septum	8	Unknown	5/50 HPF	Vimentin, CD34, CD117	Unknown	Imatinib

(2005)									
Takano et al. [19] (2006)	1	38	Vagina	7	Unknown	1-2/50 HPF	CD117, CD34, SMA	No recurrence at 1 year	Surgery
Lam et al. [20] (2006)	3	36	Vagina	4	KIT Exon 9 insertion	15/50 HPF	CD117,CD34	Local recurrence at 2 years	Surgery
		48	Vagina	6	KIT Exon 11 deletion	12/50 HPF	CD117,CD34	Local recurrence at 10 years	Surgery
		61	Vaginal septum/ rectovaginal septum	8	KIT exon 11 mutation	16/50 HPF	CD117 and CD34	Unknown	Surgery
Nagase et al. [14] (2007)	2	42	Vagina	3.5	Unknown	<1/50 HPF	CD117, CD34, Vimentin ,Caldesmon	No recurrence at 4 years	Surgery
		66	Vagina	5	KIT Exon 11.21-bp deletion,	2-3/50 HPF	CD117 ,Vimentin	No recurrence at 6 months	Surgery + Imatinib
Zhang et al. [15] (2009)	1	42	Vagina	8	Unknown	10/50 HPF	CD117, CD34	No recurrence at 11 months	Surgery
Molina et al. [23] (2009)	1	56	Rectovaginal septum	5	Unknown	25/50 HPF	CD34,CD117	No recurrence at 18 months	Surgery + Radiation
Fregmani et al. [24] (2011)	1	60	Rectovaginal septum	2	KIT exon 9 mutation	4/50 HPF	CD34 ,CD117	No recurrence at 6 months	Surgery + Imatinib
Julio et al. [16] (2012)	1	29	Rectovaginal septum	6	KIT mutation positive	10/50 HPF	CD117,CD34	No recurrence at 24 months	Surgery + Imatinib
Mario et al. [11] (2013)	1	15	Rectovaginal septum	2	Unknown	40/50 HPF	CD117 and DOG-1	Death at 19 months	Surgery + Imatinib + Sunitinib
Qiu-yu et al. [17] (2016)	1	41	Vagina	7.5	KIT Exon 11 mutation	25/50 HPF	DOG-1, CD117, CD34	No recurrence at 5 months	Surgery + Imatinib
Wissam et al. [9] (2018)	1	58	Vagina	8.9	Unknown	4/50 HPF	CD117, DOG-1, Caldesmon	No recurrence at 3 months	Imatinib
Shi et al. [22] (2020)	1	39	Vagina (recurrent case)	2.5x2	Exon 11 mutation of c-KIT	>5/50 HPF	CD117, CD34, DOG-1	No recurrence at 13 months	Surgery + Imatinib
Shuai et al. [18] (2021)	1	60	vagina	5.5	Unknown	14/50 HPF	CD117, CD34, DOG-1	No recurrence at 5 years	Surgery
Susan et al. [21] (2021)	1	55	Rectovaginal septum	20-3 (two fragments	Exon 11 mutation of the c-KIT	1/50 HPF	CD117, CD34, DOG-1	No recurrence at 28 months	Surgery + Imatinib
Our case	1	70	Rectovaginal septum	5.5	Unknown	20/50 HPF	CD117, CD34, DOG-1	No recurrence at 19 months	Surgery + Imatinib

IHC:İmmunohistochemistry HPF: High Power Field SMA: Smooth Muscle Actin

3. Discussion

EGISTs are rare tumors that occur outside the gastrointestinal tract. It conctitutes approximately 5-7% of GISTs. It is still not clear where EGİSTs originate from. The majority of EGISTs originate from the mesentery, omentum and retroperitoneum. According to our literature review, only twenty well-defined cases have been reported since 2004 including our case, originate from the vagina and rectovaginal septum (Table 1) (9-24). According to literature data GISTs are predominantly seen in elderly individuals with a median age diagnosis between 64-69 years and rarely seen in children (25-27). GISTs are rarely occur under 40 years of age (25). The median age of EGİSTs originated from the genital tract we rewieved was 50. The diameters of tumor was ranged from 2 to 20 cm. With our case nine tumors were originated from rectovaginal septum, eleven tumors were originated from vagina. In our case, the mass was at the rectovaginal septum. GISTs are mostly positive for c-KIT protein (CD117) and 60-70% of gastrointestinal stromal tumor are positive for CD34. İn addition, 30-40% of GİSTs are positive for SMA (Smooth Muscle Actin) immunohistochemically (1, 28, 29). DOG-1 is more sensitive marker than CD117 and CD34 for GISTs and can be positive in KIT-negative GISTs and its use as a diagnostic marker continues to increase (30). In the current case immunohystochemical analyses of the tumor was diffusely positive for CD117 and CD34 and DOG-1 and focal positive for SMA and Caldesmon and negative for Pansitoceratin, CK7, S100, Desmin, STAT-6, EMA and necrosis was observed in focal foci in the tumor. GISTs and EGISTs originate from the Cajal cells (31). EGISTs are more agressive than gastrointestinal stromal tumors originating from the common locations. Poor prognostic factors for gastrointestinal stromal tumors are high mitotic index (>2/50 HPF), tumor size (>2 cm), tumor rupture with the surgery, the location in the gastrointestinal tract and necrosis. In our case high mitotic counts (20/50 HPF) were observed and focal necrosis was present and tumor size was 5.5 cm suggested that the tumor is a high-risk category. CD117 positive tumors benefit more from receptor tyrosine kinaz inhibitör imatinib therapy. The cellular morphology of GISTs are ranges from epithelioid morphology to spindle cell morphology, Histologically it consists of 70% spindle cell type, 20% epithelioid type, 10% mixed type (32).

Definitive treatment of EGISTs is surgery with local excision. The standart treatment of GISTs is complete resection of the tumor and achieving negative surgical margins. In our case no farther comment could be made about the surgical margins, since tumor integrity was disrupted Imatinib, a tyrosine kinase inhibitor, is a treatment option for GISTs. Adjuvant imatinib treatment has reduced the risk of recurrence in GISTs (33). According to current guidelines and consensus regarding GIST treatment, it is recommended to continue adjuvant imatinib therapy for 3 years in high-risk patients after surgery (34). İmatinib treatment is used in tumours expressing KIT in metastatic GİSTs. Spesific mutations in KIT such as exon 11 are associated with clinical response to imatinib. Imatinib 800 mg is recommended in patients with exon 9 mutations (35). If mutation assesment cannot be performed, ımatinib 400 mg can be started and if no response is obtained, ımatinib 800 mg or sunitinib treatment can be started. Regorafenib therapy is indicated for patients resistant to imatinib and sunitinib (36). Ripretinib therapy is recommended in patients who have received at least three tyrosine kinase inhibitors, including imatinib (37). We aimed to complete the adjuvant imatinib treatment for 3 years in our patient, because our case had high risk factors.

4. Conclusions

EGISTs are rare tumors. Poor prognostic factors are high mitotic index, tumor size, the tumor rupture, the tumor location along the gastrointestinal tract and presence of necrosis. More data are needed for tumor behavior, prognosis and treatment options in patients with EGİST.

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