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Olgu Sunumu

# Is there any prognostic significance of age in gastrointestinal stromal tumor?

# Yaş gastrointestinal stromal tümör için prognostik bir önem taşır mı?

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**ABSTRACT**

**Gastrointestinal stromal tumours (GISTs) are uncommon primary mesenchymal tumors of the gastrointestinal tract mostly observed in the adults. Small intestinal GISTs are relatively rare even in adults and it can be regarded as exceptional in childhood. Most GISTs arise because of a mutation in a gene called c-kit. This gene encodes a transmembrane receptor for the growth factor termed stem cell factor.**

**An 11-month-old girl was referred to our hospital with vomiting. A small bowel mass was detected by radiological examination and the patient underwent surgery. During surgery, a 2 cm solid tumoral mass arising from the wall of the jejunum was identified. Immunohistochemical analysis of the specimen revealed to be positive for CD117 (c-KIT protein) consistent with a diagnosis of GIST. Forty two months later, a recurrent mass developed on the omentum. Specimen obtained during re-operation revealed similar features with the primary tumor. The treatment with imatinib was started following surgical resection of the recurrent tumor. After the second surgery, the patient had an uneventful course and remained disease-free during seven years of follow-up.**

**Key words: Childhood, small bowel, gastrointestinal stromal tumor**

**ÖZET**

**Gastrointestinal stromal tümörler (GIST), genellikle erişkinde gözlenen, çok sık rastlanmayan gastrointestinal traktın primer mezenkimal tümörüdür. İncebağırsak GİST'leri göreceli olarak erişkinde bile enderdir, çocukluk çağının ise sıra dışı tümörü olarak nitelenebilir. Çoğu GIST c-kit genindeki mutasyona bağlı gelişir. Bu gen kök hücre faktörü olarak adlandırılan büyüme faktörünün transmembranöz yerleşimli reseptörünü kodlar.**

**Kusma nedeniyle hastanemize başvuran 11 aylık kız çocuğunda radyolojik incelemelerle intestinal kitle saptandı ve opere edildi. Operasyonda jejunum serozasından köken almış 2 cm çapında tümör saptandı. İmmunohistokimyasal olarak CD117 (c-kit) protein pozitif bulunan olgu GIST tanısı aldı. Kırk iki ay sonra omentumda rekürrent kitle gelişti. Tümörün re-operasyon materyalinde aynı özelliklere sahip tümör saptandı. Nüks tümörün rezeksiyonundan sonra imatinib tedavisi başlandı. Olgu 7 yıldan beri hastalıksız izlenmektedir.**

**Anahtar kelimeler:** Çocukluk çağı, ince bağırsak, gastrointestinal stromal tümör

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## INTRODUCTION

The mesenchymal tumors of the gastrointestinal tract are called gastrointestinal stromal tumors (GIST). These tumors, which have quite heterogeneous histogenetical and biological features are immu-

noreactive for CD117 in common [1-3]. Patients with GIST are predominantly of middle or elderly age group (approximately 55-65 years old) and pediatric cases are rare [4,5]. Since GIST in the pediatric population is rarely reported, data for the prognosis of the tumor in this age group are scarce [4-6].

In this paper, GIST of the jejunal wall in a 11 month-old girl, which recurred on the omentum after 42 months, is presented. The diagnostic tools and prognostic factors were reviewed and discussed in consideration of pediatric cases.

## CASE

An 11 month-old girl who had discomfort and vomiting for a month before attending the hospital, was examined with ultrasonography, and an invaginated small intestine measuring 26x33 mm was detected at the umbilicus level. The jejunal mass excision and appendectomy were performed for the relief of invagination. The tumor was observed to cause mucosal ulceration and hemorrhage at the jejunal wall. It lied beneath the submucosa and was 2 cm in diameter. Segmental resection of the jejunum (10 cm length) and lymph node dissection of the perijejunal area were performed. Surgical margins and six regional lymph nodes were evaluated as disease-free. In the histopathological evaluation, the tumor was detected to show hypocellular and hypercellular areas and also storiform growth pattern. The tumor growth was expansive rather than infiltrative and the expansion was limited to the jejunal wall. Pleomorphism, necrosis and mitotic figures were not observed even in the areas of high cellularity. In these areas of high cellularity, the Ki67 proliferative index was determined to be 3% (Figure 1). Immunohistochemically, the tumor cells showed diffuse strong expression for CD117, CD34 (Figure 2) (class 2, QBEnd 10, 1/40 dilution, DAKO) and Vimentine (V9, Dako) while focally weak positive expression was detected for S100 protein (Dako). The tumor cells were negative for desmin (D33, Dako), SMA (1A4, Dako) and NSE (BBS/NC/V1-H14, Dako). The immunophenotypic characteristics of the tumor are summarized in Table 1.

With these findings, the tumor was considered to have benign behavior and the patient was inspected periodically by ultrasound. After 42 months following the initial diagnosis, a recurrent tumor of 4.5 cm in diameter was detected on the omentum (Figure 3). This tumor had identical morphologic and phenotypic features of GIST, too. Exceptionally, focal areas showing multinuclear tumor giant cells were noticeable (Figure 4). The recurrent tumor was more

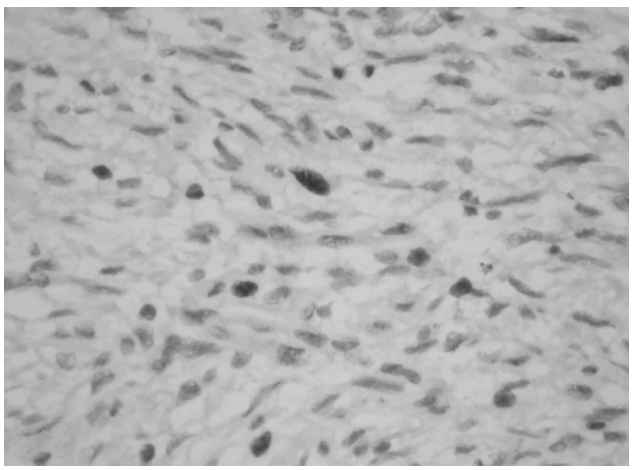

**Figure 1. Low Ki67 proliferation index of the primary tumor (x100; DAB).**

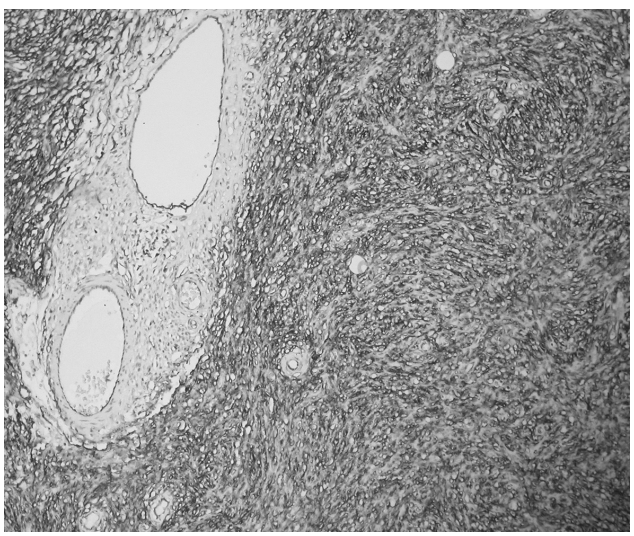

**Figure 2. CD34 immunoreactivity of the primary tumor (x40; DAB).**

**Table 1. Immunphenotyping characteristics of our case.**

| Immunphenotyping | CD117 | CD34 | Vimentin | S100 | Desmin | NSE | Ki67 % |
|---|---|---|---|---|---|---|---|
| Primary tumor | ++ | ++ | ++ | + | - | - | 3 |
| Recurrence tumor | +++ | ++ | ++ | - | - | - | 5 |

**Table 2. Prognostic factors of our primary tumor.**

| Prognosis | Diameter (cm) | Localization | Mitosis | Pleomorphisim | Necrosis | Ki67 |
|---|---|---|---|---|---|---|
| Favorable | < 5 | stomach | <5 | mild | no | <5-10 |
| Our case | 2 | jejunum | 0 | mild | no | 3 |

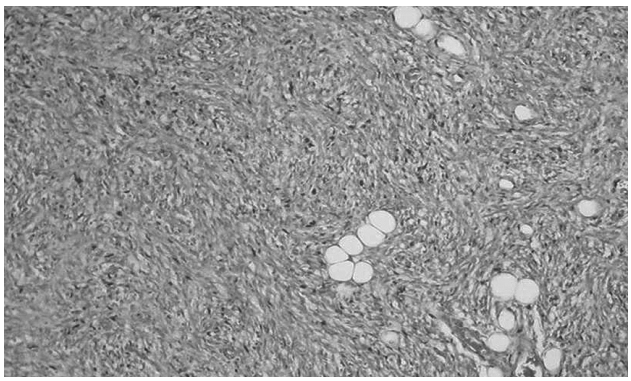

**Figure 3. The histopathological pattern of the primary tumor (x100; HE).**

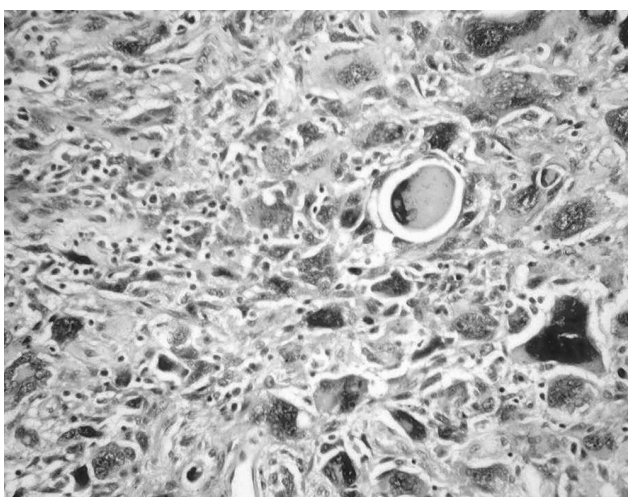

**Figure 4. The bizarre tumor giant cells in the recurrent tumor (x400; HE).**

strongly positive for CD117 (Figure 5) compared with the primary tumor. The Ki67 index was 5% and mitosis was calculated to be 5/50 HPF.

The imatinib therapy was started for the recurrent

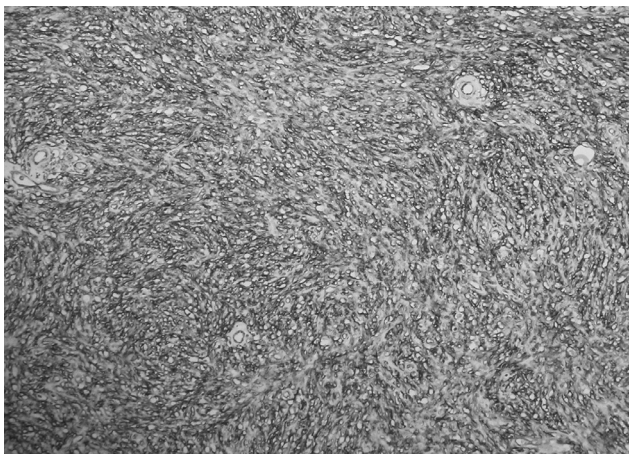

**Figure 5. CD117 immunreactivity of the recurrent tumor (x100; DAB).**

tumor, and continued for 7 years with no side effects.

## DISCUSSION

The prevalence of pediatric GIST has not been documented [4-6]. GISTs are most commonly located in the stomach in childhood. Small intestine is the second leading location. Shimamura et al. reported 11 cases of the small intestine GISTs in the literature in 2010. It is known that GISTs of the small intestine show a more aggressive behavior [1-3].

C-kit (CD117) positivity is a hallmark for this tumor [1-3,14]. Although the sensitivity of the CD117 is high, its specificity for GIST is lower. Its degree of positivity varies for many malign and benign tumors of GIS [1,3]. Some authors declare that CD34 (a stem

cell marker and surface glucoprotein) positivity is a helper for the diagnosis of GIST [3]. Our primary and recurrent tumors were shown to be strongly positive for CD34 and CD117.

Some of the pediatric GIST tumors published in the previous papers reported negative expression for CD117 and CD34 and variability for positive expression of S100, NSE and SMA [1,4,6,8,9]. The diagnosis of these tumors may not be GIST. Miettinen et al. noted that some of these tumors might be inflammatory myofibroblastic tumors [1].

Some of the clinical, histological, immunophenotyping and genotyping parameters were used in estimating prognosis [1-9]. Localization, diameter, cellular typing, cellularity, pleomorphism, necrosis, mucosal infiltration, mitosis, proliferation index and p53 positivity of the tumor are independent factors in the univariate statistical analysis. But in the multivariate analysis, diameter, mitosis, necrosis and proliferation index of the tumor are the major determinants of the behavior of the GIST [3,10,11]. The determination of the biological behavior of the borderline or suspect tumors is difficult. Typical histologically benign tumors can be recurrent and show metastasis, as seen in our case. For this reason, none of the histopathological parameters alone can be considered sufficient for the prediction of the biological behavior [1,2,5]. The interpretation of mitosis, diameter and necrosis should be combined with the results of the proliferation markers (PCNA, Ki67) [10,11]. In our case, the primary tumor diameter was 2 cm and the prognostic markers were favorable. However, recurrence was determined after 42 months from the initial diagnosis. In the literature, five centimeter is accepted as the critical diameter of the tumoral mass discriminating between benign, and malign cases [1,2]. In our case; the recurrent tumor in the omentum was 4.5 cm in diameter. We think that, our tumor localization is the major factor for the recurrence. There are a lot of papers about unpredictable survival of the pediatric GISTs [2,4,5,14]. The prognostic factors of our tumors are summarized in Table 2.

Multinuclear giant cells were seen in the focal areas of the recurrent tumor which were stained negative for CD68 and positive for CD117. These results were in favor of neoplastic nature. But contradicting opinions have been reported in the literature [2,12]. We think that, this phenomenon is due to de-differentiation or cellular anarchy.

The essential therapy of the GIST is surgery. Selective KIT tyrosine kinase inhibitors were beneficial in these cases. Some papers report that, c-KIT tyrosine kinase inhibitor; imatinib mesylate usage partially controls metastasis and dissemination in 50-96% of the tumors [13]. But application lasting longer than 2 years is not advised because of its toxic effect and the cost. There is not an agreement on duration of treatment of recurrent tumors. Neither side effects nor recurrences have been seen in our patient for 7 years.

The usefulness of the prognostic criteria in the adult GIST is controversial for the childhood period. For this reason, we recommend an initial aggressive surgery and periodical radiological and clinical follow up in pediatric GIST.

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