Intussusception due to gastrointestinal stromal tumor with neural differentiation in a patient with Von Recklinghausen Neurofibromatosis (NF-1):
A case report

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Von Recklinghausen Neurofibromatosis is a fairly common disorder characterized with café au lait spots of the skin and neurofibromas of the skin and viscera. Neurofibromas can be observed throughout the gastrointestinal tract and lead to various complications. These neurofibromas can be diagnosed with immunohistochemical studies in order to exclude other type of tumors. We document clinical and pathological aspects of a patient with Von Recklinghausen Neurofibromatosis presented with jejunojejunal intussusception due to a stromal tumor with neural differentiation. [Turk J Cancer 2001;31(4):172-176]

Key words: Von Recklinghausen Neurofibromatosis, stromal tumor, intussusception

Von Recklinghausen Neurofibromatosis (known as NF-1) is a fairly common disorder with an incidence of 1 in 4000 live births in the United States. It is characterized with café au lait spots of the skin and neurofibromas of the skin and viscera (1). Neurofibromas in the bowel commonly occur in the ileum and can ulcerate into the lumen resulting in severe bleeding. Upper digestive tract involvement by NF-1 occurs in 2% to 25% of patients with this disease and much of it is asymptomatic. Typically, submucosal neurofibromas and rarely duodenal paragangliomas have been reported (2).

Most of the stromal tumors of small intestines are observed in adults. But pediatric cases were also reported in the literature (3). Most of these cases are HIV–infected persons (4). Although these tumors can be observed in any segment of the small intestine, tumors with smooth muscle differentiation are mostly distally located. Generally only one tumoral mass is observed. But multiple nodules were established in both small intestine and colon (5).

Macroscopically, they are very limited and show submucosal or subserosal growth pattern. Central ulceration is observed generally, in submucosally located types. Immunohistochemically and ultrastructurally, differentiation
towards smooth muscle and/or nerve tissue can be observed in these tumors like the ones located in stomach. Most frequent differentiation is towards the nerve tissue.

They are classified as benign, borderline and malignant according to some macroscopic and microscopic criterias.

Great diameter (over 5 cm), tumoral necrosis, prominent cellularity, atypia, high mitotic index (10 in high-power fields), presence of 5 or more mitosis in 10 great magnification areas are in favor of malignancy (6). High mitotic activity is the only most important criteria in differentiating the tumor as low or high grade.

Stage, microscopic grade and DNA ploidy are correlated with the prognosis. Stromal tumors that are located in the small intestine show a higher rate of malignant behavior contrary to the tumors that are located in the stomach (7).

We document clinical and pathological aspects of a patient with NF-1 presented with jejunoojejunal intussusception due to a stromal tumor with neural differentiation.

**Case Report**

A 38-year old female with NF-1 presented with recurrent abdominal discomfort and profuse bile stained vomiting. Contrast enhanced CT revealed an intussusception in proximal jejunum. The patient underwent emergency surgery because of signs of impending acute intestinal obstruction. Segmental resection of jejunum performed. Following reduction of the intussusception two polypoid masses with 3.5 cm and 1.5 width and 2 cm height, respectively were observed (Figure 1). The lesions were 1 cm apart from each other and covered with serosa.

![Fig 1. The macroscopic appearance of operation material: Two polypoid masses covered with serosa observed after reduction of the intussusception](image)
Histologically, sections showed relatively normal small bowel mucosa and muscularis mucosa encompassed by a predominantly spindle cell tumor that completely replaces the submucosa and outer muscle coat. The outer serosal surface was covered by necrotic debris and bacterial colonies, presumably as a consequence of the intussuception. The tumor itself also showed hemorrhagic necrosis which may be a consequence of the intussuception. The viable tumor was composed of bundles of long, thin, strap-like spindle cells with fibrillar eosinophilic cytoplasm and relatively small, central, oval nuclei. There was a variable pattern. In places the cells lied in parallel arrays, elsewhere cells intersected at different angles. Some parts were highly vascular with anastomosing capillary channels lined by plump endothelium. Some areas had a moderate interstitial collagenous stroma in which there was scattered small amorphous eosinophilic deposits. The latter were strongly PAS positive and diastase resistant. A battery of immunostains have been performed and revealed that the tumor was strongly and universally positive for CD 34, a proportion of cells stained strongly for neuron specific enolase (NSE), PGP 9.5 and very few for smooth muscle actin. There was no demonstrable immunoreactivity with desmin. The immunoreactivity pattern and the location of the tumor are in keeping with a gastrointestinal stromal tumor with neural differentiation.

**Discussion**

Gastrointestinal stromal tumor is the generic term for mesenchymal tumors of the gastrointestinal tract and have previously been recognized in association with neurofibromatosis (NF-1) (11). These tumors variably express neural and smooth muscle markers and have been subdivided accordingly (9,10). Thus, those with neural expression have been called myenteric plexomas or gastrointestinal autonomic nerve tumors (GANT) and dense core granules have been demonstrated by electron microscopy in some cases (10). Other authors consider the subdivision to be artificial and propose the stromal tumors to be the same entity with a spectrum of differentiation.

Immunohistochemistry provides further supportive evidence of GANT and is important in excluding other possibilities. Shanks et al. (10) and Segal et al. (12) found NSE expression in 100% of cases in their series. PGP 9.5 positivity was described by Newman et al. (13) in 7 of 60 gastrointestinal stromal tumors. Shanks et al. (10) reported positive immunostaining for PGP 9.5 in all of 9 cases with GANT in his series (11). The strong PGP 9.5 (Figure 2), NSE (Figure 3), CD34 staining in the absence of immunoreactivity for muscle specific actin and desmin in this case suggest it was a stromal tumor with neural differentiation.

Consistent with our opinion, immunohistochemical positivity for NSE, PGP 9.5, CD34 and vimentin in the absence of immunoreactivity for muscle specific actin and desmin, cytokeratin, chromogranin and S-100 protein is recommended for the diagnosis of gastrointestinal stromal tumors with neural differentiation (GSTND) (9,10,12).
These tumors are generally regarded as slow growing malignancies but prognosis appears to relate with size and mitotic activity (8,10,12). Large tumors and those with high mitotic rate tend to recur and metastasize. Inai and colleagues (8) reported a case of duodenal paraganglioma with regional lymph
node metastases. Follow up for this case is 12 months. Laparoscopic exploration at the end of this period revealed no recurrences at the line of anastomosis and in the abdomen. Although this is a relatively short period, mitosis was very sparse in this case and as the two tumor nodules have been completely resected, the prognosis would be expected to be favorable.

References