Diffuse Cecal Ganglioneuromatosis in a Patient with von Reklinghausen's Disease: Case Report

von Recklinghausen Hastalığı Olan Bir Olguda Diffüz Çekal Ganglionöromatozis

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ABSTRACT A 41-year-old female with 'cafe au lait' and multiple skin neurofibromas was admitted with a complaint of constipation, abdominal pain and distention. The colonoscopic investigation was normal, however computed tomography revealed a mass in the cecal wall. Thereon, right hemicolectomy was performed to the patient. Histopathologic examination revealed ganglioneuromatosis of the cecum. There was not any recurrence after three years of follow-up. An intestinal manifestation of von Recklinghausen's disease should be kept in mind in a patient who has multiple neurofibromas and 'cafe au lait' spots with intractable constipation and intestinal obstruction.

Key Words: Cecum; neurofibromatosis 1

ÖZET 'Cafe au lait' lekeleri ve multipl cilt nörofibromları olan 41 yaşında bir kadın hasta konstipasyon, karın ağrısı ve distansiyonu yakınmalarıyla başvurdu. Kolonoskopik inceleme normaldi, bununla birlikte bilgisayarlı tomografide çekum duvarında bir kitle görüldü. Bunun üzerine hastaya sağ hemikolektomi yapıldı. Histopatolojik incelemede çekumda ganglionöromatoz tanısı kondu. Üç yıllık izlemde rekürens gözlenmedi. Multipl nörofibromatozis ve 'cafe au lait' lekeleri ile birlikte tedaviye yanıtsız konstipasyon ve intestinal obstrüksiyonu olan bir hastada von Recklinghausen hastalığının intestinal tutulumu akılda tutulmalıdır.

Anahtar Kelimeler: Çekum; nörofibromatozis 1

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Neurofibromatosis (NF) is an autosomal dominant hereditary disorder that includes two types; Type 1 and 2. Type 1 (NF1), known as von Recklinghausen disease, was first described in 1882 by Frederick von Recklinghausen. NF1 is fundamentally characterized by the existence of multiple mucocutaneous neurofibromas, 'cafe au lait' spots, and Lisch nodules.[1] It occurs with a prevalence of 1 in 3000 in Western populations. Approximately 50 percent of individuals with NF1 have no family history and are presumed to represent new mutations. The café au lait spots usually manifest immediately after birth. Neurofibromatosis is not a deadly or contagious disease; however, it is associated with malignant neoplasm of neural crest origin. Up to 25 percent of patients with NF1 develop intestinal neurogenic tumors; the most common sites of involvement are the jejunum and stomach, followed by the ileum, duodenum, and colon.[2,3] Intestinal diffuse ganglioneuromatosis is very rare in NF1 patients. We re-

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port this patient with NF1 and diffuse cecal ganglioneuromatosis in order to analyze her symptoms according to the relevant literature.

CASE REPORT

A 41-year-old female presented with a history of constipation, intermittent colicky abdominal pain and distension. Physical examination revealed typical café au lait spots as well as multiple skin neurofibromas. The same skin lesions were present in her grandmother, father, brother and two of her brother's three children. The only relevant laboratory finding was mild anemia (hemoglobin: 11.1 g/dl). There were intestinal obstruction signs on the abdominal plain radiography. The first colonoscopy was normal; however, computerized tomography (CT) demonstrated concentric thickness at the cecum wall (Figure 1). Hereon, a second colonoscopy was performed, and along the way mucosal and submucosal deep biopsies were taken. Histopathologic examination revealed schwannoma. Right colon resection was performed. Bowel continuity was restored by means of ileocolostomy. Macroscopically, there was a large submucosal lesion (Figure 2). Microscopic examination detected a diffuse spindle cell tumor with ganglion differentiation infiltrating from mucosa to serosal surface of the cecum (Figure 3). Immunohistochemically, S-100, neurofilament, smooth muscle actin, desmin, CD-117 antibody tests were performed. S-100 and neurofilament were stained positively, while the others were negative in the

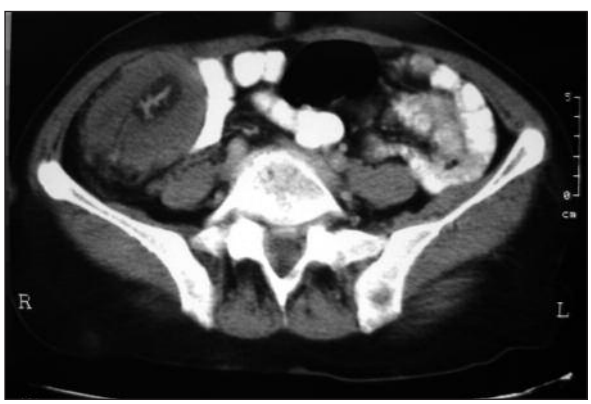

FIGURE 1: Concentric thickness of cecal wall in computed tomography.

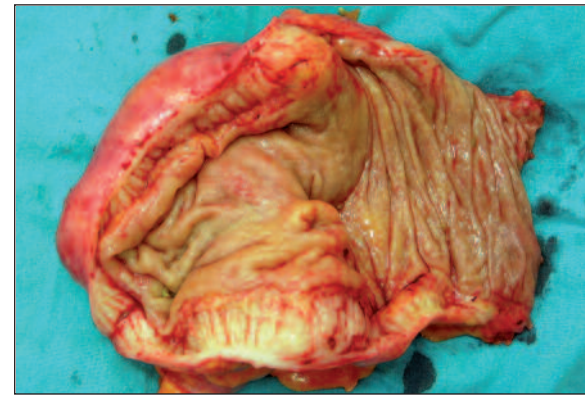

FIGURE 2: Submucosal large tumor.
(See for colored from http://tipbilimleri.turkiyeklinikleri.com/)

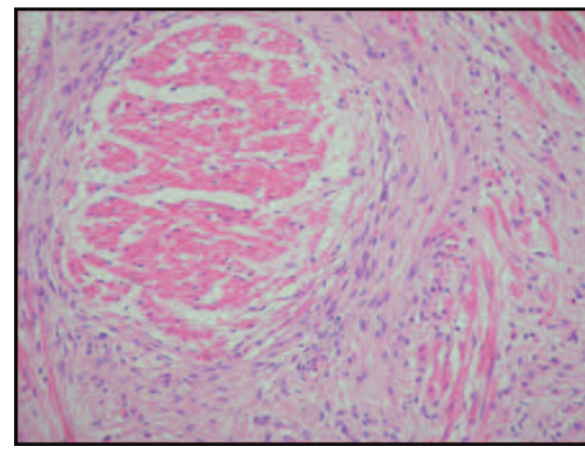

FIGURE 3: Microscopic examination detected diffuse spindle cell tumor with ganglion differentiation infiltrating from mucosa to serosal surface of the cecum(H&E X200).,
(See for colored from http://tipbilimleri.turkiyeklinikleri.com/)

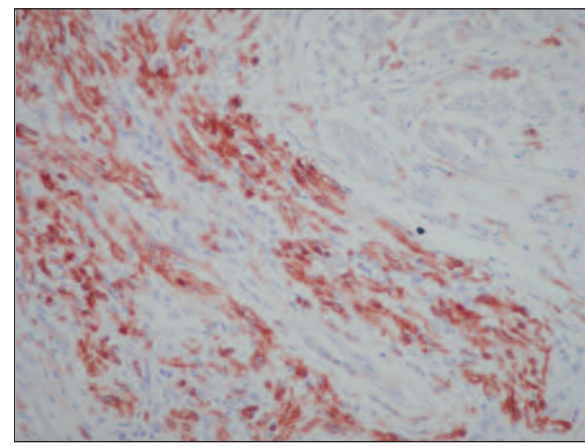

FIGURE 4: Diffuse staining with S-100 in neural crest cells (S100 X100).
(See for colored from http://tipbilimleri.turkiyeklinikleri.com/)

tumor cells (Figure 4). The tumor was diagnosed as diffuse ganglioneuromatosis (Figure 4). There was no metastasis to the mesenteric lymph nodes. The postoperative period was uneventful. No recurrence of disease was detected during three years of follow up.

DISCUSSION

The National Institute of Health (NIH) has created specific criteria for the diagnosis of NF1. Two of these seven criteria (Cardinal Clinical Features) are required for positive diagnosis.[4] They include: skin lesions such as café-au-lait spots, axillary and inguinal freckling, multiple neurofibromas, Lisch nodules (pigmented iris hamartomas), optical gliomas and bone lesions, and a first degree family history.[5] Our patient was not diagnosed as NF1 previously, but she had more than two criteria.

In cases of NF1, the gastrointestinal involvement occurs in four forms: 1) stromal tumors, 2) neuronal hyperplasia and ganglioneuromatosis, 3) endocrine tumors in the duodenum and periampullary region, and 4) other gastrointestinal neoplasms (adenocarcinoma of the small intestine and pancreas, cholangiocarcinoma).[6] Our patient`s gastrointestinal involvement was ganglioneuroma, a neoplasm of peripheral nerves with ganglion cells. Intestinal ganglioneuromas can be divided into three groups: solitary ganglioneuroma, ganglioneuromatous polyposis, and diffuse ganglioneuromatosis.[7] The first two conditions have no proven association with NF1.

In a recent review, it was reported that the association of diffuse intestinal ganglioneuromatosis with NF1 is much rarer, and there were only 14 documented previous cases.[8] The colon was the site of involvement in 8 of those 14 cases. Our patient was the ninth case of NF1 with diffuse intestinal ganglioneuromatosis located in the colon.

Those patients' clinical features are abdominal pain, constipation, melena and bowel obstruction.[8] Diffuse ganglioneuromatosis can be detected radiologically, but may be underdiagnosed because of its rarity and lack of recognition. Because of the submucosal location of diffuse intestinal ganglioneuromatosis, a colonoscopy may be reported as normal. An abdominal CT might be helpful to the diagnosis in conditions as in our case.

Although a connection between colorectal cancer and intestinal ganglioneuromatosis is controversial, intestinal ganglioneuromatosis in NF1 has the potential to become malignant.[9] The gene corresponding to NF1 is a tumor-suppressor gene, and it has been identified on chromosome 17 (17q11.2).[10]

Surgical resection is the treatment of choice in this type of tumor. Surgical examination of the digestive tract is very important during surgery to discount the presence of other similar lesions.[9] The coincidence of ganglioneuroma and adenocarcinoma in the colorectal region was previously reported by Tomita et al.[11] There was not any other intestinal lesion in our patient.

As a result, in a patient with multiple neurofibromas and 'cafe au lait' spots with intractable constipation and intestinal obstruction, intestinal manifestation of von Recklinghausen's disease should be kept in mind. If the colonoscopy is normal, a CT might be taken in order to screen for submucosal diffuse ganglioneuromatosis in those patients.

REFERENCES

1. Riccardi VM. Von Recklinghausen neurofibromatosis. N Engl J Med 1981;305(27): 1617-27.
2. Fenoglio-Preiser CM, Lantz PE, Listrom MB, Davis M, Rilke FO. Gastrointestinal mesenchymal neoplasms. In: Fenoglio-Preiser CM, ed. Gastrointestinal Pathology: An Atlas and Text. 1st ed. New York: Raven Press; 1989. p.558-61.
3. Urschel JD, Berendt RC, Anselmo JE. Surgical treatment of colonic ganglioneuromatosis in neurofibromatosis. Can J Sur 1991;34(3):271-6.
4. Huson SM. Neurofibromatosis 1: A clinical and genetic overview. In: Huson SM, Hughes RAC, eds. The Neurofibromatosis: A Pathogenic and Clinical Overview. London: Chapman and Hall Medical; 1994. p.160-204.
5. Keese M, Riester T, Schwenke K, Dinter D, Back W, Palma P. Acute GI bleeding by multiple jejunal gastrointestinal autonomic nerve tumour associated with neurofibromatosis type I. Rev Esp Enferm Dig 2007;99(10):608-11.
6. Artaza T, García JF, González C, Amengual M, Mazarro A, Rodríguez R, et al. Simultaneous involvement of the jejunum and the colon by type-1 neurofibromatosis. Scand J Gastroenterol 1999;34(3):331-4.

7. Shekitka KM, Sobin LH. Ganglioneuromas of the gastrointestinal tract. Relation to Von Recklinghausen disease and other multiple tumor syndromes. Am J Surg Pathol 1994;18(3):250-7.
8. Thway K, Fisher C. Diffuse ganglioneuromatosis in small intestine associated with neurofibromatosis type 1. Ann Diagn Pathol 2009; 13(1):50-4.
9. Chan OT, Haghighi P. Hamartomatous polyps of the colon: ganglioneuromatous, stromal, and lipomatous. Arch Pathol Lab Med 2006; 130(10):1561-6.
10. Barker D, Wright E, Nguyen K, Cannon L, Fain P, Goldgar D, et al. Gene for von Recklinghausen neurofibromatosis is in the pericentromeric region of chromosome 17. Science 1987;236(4805):1100-2.
11. Tomita H, Miya K, Tanaka H, Shimokawa K. Ganglioneuroma and adenocarcinoma associated with neurofibromatosis type 1 in the colorectal region. Int J Colorectal Dis 2006; 21(1):89-91.