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Case Report

A Study on the Challenges of Diagnosis and Interpretation in the Subject with Intestinal Ganglioneuromatosis

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Abstract

Diffuse intestinal ganglioneuromatosis is hamartomatous polyposis distinguished by a scattered, intramural or transmural proliferation of neural elements involving the enteric plexuses. This condition may involve any segment of the gastrointestinal tract, but the ileum, colon, and appendix are most frequently affected. It is a rare, benign neoplastic condition that has a well known association with multiple endocrine neoplasia type 2b, Cowden syndrome and a rare but documented association with neurofibromatosis type 1. We reported the case of a female patient's history of a neurofibromatosis who presented with chronic diarrhea. On the CT scan of the abdomen, thickening of the wall up to 2 cm, air-fluid leveling and dilatation reaching up to 6 cm at its maximum in the ileal segments and mesentery lymphadenopathies and intraperitoneal effusion were reported. There was not any peculiarity except ileal oedema and erythema on the colonoscopic examination. Endoscopic biopsy specimens obtained from the terminal ileum showed acute inflammation without any definitive findings of Crohn's disease. Due to intestinal obstruction, the patient underwent surgical resection. Diffuse ganglioneuromatosis was observed in the resected specimen.

Keywords: Intestinal Ganglioneuromatosis; Neurofibromatosis; Diarrhea; Crohn's Disease

Introduction

Diffuse ganglioneuromatosis is a rare, benign neoplastic condition that has a well known association with other pathologies like multiple endocrine neoplasia type 2 and neurofibromatosis type 1 (NF 1). It includes hyperplasia of the myenteric plexus and infiltration of ganglioneuromatous tissue in the guts wall. This condition may affect any portion of the gastrointestinal tract but the ileum, colon and appendix are more frequently involved. Affected persons may present with marked diarrhea, acute intestinal obstruction and/or nonspecific symptoms owing to motility disturbances [1,2]. Because of its rarity, diffuse intestinal ganglioneuromatosis is straightforwardly overlooked or misdiagnosed. We reported the case of diffuse ganglioneuromatosis which caused diagnostic difficulties.

Case Report

A 43-year-old woman presented to our clinic with the complaint of diarrhea. The physical examination performed in this patient with a medical history of neurofibromatosis revealed a swelling of the abdomen and visible intestinal loop movements. Diffuse neurofibromas and cafe au lait pigment changes were observed in her body (Figure 1). The biochemical values were as follows: to-

tal protein: 5.43 gr/dl (6.4 - 8.3), albumin: 2.80 gr/dl (3.5 - 5.2), IgG: 679 mg/dl (700 - 1600), IgA: 69.2 mg/dl (70 - 140), C-reactive protein (CRP): 24.6 mg/dl (0 - 5). On the abdominal pelvis tomography, thickening of the wall up to 2 cm, air-fluid leveling and dilatation reaching up to 6 cm at its maximum in the ileal loops and mesentery lymphadenopathies and intraperitoneal effusion were observed. The conventional enteroclysis revealed marked coarsening and thickening of the plicae in the ileal curves together with submucosal nodular pattern becoming evident (Figure 2). The colonoscopy investigation showed no peculiarity except the ileal edema and erythema. Biopsy of the ileum detected no findings that could be definitive of the Crohn's Disease except the mild acute inflammation. Given the patient's lymphopenia detected at 760/microliters (1300 - 3500), a potential presence of common variable immunodeficiency was considered and thus flow cytometry was performed on peripheral blood, which revealed no pathology (CD4+: 60.2%, CD3+: 80.1%, CD8+: 24.1%). On the macroscopic investigation of the ileocecal segment obtained following the surgical resection, the wall of the small intestine and the large intestine was observed to be markedly thickened reaching up to 2 cm, respectively along a length of 100 cm and 6 cm. A large number of polypoid lesions with a diameter ranging between 5 mm and 60 mm, which were either isolated or showed a tendency to unite with each other and blistered from the mucosa were observed. They had a grey-white cross-section surface, elastic-hard consistency and a filamentous appearance. Microscopic investigation showed that proliferation consisting of fusiform cells and individual or grouped mature ganglion cells occupied all the wall layers starting from the lamina propria. No cellular atypia, pleomorphism, mitosis or necrosis was detected. The fusiform cells exhibited diffuse positive staining with S100 and NSE and focal positive staining with synaptophysin (Figure 3). The patient was put on outpatient follow-up and discharged.

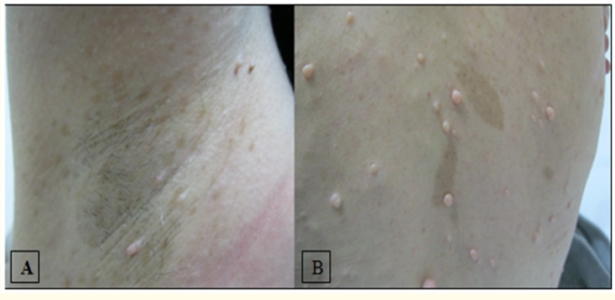

Figure 1: A. Axillary freckles observed in the patient, B. There were cafe au lait spots and multiple neurofibromas on the patient's back.

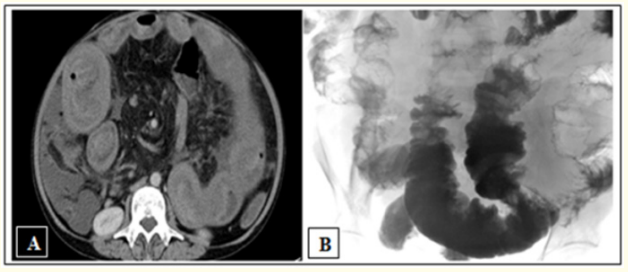

Figure 2: A. Computerized Tomography scan of the abdomen revealed thickening of the wall of the distal ileal loops with mild ascites, B. The conventional enteroclysis revealed marked coarsening and thickening of the plicae in the ileal curves together with submucosal nodular pattern becoming evident.

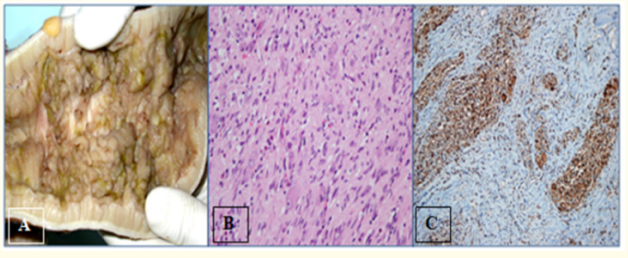

Figure 3: A. Small intestine wall thickening up to 2 cm was observed. B. Fusiform cell proliferation was detected (X400, Hematoxylin-eosin) C. Fusiform cells exhibited diffuse S-100 and neuron-specific enolase staining.

Discussion

Although the imaging investigations revealing ileal wall thickening together with the complaint of diarrhea primarily suggested the presence of Crohn's disease, the colonoscopic findings or the conventional enteroclysis findings did not confirm this diagnosis. The pathological investigation performed following surgery revealed findings consistent with diffuse ganglioneuromatosis.

Intestinal ganglioneuromatosis ganglion cells represent a rare neoplastic condition resulting from the schwann and nerve fibers. These tumors may be solitary or manifest as a part of a syndrome (Cowden, Neurofibromatosis). 25% of the patients with neurofibromatosis may develop intestinal neurogenic tumours; these tumours are primarily located in the jejunum, stomach and at a decreasing frequency, in the ileum and colon [3]. Also, diffuse ganglioneuromatosis observed in our patient mostly involves the colon, terminal ileum and the appendix [4]. In their literature review, Iwamura and coworkers showed that the most common symptom

of the patients was abdominal pain (33%) and the most frequently involved site among bowel segments was the colon (56.3%) [5]. Thyway., *et al*. described that intestinal ganglioneuromatosis could accompany neurofibromatosis with other investigators reporting that 6.7% of the cases of neurofibromatosis-associated ganglioneuromatosis had diarrhea [6]. Charagundla., *et al*. reported that this association could mimic the Crohn's disease [1]. In the literature, there was only one patient reported with diffuse intestinal ganglioneuromatosis associated with neurofibromatosis type 1 from our country [7]. Our case had both chronic diarrhea and radiologic findings suggesting the Crohn's disease. However, the biochemical values caused us to consider protein-losing enteropathy in the differential diagnosis. On the other hand, the low level of immunoglobulins and lymphopenia alarmed us for common variable immunodeficiency (CVID) however, peripheral flow cytometry study helped us to exclude this diagnosis. Protein-losing enteropathy manifests with hypoproteinemia, hypoalbuminemia and with lymphopenia, particularly in the presence of lymphatic obstruction [8].

Conclusion

In conclusion, the diagnosis of the diffuse intestinal ganglioneuromatosis represents a challenge**.** The most frequently reported symptoms are diarrhea, abdominal pain and change in bowel habit, which mimics Crohn's disease and CVID. While this clinical manifestation is rare, the clinician should still strongly suspect the presence of ganglioneuromatosis based on the patient's medical history, the mode of presentation and the radiological findings. The treatment should be surgical as is the case in our patient.

Bibliography

1. Charagundla SR., *et al.* "Diffuse intestinal ganglioneuromatosis mimicking Crohn's disease". *American Journal of Roentgenology* 182 (2004): 1166-1168.

2. Lefere I., *et al.* "Diffuse intestinal ganglioneuromatosis of the ileum". *Journal of the Belgian Society of Radiology* 95 (2012): 152-153.

3. Fenoglio-Preiser CM., *et al.* "Gastrointestinal mesenchymal neoplasms". Gastrointestinal pathology: an atlas and text. NY: Raven Press (1989): 558-561.

4. Shekitka KM and Sobin LH. "Ganglioneuromas of the gastrointestinal tract: relation to Von Recklinghausen disease and other multiple tumor syndromes". *The American Journal of Surgical Pathology* 18 (1994): 250-257.

5. Iwamuro M., *et al.* "Diffuse Intestinal Ganglioneuromatosis Showing Multiple Large Bowel Ulcers in a Patient with Neurofibromatosis Type 1". *Internal Medicine* 56.24 (2017): 3287-3291.

6. Thway K and Fisher C. "Diffuse ganglioneuromatosis in small intestine associated with neurofibromatosis type 1". *Annals of Diagnostic Pathology* 13 (2009): 50-54.

7. Kilincalp S., *et al.* "Double-balloon enteroscopy for the detection of diffuse small-bowel polypoid ganglioneuromatosis mimicking Crohn's disease in a patient with von Recklinghausen disease". *Endoscopy* 47.1(2015): E4-E5.

8. Umar SB., *et al.* "Protein-losing enteropathy: case illustrations and clinical review". *The American Journal of Gastroenterology* 105 (2010): 43-49.