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CASE REPORT

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Adult Hirschsprung's Disease Diagnosed During Forensic Autopsy

ABSTRACT: We report a case of fatal Hirschsprung's disease (HD) discovered at autopsy. A 20-year-old man collapsed at home. Emergency medical personnel found him in cardiac arrest and all resuscitative efforts failed. He had a past history of chronic constipation since infancy. Forensic autopsy revealed a megacolon full of gas and stools. Microscopic examination showed absence of ganglion cells in a short segment of the rectum and enterocolitis in the left and transverse colon. HD is rarely described in adults. In many cases, patients complained of constipation since infancy but the affection remained misdiagnosed. The relative good tolerance of the disease is usually due to a short aganglionic bowel segment. Enterocolitis is a frequent and severe complication of HD in children but is rarely described in adults. This case suggests the importance of HD diagnosis in childhood in order to avoid fatal complications with forensic consequences.

KEYWORDS: forensic science, forensic pathology, Hirschsprung's disease, adult, autopsy

Hirschsprung's disease (HD), also known as congenital aganglionic megacolon, is characterized by the absence of ganglion cells in the submucosal and myenteric plexus of the distal bowel (1). HD is usually diagnosed and therefore surgically treated in infancy, in children presenting complete large bowel obstruction at birth, enterocolitis, or chronic constipation (2). In rare cases, the diagnosis of HD may be made in adults (2). We report the postmortem pathological and histological findings of a case of HD complicated by enterocolitis in a young adult.

Case Report

A 20-year-old man's father called the emergency service after discovering his son who had fainted in his shower after having a foul-smelling diarrhea. On arrival in a poor condition home, they found a young man lying on the floor of the bathroom in respiratory and cardiac failure. Despite intensive resuscitation, no cardiac activity reappeared and death was certified 30 min later. Because the circumstances of death appeared suspicious to the treating emergency physician, a forensic investigation was initiated. The Public prosecutor ordered a forensic necropsy.

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Autopsy Findings

The man was 20 years old, measuring 1.75 m and weighing 60 kg. External examination showed a huge abdominal distension with no bruising. Laparotomy showed a dilated colon, full of gas and stools. The left colon had a thickened wall and there was an accumulation of hardened feces in the colon and rectum (fecaloma). The recto-sigmoid colon was considerably distended, measuring 40 cm in diameter. Mucosa of the left and transverse colon was fragile and darkened (Fig. 1). Microscopic examination showed a 1 cm aganglionic bowel located 2 cm above the level of the dental line associated to hypertrophic nerve trunks (Fig. 2). Microscopic examination of the left colon revealed a thickened fibrous wall with rare ganglion cells in the plexus. The transverse and left colon showed microscopic lesions of enterocolitis. They consisted of ulcerative and necrotized mucosa with micro-abscesses in the submucosa (Fig. 3). The lungs were congestive. The heart weighed 340 g and had a normal gross and microscopic appearance. The other organs had a normal gross and microscopic appearance and showed no septic lesions. Samples of blood from the femoral vein and the heart, urine, bile, gastric contents as well as the liver, brain, heart, kidney, lung, and hair samples were collected at autopsy for toxicological analyses. Urine and blood contents were analyzed for drugs by high-pressure liquid chromatography with UV and mass spectrometric detection as well as gas chromatography coupled to a mass spectrometric detector. Ethanol, opiate-type drugs, amphetamines, benzodiazepines, neuroleptics, tricyclic antidepressants, cannabinoids, cocaine metabolites, LSD, and methadone were not detected in blood or urine. No postmortem bacteriological cultures were performed on the heart blood, spleen, and colon.

Death was attributed to septic shock due to enterocolitis complicating HD.

FIG. 1—*The opened formalin-fixed colon shows the dilated (40 cm diameter) recto-sigmoid on the right. Note the dark discoloration of the mucosa of the left and transverse colon, compared with the relatively normal mucosa of the right colon (seen on the left hand side of the figure).*

History of Disease

The medical file of the young man showed that he was a mentally handicapped child, abandoned by his parents, and living under precarious socioeconomic conditions. He had been living in special institutions for the disabled during infancy and adolescence. He had been admitted at hospital twice at the age of 11 and 13 for fecal impaction. Barium enema showed dilation of the colon (dolichocolon) with retention of barium for 24 h in the rectosigmoid. The diagnosis of short HD was made but not confirmed because rectal examination and ano-rectal manometry were considered normal. A Diagnosis of decreased distal colonic motility was made and laxatives were prescribed. No rectal biopsy was performed. The physicians lost contact with the child. He had left the institution a few months before his death and had gone home, and was living under precarious socioeconomic conditions.

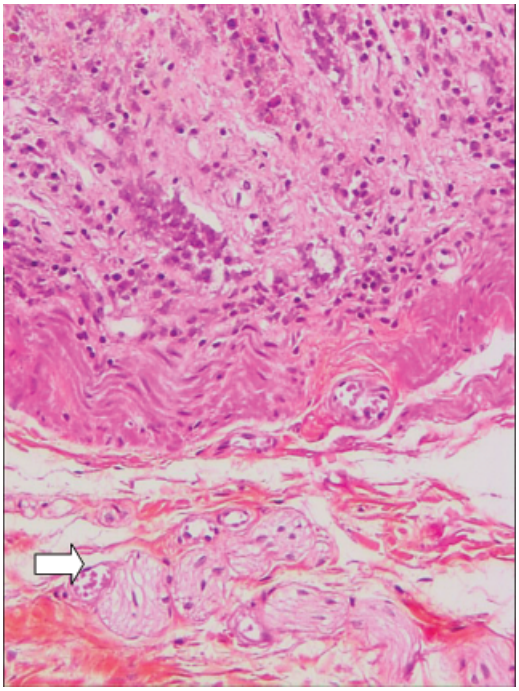

FIG. 2—*Rectal aganglionic segment showing lytic mucosa with absence of ganglion cell and hypertrophic nerve trunks in the submucosa (arrow) (Hematein Phloxin Saffron × 10).*

Discussion

The first description of congenital megacolon was given by Ruysch in a 1691 autopsy report (3), but the classic description of this condition was reported in 1887 by Harald Hirschsprung, a Danish pediatrician (4). The absence of ganglion cells in the rectal wall nerve plexuses on microscopic examination was described by Tittel in 1901 (5).

HD is the most common cause of neonatal intestinal obstruction and occurs in approximately 1 per 5000 live births, with a 4:1 male to female predominance (1). Several gene mutations have been suspected in the genesis of the disease, such as endothelin B receptor gene, endothelin 3, RET proto-oncogene, and glial cell-linked-derived neurotrophic factor gene (1,6). Aganglionosis extends from the dental line proximally to the level of the upper rectum or rectosigmoid in 80% of patients and to the proximal colon in 15% of patients (6). In 5% of patients, aganglionosis involves the entire colon with variable extension into the small bowel (6).

The cause of aganglionosis remains uncertain. Failure of ganglion cells' migration from the vagal neural crest to the distal bowel during embryonic life has been suspected (1,6). Microenvironmental changes with modifications of the composition of the extracellular matrix, cell adhesion molecules, and neurotrophic factors could alter migration, differentiation, and maturation of the ganglion cells. Ischemic or immunologic injury may also destroy ganglion cells (1,6). The absence of ganglion cells in the colonic

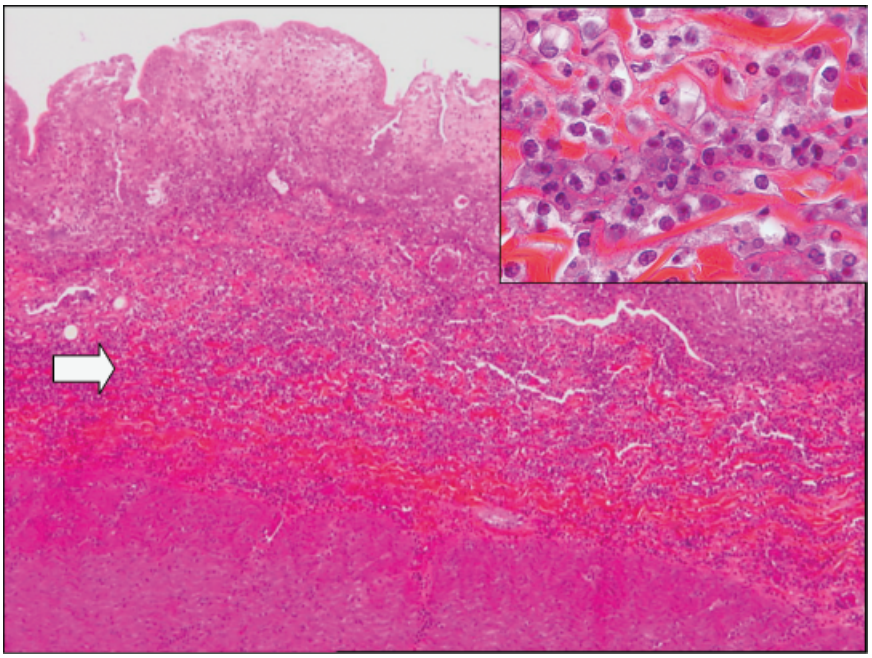

FIG. 3—*Enterocolitis with necrotic mucosa and abscesses in the submucosa (arrow) consisting of numerous macrophages and neutrophils (inset) (Hematein Phloxin Saffron × 2.5 and × 20).*

neural plexuses results in an imbalance of bowel innervation leading to a permanent spasm of the aganglionic segment. The aganglionic distal bowel in HD lacks peristalsis, and secondary dilation in the upstream bowel due to functional obstruction occurs. Patients present complete obstruction at birth or chronic constipation in infancy and childhood (1). The diagnosis of HD is based on radiological studies, anorectal manometry findings, and histological examination of rectal wall biopsies (1). Barium enema usually demonstrates a small-caliber aganglionic rectum transiting with a larger and obstructed proximal ganglionic colon (1). Barium retention for 2–3 days in the rectosigmoid helps to diagnose the disease (1). Manometric examination shows an absent anorectal response characterized by a lack of relaxation of the internal anal sphincter with transient rectal distension (1). The diagnosis of HD requires histologic confirmation of the absence of ganglion cells in the submucosa on a rectal biopsy (1). The current criteria for the microscopic and histochemical diagnosis of the disease are failure to demonstrate ganglion cells in serial sections from a suction rectal mucosal biopsy and an increase in the amount of acetylcholinesterase-containing nerve bundles fibers in the affected segment (1). Curative surgery consists in total resection of the aganglionic segment, followed by anastomosis of the normally innervated intestine (1).

In some patients, the diagnosis of HD is delayed until adulthood (2,7–11). Patients complain of chronic constipation. Some have sought medical attention earlier but without any diagnosis as in our case (7). Powell (7) showed that the delay in diagnosis could also result from physician misinformation of the child's family concerning the severity of the disease. Miyamoto et al., (2) in their review of the literature, found 229 cases of adult's HD reported from 1950 to 2005. Adults with HD are usually males, with a male to female ratio of 4:1 (2,9). Their mean age is 24 years, and the oldest patient was a 69-year-old woman (2,8,9). Patients usually complain of severe constipation since infancy, with episodes of abdominal pain and colonic distension (2,9). Defecation ranges from once a week to once every 2 months (2,9). Palpable fecal masses or fecal impaction are frequent (2,9). Patients frequently take cathartics and enemas or sometimes use digital evacuation (2,9). The diagnosis of HD is rarely considered in adults but could represent 2% of chronic refractory constipation (10). The relative good tolerance of HD in patients reaching adulthood without surgical procedure is usually due to a short aganglionic bowel segment, usually less than 10 cm long, and hypertrophy of the proximal normal colon that overcomes the distal obstruction of the bowel (2). When the dilated colon is no longer able to propel the feces distally, the patients present with acute obstruction. Complications such as colonic perforation or respiratory failure due to compression of the diaphragm by the distended colonic bowel are rare in adults (11). Sepsis due to enterocolitis, as in our case, is a frequent complication in children (12). Meanwhile, it remains a very rare complication of adult's HD with a single case reported in the literature to our knowledge in a 17-year-old man (7). Patients dying from enterocolitis usually have no evidence of sepsis in other organs at microscopic examination; occurrence of abscesses in other organs is a rare finding in patients who die from gastro-intestinal tract-induced sepsis (13). The underlying causes of enterocolitis include ischemia secondary to huge intestinal dilation and intestinal stasis, which promote the proliferation of luminal pathogens and subsequent mucosal invasion (12).

Adult's HD usually does not lead to death and the diagnosis is rarely made at autopsy (8). The diagnosis of HD in adults, as well as infants, is based on radiological studies, anorectal manometry findings, and histological examination of rectal wall biopsies (2,9). However, the typical rectal narrowing can be absent in adult's HD and anorectal manometry can be interpreted as normal as in our case, due to a short aganglionic segment (9).

Conclusion

To our knowledge, we report the first case of adult's HD diagnosed during forensic autopsy. The patient died of sepsis due to enterocolitis which is a classic complication of HD in infants, but very rare in adults.

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