Rare disease

Diffuse ganglioneuromatosis of intestine in a 15-year-old girl

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Summary

The authors present the case of a 15-year-old girl with diffuse ganglioneuromatosis, principally involving the caecum. This is a rare condition and usually associated with multiple endocrine neoplasm IIb and neurofibromatosis type I. In our case, the myentric nerve plexus was exclusively involved. The patient presented with episodes of vomiting and weight loss. So far, to our knowledge no other manifestations of the above mentioned genetic conditions have become apparent in this patient.

BACKGROUND

Many types of neuronal tumours occur in the gastrointestinal tract. These may develop sporadically or in association with syndromes such as neurofibromatosis type I (NF1) and multiple endocrine neoplasm (MEN).^{1 2} These tumours include neuromas, ganglioneuromas, neurofibromas (including plexiform neurofibromas) and even malignant peripheral nerve sheath tumours. Ganglioneuromas may occur as single or multiple polypoidal lesions, the latter condition is called ganglioneuromatous polyposis; or as a diffuse involvement of the intestinal wall, referred to as intestinal ganglioneuromatosis.³ Single polypoid ganglioneuromas are normally not associated with the above mentioned genetic syndromes, but lesions occurring as multiple polyps or as diffuse involvement of the wall

often occur in association with NF, MEN II, juvenile polyposis, etc.⁴ Gastrointestinal ganglioneuromatous tumours are rare tumours and solitary polyps involving the mucosa and submucosa are the most common.⁵ Diffuse intestinal ganglioneuromatosis is diffuse hyperplasia of the neural plexuses of the intestinal wall.⁶ It has two variants, transmural and mucosal.⁴ We report the case of a 15-year-old girl from Peshawar in the troubled northern part of Pakistan.

CASE PRESENTATION

We received the surgical specimens of a 15-year-old girl from Peshawar in North Pakistan coded as 'right hemicolectomy' specimen. She had presented with a few weeks history of episodic, ill-defined abdominal pain, vomiting, loss

Figure 1 Diffuse and prominent infiltration of muscularis propria by large nerve bundles with ganglia. H&E × 20.

Figure 2 Diffuse and prominent infiltration of muscularis propria by large nerve bundles with ganglia. H&E $\times$ 40.

of appetite and progressive weight loss. The exact degree of weight loss was not known; however, it was significant. Family history was unremarkable. She was referred to a surgeon in Peshawar. On examination, she had abdominal distention. No skin nodules were found and there was no cranial nerve involvement. Ultrasound report from a local imaging centre in Peshawar reported a large, cystic dilatation of the caecum and terminal ileum. Gas was present in the dilated area. Plain abdominal x-ray, CT scan or colonoscopy were not performed. At laparotomy, diffuse thickening of the caecal wall was found which extended for a few centimetres into the terminal ileum with resulting narrowing of the lumen. However, the ileum proximal to the thickening was thin walled and dilated. These findings corresponded with the ultrasound findings. The caecum and terminal ileum were adherent to part of ascending colon. There was no evidence of peritonitis.

INVESTIGATIONS

The specimen we received consisted of caecum, terminal ileum and adherent loops of ascending and proximal transverse colon. The specimen measured 55 cm in length. No discrete mass was identified in the caecum; however, there appeared to be a diffuse thickening of the wall and this thickening extended through the ileocaecal wall into the terminal ileum. The proximal terminal ileum was dilated and thin walled. The terminal ileum and caecum appeared to be adherent to part of the ascending colon. There was no evidence of perforation. Multiple representative sections were submitted from the thickened part of caecum and terminal ileum as well as from the adherent loops of large bowel. Representative sections were also submitted from the peripheral proximal and distal resection

margins which were 5 cm and 18 cm respectively from the thickened area in the caecum. Histological examination revealed no significant histological abnormality in the adherent loops of large bowel and the peripheral resection margins also were histologically unremarkable. However, histological examination of thickened part of caecum and terminal ileum revealed a diffuse prominent infiltration of muscularis propria by large nerve bundles with ganglia (figures 1 and 2). There was no involvement of the submucosa or the serosal fat. On immunohistochemistry, there was strong reactivity for S 100 protein (figure 3) while staining for CD117 was negative. The positivity for S100 protein confirmed the neural origin of the cells, while negative CD117 ruled out the possibility of gastro intestinal stromal tumour. The nerve bundles were seen to infiltrate between the layers of muscularis propria. However, no significant nuclear pleomorphism or mitotic activity was seen. The overlying epithelium was mostly intact. All 18 recovered lymph nodes showed reactive changes only. The sections from adherent loops of large intestine were also unremarkable except for mild inflammation and fibrosis. A diagnosis of diffuse intestinal ganglioneuromatosis was made. The possibility of the patient suffering from NFI, MEN II, etc was raised in the report and we recommended that such a possibility should be excluded by appropriate clinical examination.

TREATMENT

The patient underwent surgery.

OUTCOME AND FOLLOW-UP

The patient underwent surgery, follow-up was not available.

Figure 3 The hyperplastic nerve plexus in the muscularis propria showing strong positivity with immunohistochemical stain S100 protein. $\times 20$.

DISCUSSION

Ganglioneuromas of the gastrointestinal tract may be single, multiple (ganglioneuromatous polyposis), or may present as a diffuse involvement of the intestinal wall (diffuse ganglioneuromatosis).³ Diffuse ganglioneuromatosis can be mucosal or transmural.⁴ In children, either variant can be seen, while in adults the condition mostly involves the mucosa.⁷ Histologically, diffuse ganglioneuromatosis appears as a diffuse, band like enlargement of nerve fibres and ganglion cells of the submucosal and myenteric plexuses and the changes are more pronounced in the latter.^{3 6 8} Most reports have described the tumour cells as bland and mature, with no significant mitoses or nuclear pleomorphism.^{4 8} Our case showed similar findings. Diffuse ganglioneuromatosis is often the first manifestation of MEN IIb.⁹ Analysis for specific genetic mutations of MEN IIb was not performed as such facilities are not available in our country. However, apparently the girl is so far free from any manifestation of NF1, MEN IIb, etc. Most reports have observed that it is the solitary gastrointestinal ganglioneuromatous polyps which are not associated with NF1 or MEN IIb while multiple ganglioneuromatous polyps and diffuse ganglioneuromatosis are usually associated with the same.^{4 6} However, Ledwidge *et al*⁴ have also observed that adult transmural intestinal ganglioneuromatosis is not always associated with multiple endocrine neoplasm or neurofibromatosis. Malignant transformation in the ganglioneuromatosis itself has not been documented, and there are only occasional case reports of an association with malignant peripheral nerve sheath tumour.^{3 8}

The girl who is apparently well now needs to be followed up so that any subsequent manifestations of the usually associated genetic disorders are recognised early.

Although, it may be possible to suspect ganglioneuromatosis radiologically, it is not often diagnosed because it is very rare and may not be recognised. It may present as intestinal obstruction due to unknown cause. Initially, surgical resection is the main treatment. If disease recurs, or if further surgery is not feasible, chemoradiation therapy can be given. It is very important to recognise the histopathological features as these may be very subtle. The diagnosis is essentially morphological.⁸ It is sometimes diagnosed in the absence of any clinical features of NF1 and so its recognition at this early stage may be of great help for investigation of NF1 as such a possibility can lead to problems for the whole family.^{3 8}

Learning points

- It is a rare disease presented to us.
- It needs follow-up, surveillance of siblings may also be needed in such cases.

Competing interests None.

Patient consent Obtained.

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AHmad Z, Khan R, Barakzai A, Ahmed A, Qureshi A. Diffuse ganglioneuromatosis of intestine in a 15-year-old girl. *BMJ Case Reports* 2011; 10.1136/bcr.04.2011.4151, date of publication

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