Pathology of an East African megacolon¹

G. M. BÖHM² AND BARBARA SMITH

From the Pathology Department, St. Bartholomew's Hospital, London

EDITORIAL COMMENT This paper provides further evidence of the value of studying the epidemiology of diseases. Attention is drawn to a local cause of megacolon and it is postulated that there may be degenerative changes in the sacral para-sympathetic nerve supply.

In 1952 Burkitt called attention to the frequency of volvulus of the sigmoid colon amongst the Baganda tribe in Uganda. Hall-Craggs (1960) reported 104 cases in five years at Kampala, and Shepherd and Wright (1965) stated that from 1961 to 1963 over 120 cases were admitted to the Mulago Hospital, Kampala. In Hall-Craggs' experience patients with volvulus were between 30 and 60 years of age, 94.2% of the patients were males, and 77% of them were Baganda. He suggested that a long mobile sigmoid colon, common in Africans, predisposed to torsion of the gut.

Shepherd and Wright (1965) considered that the hypertrophy and dilatation in these cases were rather the cause of the torsion than its consequence, the primary disease being a megacolon which frequently caused volvulus. The same authors observed that the symptoms do not date from birth and that a distal narrowed aganglionic segment was not present. Dilatation and hypertrophy of the sigmoid colon have been encountered in patients without a history of obstruction and in some cases were incidental radiological or surgical findings. Coordinated contraction rings were not seen either radiologically or at laparotomy. Usually only the distal two-thirds of the sigmoid colon was affected and involvement of the other segments of the colon was not observed. At laparotomy the appearance of the affected part was flabby and stimulation by pinching did not result in contraction. The wall of the dilated pelvic colon was greatly thickened; in 10 cases in which it was resected for volvulus it was found to be 150-200% thicker than that of the descending colon. The meso-

colon was thickened as well as elongated and its blood vessels and lymphatics were enlarged. Shepherd and Wright (1965) suggested that megacolon, defined by Adamson and Aird (1932) as 'dilatation and hypertrophy of a part of the colon or of the whole colon, occurring in the absence of a gross obstructive lesion', is very frequent in Uganda.

The purpose of this paper is to present the pathological findings in the colon in this condition.

MATERIAL AND METHODS

Material from two cases was obtained by one of us (G.M.B.). Both patients were males, one (no. 591/64) was 27 years old and the other (no. 5084/64) was 55. In the first patient the total sigmoid colon was measured and was 65 cm. long; the dilated part was 27 cm. long and 10 cm. wide in its widest portion. The second sigmoid colon was 75 cm. long and the dilated part 40 cm. in length and 9 cm. in its greatest diameter. In both cases the dilatation occurred in the distal part of the sigmoid colon and the rectum appeared normal, although no biopsy was taken.

The specimens were fixed in formol-saline, paraffin sections were stained with haematoxylin and eosin, and thick frozen sections by Schofield's silver impregnation method. Köberle's (1963a) technique, which counts all neurones in a ring of 1 mm. thickness, was used to assess the number of ganglion cells in Auerbach's plexus. This was done at four levels in each case.

RESULTS

The histological appearances of the mucosa and submucosa were normal. The muscle coats were hypertrophied, particularly the circular fibres. The circular muscle coat contained a few vacuolated fibres and some of the nuclei were large and pale with pronounced nucleoli similar to those seen in regenerating skeletal muscle.

¹This work is supported by the Conselho Nacional de Pesquisas (Brazil) and Fundação de Amparo à Pesquisa do Estado de São Paulo (Brazil).

²Present address: Department of Pathology, Medical School of Ribeirão Preto, University of São Paulo, Brazil.

FIG. 1. Swollen and vacuolated neurones from Auerbach's plexus in a megacolon. Haematoxylin and eosin $\times 600$.

FIG. 3. Circular unmyelinated fibres from Auerbach's plexus in a normal colon. Schofield $\times 300$.

FIG. 2.

FIG. 4. Part of the fine fibre network in Auerbach's plexus in a normal colon. Only a small amount can be brought into focus at the same time. Schofield $\times 300$.

Ganglion cells were present in the intermuscular and submucosal nerve plexuses and although many showed normal appearances, some were swollen with chromatolysis or vacuolation of their cytoplasm (Fig. 1). Figure 2 shows the results of the ganglion cell counts in Auerbach's plexus. These numbers are similar to those found in normal Brazilian subjects. The average number found in a ring 1 mm. in diameter is 5,785 for normal sigmoid colon and 4,036 for normal rectum (Köberle, 1960).

The quantity of unmyelinated nerve fibre in the intermuscular plexus was reduced compared both with a normal gut and with gut distended behind a neoplastic obstruction. The Schwann cell nuclei were large and more rounded than normal and considerably reduced in numbers. The plexus was infiltrated in places by a number of eosinophils but there was no other inflammatory reaction.

Silver impregnations of normal large intestine show two types of unmyelinated axons. One type is relatively thick and runs in the same direction as the circular muscle fibres (Fig. 3). The other type consists of an interlacing network of very fine fibres (Fig. 4). In the two cases of megacolon studied, the thick axons could still be seen, but they were fragmented and in some cases very swollen (Figs. 5 and 6). The fine network was absent except for a little axonal dust (Fig. 7).

DISCUSSION

This is a true megacolon as suggested by Köberle (1963a), namely, dilatation and hypertrophy, not due to any obstruction, either mechanical or functional, and the dilated segment itself is diseased. The finding of muscular hypertrophy does not need any

FIG. 5.

FIG. 6.

FIGS. 5 and 6. *Greatly swollen circular fibres from Auerbach's plexus in a megacolon. Schofield $\times 300$.*

FIG. 7. *Axonal remnants in Auerbach's plexus in a case of megacolon. Schofield $\times 300$.*

obstruction and overwork for its explanation. Meyer (1921) and Froboese (1922) have shown that distension of the immobilized muscle leads to hypertrophy without an increased work load. In the colon failure of peristalsis will lead to chronic distension of the viscus and muscular hypertrophy (Köberle, 1963a). This explanation is consistent with the more accentuated hypertrophy of the circular muscular coat which suffers the greater distension found in our cases and other enteromegalies (Köberle, 1963b).

The histological changes in these intestines are quite different from those described in Hirschprung's disease where the pathological section of the gut is contracted and aganglionic. The dilated and hypertrophied bowel lies proximal to this and is the result of a physiological obstruction. Hirschprung's disease is thus not a megacolon.

Siegmund (1935) showed that patients treated with atropine developed megacolon, thus calling attention to the importance of normally functioning ganglion cells in preventing this condition. In Chagas disease a true megacolon occurs as a late manifestation of the condition due to the destruction of neurones in Auerbach's plexus by a neurotoxic substance produced by the disintegrated leishmanias (Köberle, 1956a; 1956b).

In these two cases the number of neurones is within normal limits, but they do show histological changes, namely, vacuolation and chromatolysis. These changes could be due to direct damage to the cell, damage to their axons resulting in retrograde cell change, or to loss of the preganglionic innervation resulting in transneuronal degeneration (Jacob, 1957). Direct damage to the neurone is unlikely, as one would expect cell fall-out with so much functional derangement. However, infectious diseases are endemic in East Africa and it is possible that one might produce a toxin damaging, but not destroying, neurones. The presence of a chronic volvulus with ischaemia could also damage them.

A great deal of the normal fine nerve network has disappeared in these cases and the long thick fibres show evidence of damage. Cajal (1954) states that the preganglionic fibres are much thicker than the intrinsic fibres of Auerbach's plexus, although he does not distinguish between sympathetic and parasympathetic innervation. The presence of these circular fibres in Hirschprung's disease where there are no ganglion cells would tend to confirm that they may be preganglionic fibres. If so, in these cases it is possible that the lesion lies not in the colon but in the preganglionic neurones. This would account for the presence of normal numbers of ganglion cells and for the damage to the thick circular axons, the loss of the nerve net being a secondary phenomenon.

The descending and sigmoid portions of the colon

receive their parasympathetic supply from the second, third, and fourth sacral segments (Woodburne, 1956) and a degenerative lesion of neurones in the lateral columns of these segments of the cord could produce this type of lesion. The fact that this disease occurs mainly in one tribe and in the male sex suggests a genetic factor (associated or not with an infectious agent) perhaps similar to that in Kuru (Gajdusek, 1963) or the melanesian amyotrophic lateral sclerosis (Kurland, 1957). These diseases occur also in a single tribe, mainly in the same sex, and have been shown to be a neuronal degeneration coming on in adult life. Degenerative changes in central autonomic cells can occur with the production of symptoms. Shy and Drager (1960) described cell loss in the intermediolateral columns in a case of postural hypotension. Two further cases of progressive autonomic failure with a similar pathology have been published by Johnson, Lee, Oppenheimer, and Scadding (1966). In all three cases there were other degenerative changes in the nervous system.

In these cases of megacolon the examination of the spinal cord could confirm or eliminate this possibility.

SUMMARY

The pathology of the gut is described in two cases of dilatation and hypertrophy of the sigmoid colon from East Africa, occurring predominantly in the males of a single tribe. The pathological findings confirm other workers' impressions that this entity is a true megacolon. The possibility that it may be a system degeneration affecting the sacral parasympathetic outflow is suggested.

The authors are indebted to Dr. J. J. Shepherd (Makerere University College, Department of Surgery, Kampala) for the permission to use his material, to Mr. P. Crocker

for the photographs, and to Mr. J. W. Miller and Mr. R. A. Dunbar for technical assistance.

REFERENCES

- Adamson, W. A. D., and Aird, I. (1932). Megacolon: evidence in favour of a neurogenic origin. *Brit. J. Surg.*, 20, 220-233.
- Burkitt, D. P. (1952). Acute abdomens—British and Baganda compared. *East Afr. med. J.*, 29, 189-194.
- Froboese, C. (1922). Ueber echte Hypertrophie inaktiver Muskeln. *Beitr. path. Anat.*, 71, 170-181.
- Gajdusek, D. C. (1963). Kuru. *Trans. roy. Soc. trop. Med. Hyg.*, 57, 151-166.
- Hall-Craggs, E. C. B. (1960). Sigmoid volvulus in an African population. *Brit. med. J.*, 1, 1015-1017.
- Jacob, H. (1957). Sekundäre Retrograde und transsynaptische Degeneration. In *Handbuch der speziellen pathologischen Anatomie und Histologie*, edited by O. Lubarsch, F. Aenke, and R. Rössle. Band 13, Teil I, Bandteil p. 266. Springer, Berlin.
- Johnson, R. H., Lee, G. de J., Oppenheimer, D. R., and Scadding, J. M. K. (1966). Autonomic failure with orthostatic hypotension due to intermediolateral column degeneration. *Quart. J. Med.* In press.
- Köberle, F. (1956a). Die Chagaskrankheit: eine Erkrankung der neurovegetativen Peripherie. *Wien. klin. Wschr.*, 68, 333-339.
- (1956b). Über das Neurotoxin des Trypanosoma Cruzi. *Zbl. allg. Path. path. Anat.*, 95, 468-475.
- (1960). Pathologic anatomy of enteromegaly in Chagas disease. *Proc. 2nd Meeting Bockus Alumni Intern. Soc. Gastroent.*, pp. 92-103. Universidade de Minas Gerais, Belo Horizonte.
- (1963a). Enteromegaly and cardiomegaly in Chagas disease. *Gut*, 4, 399-405.
- (1963b). Patogenia do megaesôfago brasileiro e europeu. *Rev. goiana Med.*, 9, 79-116.
- Kurland, L. T. (1957). Epidemiologic investigations of amyotrophic lateral sclerosis. III. A genetic interpretation of incidence and geographic distribution. *Proc. Mayo Clinic*, 32, 449-462.
- Meyer, A. W. (1921). Experimentelle Untersuchungen über Muskelkontrakturen nach fixierenden Verbänden. I Versuche an Kaltblütern. *Dtsch. Z. Chir.*, 162, 122-138.
- Ramon y Cajal, S. (1954). *Histologie du Système Nerveux de l'Homme et des Vertébrés*, Vol. 2, p. 921. Consejo Superior de Investigaciones Científicas, Madrid.
- Shepherd, J. J., and Wright, P. G. (1965). Observations on megacolon. *East Afr. med. J.*, 42, 401-406.
- Shy, G. M., and Drager, G. A. (1960). A neurological syndrome associated with orthostatic hypotension. *Arch. Neurol. (Chic.)*, 2, 511-527.
- Siegmund, H. (1935). Anatomisch nachgewiesene Folgen von Tonus- und Motilitätsstörungen des Verdauungskanaals bei Enzephalitiden, die mit Atropin behandelt wurden. *Münch. med. Wschr.*, 82, 453-454.
- Wodbourne, R. T. (1956). The sacral parasympathetic innervation of the colon. *Anat. Rec.*, 124, 67-76.