A summary of ultrasonic findings of
*Oesophagostomum bifurcum*-induced nodular lesions
in northern Ghana

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Submitted for publication
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Abstract

Objective:

To describe the ultrasonic appearance of *O. bifurcum*-induced nodular lesions visualised by abdominal ultrasonography in an endemic area of northern Ghana.

Method:

Cross sectional surveys were carried out in September 2001 and 12 months later in an *O. bifurcum* endemic focus of northern Ghana involving a random sample population of 1470 patients. Patients were subjected to coproculture and abdominal sonography investigations to detect the presence of egg-producing adult *O. bifurcum* worms and ultrasonically detectable *O. bifurcum*-induced nodular lesions in the colon wall respectively. All patients were investigated by ultrasound irrespective of their parasitological status. Qualitative description of ultrasonically- visible lesions is presented together with semi-quantitative analysis of the number of cases detected.

Results:

Ultrasonic examinations identified a total of 637 anechoic lesions with posterior wall acoustic enhancement. Overall, solitary lesions were commonly detected compared to lesions in complex. Complex lesions were either detected in chains along the colon wall (arranged circularly or longitudinally) or they were seen as a grape-like cluster constituting a tumour. The lesions were mostly detected in the colon wall and frequently the adjacent colon wall appeared hyperechogenic and showed signs of pericystic oedema. Only 3 lesions were detected in the anterior abdominal wall.

Conclusion:

*O. bifurcum* infection causes cystic nodules along the colon wall which in most cases can be detected by ultrasound. The sonographical manifestation is characterized by the appearance of anechoic lesions either solitary or in complex showing typical pattern of distribution surrounded by hyperechoic material of the bordering tissue.

Abbreviations:

NS: Nestor Spannbrucker
**Introduction**

Human oesophagostomiasis caused by infection with *Oesophagostomum bifurcum* is focally endemic in northern Ghana and northern Togo but rare on the global scale. Approximately 250,000 persons living in the endemic area are known to harbour the infection and it is estimated that a million more are at risk of being infected (Polderman *et al*., 1991; Polderman *et al*., 1999).

Adult *Oesophagostomum* worms dwell in the host’s intestinal lumen and produce eggs which are passed out with host faeces into the environment. With adequate soil moisture and temperature, the eggs hatch and develop into infective larvae (*L*$_3$-larvae) within 3–7 days. It is assumed that humans get infected through oral ingestion of *L*$_3$-larvae. *L*$_3$-larvae invade the colon wall to assume a histotropic stage of infection but occasionally tissues of other organs such as the lungs, liver and muscles of the trunk may be invaded. Palpable and painful protruding masses are formed as a result of intense tissue reactions around a nodule containing juvenile *Oesophagostomum* worms. The resulting clinical picture is referred to as a ‘Tumour de Dapaong’. Sometimes, the colon wall is extensively invaded by *L*$_3$-larvae producing many pea-sized, pus-filled and worm containing nodular lesions within a grossly thickened and oedematous colon wall; “multi-nodular disease” may be the result. The clinical manifestations of oesophagostomiasis may range from fever and mild abdominal pain to acute abdomen. Symptoms and severity of clinical oesophagostomiasis are related to the development of nodular lesions in the colon wall or in the anterior abdominal wall (Gigase *et al*., 1986; Storey *et al*., 2000a; Polderman and Blotkamp, 1995).

In the endemic area, it has been found that about 40% of the population develop sub-clinical nodular pathology of which some are likely to progress to clinical oesophagostomiasis Ziem *et al*., 2005a).

Treatment depends on the stage of infection and presentation of the disease; in uncomplicated oesophagostomiasis albendazole is the drug of choice but when acute abdomen presents laparotomy with partial colectomy used to be indicated Gigase *et al*., 1986; Storey *et al*., 2000a; Krepel *et al*., 1993).

The coproculture procedure which detects the characteristic third-stage *O. bifurcum* larvae (*L*$_3$-larvae) is routinely used to attain a differential diagnosis of *O. bifurcum* and hookworm infections because eggs of both nematodes are morphologically identical rendering diagnosis through egg identification.
impossible (Blotkamp et al., 1993). Abdominal ultrasound investigation is used to detect nodular lesions caused by the histotropic stage of infection. Abdominal ultrasound screening of infected persons demonstrates the presence of O. bifurcum-induced nodular lesions in the colon and abdominal walls. This method is employed in epidemiological studies in the endemic area (Ziem et al., 2005a,b; Storey et al., 2001; Storey, Spannbrucker et al., 2000; Storey, Faile et al., 2001).

Previously, ultrasonic screening of the infected population mainly concentrated on quantitative interpretation of pathological lesions in infected persons (Ziem et al., 2005; Storey, et al., 2001c; Storey et al., 2000b). Description of the ultrasonic appearance of O. bifurcum-induced nodular lesions was reported in case studies involving 3 patients who presented with acute abdomen (Storey et al., 2000b). Because of the limited imaging quality of the ultrasound machine belonging to the first generation portable devices (Siemens Sonoline LS, 1986), information on the echotexture of lesions and neighbouring tissue could not be obtained in these studies. The aim of the present study was the assessment of the characteristic sonographic features of O. bifurcum lesions using an up to date portable device with a greatly improved pictorial resolution. The qualitative description of the ultrasonic findings was based on the examination of a large representative collection of people presenting a whole region in an endemic area.

**PATIENTS AND METHODS**

The study was carried out in the present Garu district of the Upper East Region of Ghana in September 2001 and September 2002 as part of research into the control of human oesophagostomiasis in northern Ghana and Togo. As part of the research design, all persons living in the area were registered. The exact borders of the study area were chosen to limit the study population to some 18,000 persons. In September 2001, a cross sectional survey of 10% of the registered inhabitants of the area was conducted which parasitological data was obtained by coproculture to determine the prevalence of O. bifurcum infection. In September 2002, another cross sectional survey was carried out involving only 5% of the registered population. The persons included in both the 2001 and 2002 surveys were randomly chosen from the total population and nobody was included twice. A detailed description of the demographic registration and the sampling procedure has been described elsewhere (Ziem et al., 2005a). A total of 2019 persons who
underwent coproculture examination in September 2001 and the year after were also invited for abdominal ultrasound investigation to detect the presence of *O. bifurcum*-induced pathology. Overall, 1470 of them turned up for ultrasound investigations representing a recruitment rate of 73%.

**Ultrasound Investigation**

A standardized imaging protocol was used during ultrasound investigations. Bimanual abdominal palpation to elicit masses suspected to be *O. bifurcum*-induced nodular lesions preceded all ultrasound investigations. Using a portable LS-ultrasound machine (Kretztechnik AG, Zipf, Austria) equipped with a 3.5 to 4.5 MHz convex array transducer and powered by a generator, the abdomen of each patient was systematically scanned in the supine position. The large intestine was identified by gas or faeces distending the bowel with detectable haustral folds located close to the right and left kidneys (ascending and descending colon) or close to the stomach from the Murphy’s point in the right upper quadrant to the splenic flexure in the left upper quadrant (transverse colon). The caecum was identified as the most proximal part of the colon at the Mac Burney’s point where the small intestines just enter the colon. The liver and spleen served as additional landmarks for investigating the colon. Patients were all scanned in the fed state without any specific bowel preparation. The presence of hypoechoic or anechoic masses in the abdominal wall and in the colon was looked for, scanned in various planes to avoid misdiagnosis from tubular structures and the diameter measured in two dimensions.

The appearance of masses were described and recorded on a printer and with a digital camera. To avoid intraobserver variation, ultrasound examination was performed by one investigator (NS) but without previous information about the patients’ parasitological data.

**Image and data analysis**

The characteristic ultrasonic features are described and presented as pictures. *O. bifurcum*-induced nodular lesions were identified as a hypoechoegenic or anechoic structures with particulate materials and showed posterior wall acoustic enhancement. The lesions were classified according to type, number per person and location in the anatomical regions of the abdomen and colon. A lesion was described as solitary if only one lesion was detected or it was described as a
complex if two or more lesions were detected together in a cluster in the same location.

Uni-nodular pathology was subsequently defined as the presence of only one solitary lesion in the colon wall whereas multi-nodular pathology was characterised by the presence of a complex or multiple solitary lesions at different locations.

Statistical analysis was performed using SPSS statistical package, version 11.01 (SPSS Inc, Chicago, IL, USA). The presence of pathology was expressed as prevalence figures stratified by lesion-type and -location according to the anatomical region.

The average diameter of ultrasonically-visible lesions was calculated and categorised by lesion type. Values in millimetres are presented as medians with corresponding inter-quartile ranges (IQR) as data on lesion diameter are not normally distributed. Differences between groups were analysed using non-parametric tests (Kruskal–Wallis). A $P$-value of less than 0.05 was used to imply statistical significance for all tests.

**Ethical Clearance**

All participants of the study were previously informed about the purpose and procedure of the investigations and their consent to participation was obtained. The Ghana Health Services Ethics Committee in Bolgatanga approved the strategies and objectives of the study. The project also got the recommendation of the Danish Central Scientific-Ethical Committee.

**Results**

For the 1470 subjects examined, 637 anechoic lesions were detected in 363 (24.7%) patients and third stage larvae of *O. bifurcum* were detected in 465 (31.6%) of them.

Ultrasonically, *O. bifurcum*-induced lesions appeared anechoic in nature with a characteristic triangular-to-oval shape. The number of lesions detected per person varied from 1 to 13; the median number of nodules per person was 1 (IQR= 1 to 2). Over 99% of lesions were detected in the colon wall and only 3 lesions were detected in the anterior abdominal wall around the periumbilical region. Lesions typically present as either solitary or as complex lesions and show posterior wall acoustic enhancement. Many lesions contained particulate materials and showed some scattered reflexes. L$_4$-larvae or juvenile worms that can always
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be found in pathological specimens of the nodules, were never detected by ultrasound. Solitary lesions were more common than complex lesions (83.3% vs. 16.7%, \( P = 0.001 \)). The maximum diameter of solitary lesions varied from 7 mm to 30 mm, with a median maximum diameter of 13 mm (IQR = 11 to 16 mm) and that for complex lesions varied from 18 mm to 92 mm; the median maximum complex diameter was 38 mm (IQR = 28.0 to 48.3mm). Overall, the median diameter measured for complex lesions was significantly greater than that for solitary lesions (13.0 mm vs. 38.0 mm, \( P = 0.001 \)). For abdominal-wall lesions, the maximum diameter varied from 38 to 54 mm, much bigger than the maximum diameter of isolated lesions in the colon wall (Fig 4.1). A cross sectional view of a characteristic anechogenic solitary lesion with posterior wall acoustic enhancement (arrows) detected in the transverse colon near the splenic flexure is shown in fig. 4.2-4.3. Mostly, the hyperechogenic thickening of the colon wall adjacent to lesions was ultrasonically discernible as illustrated by the figure.

Ultrasonically, complex lesions were observed in three different patterns as shown by fig. 4.4a-c. Primarily, most complexes were observed as lesions occurring in a chain with a characteristic mild hyperechogenic mucosa reaction. Fig. 4.4a gives a cross sectional view of the ascending colon showing 2 adjacent lesions in chains. In the second type of complex formation, an anechogenic mass consisting of several lesions aggregated in “grape-like” clusters with visible scattered reflexes was observed (fig. 4.4b). In the last but rare type of complex formation, the entire length of the colon was studded with several aggregates of lesions associated with decreased diameter of the bowel lumen (figure 4.4c) and characteristically, the colon wall showed an enlarged echo low band, an indication of mucosa distension. Ultrasonically, lesions differed with regard to their bordering rim; in some cases the edges were sharply discernible without neighbouring tissue reaction as shown in fig. 4.2, but in most cases, the adjacent neighbouring colon wall showed increased tissue reactions (arrows in fig. 4.2). Occasionally, lesions were surrounded by a thin wall and the neighbouring tissue showed increased echogenicity.
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Fig. 4.1
Cross sectional view of cyst in the abdominal wall.
Note the abdominal aorta (A A)

Fig. 4.2
Cross sectional view of an anechoic solitary lesion located in the transverse colon near the splenic flexure.
Note the posterior wall acoustic enhancement and the increased thickness in the adjacent colon walls (arrows).

Fig. 4.3
Long axis view of a solitary cyst in the ascending colon surrounded by an echo dense inflammatory material. It has the characteristic appearance of a thyroid parenchyma.
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Fig. 4.4-a
Cross sectional view showing 3 cysts in chains located in the ascending colon

Fig. 4.4-b
Grape-like cluster of cysts in a tumour.

Fig. 4.4-c
Long axis view of a polycystic mass impressing the gas filled lumen of the colon
Discussion

Earlier, definitive diagnosis of the histotropic stage of *O. bifurcum* infection in humans was established through histological findings following laparatomy (Gigase *et al.*, 1986; Storey *et al.*, 2000a; Bogers *et al.*, 2001). Figure 4.5 shows a cross section view of a resected colon specimen from a severely infected patient. It exhibits numerous pus filled cystic lesions within the bowel wall. Upon microscopic analysis the cavities appear to be filled with necrotic material and fragmented granulocytes. In some of the cysts a juvenile worm could be seen. They are surrounded by fibrous tissue containing eosinophilic and neutrophilic granulocytes Bogers *et al.*, 2001).

Previous area-wide ultrasonic screening of the endemic population demonstrated anechogenic lesions, but technical limitations of the ultrasound machine used in those surveys prevented ultrasonic visualisation of detailed histological changes in the colon wall associated with lesions formation Storey *et
The sonographical findings in the present study match the pathological observations of dissected specimens from severely infected patients. Although the changes in most of the individuals were more discrete, portions of bowel in close proximity to nodular lesions appear ultrasonically hyperechoic, indicating inflammation and associated fibrosis caused by the histotropic stage of infection. Associated oedema of the neighbouring pericolic tissue was observed to have a diffuse hyperechogenic texture similar to the ultrasonic appearance of a thyroid parenchyma described as “a thyroid in the abdomen” (Se Hyung Kim et al., 2003).

Most lesions were detected as solitary lesions, but polycystic masses were also detected. Ultrasonically, these masses were observed to protrude into the intestinal lumen and decrease the lumen diameter. It would have been expected that some patients with polycystic masses during the September 2001 survey would progress to acute abdomen as a result of bowel obstruction over the one-year period, but as all persons in the study area received albendazole treatment in the fall of October 2001 and April 2002 as part of our study protocol, no incident of acute abdominal emergencies were recorded.

The colon remains the only abdominal organ where ultrasonically visible nodular lesions were frequently detected even though some extra-intestinal lesions were detected in the anterior abdominal walls of three patients. Slow peristaltic waves in the colon compared to the much stronger peristaltic waves of the small intestines was one of the explanation given for the predilection of colon to *O. bifurcum* infection (Ziem et al., 2005a; Storey et al., 2001c). However, it can not be excluded that in some portions of the small bowel these lesions might be present as well. Indeed, in an earlier case study involving some patients who underwent open abdominal surgery, some nodules were detected in the terminal ileum (Storey et al., 2001c; Bogers et al., 2001). The presence of chyme in the small bowel makes it unsuitable for ultrasonic identification of cystic lesions. On the contrary, accumulation of gases in the lumen of the colon due to bacterial activities serves as an ideal contrast to aid ultrasonic detection of fluid filled lesions.

It is very unlikely that the lesions described in this study are due to some pathological processes of the colon wall other than *O. bifurcum* infection. Evidence from previous ultrasonic investigations involving some selected villages in this endemic area showed that similar lesions were commonly detected. However,
ultrasound investigations in neighbouring villages located only 100km south of the
*O. bifurcum*-endemic area where coprocultures were negative for *O. bifurcum*
revealed no such lesions. In the present study, individuals who underwent
abdominal ultrasound investigation equally had their stool examined by
coproculture to determine the presence of the intestinal stage of infection.
Individuals who were stool culture positive had a higher risk of developing
ultrasonically detectable nodular lesions. A cross-tabulation of infection with any
nodular pathology provided an odds ratio (OR) of 4.5 (95% CI 3.6-5.9, \( P = 0.001 \)),
indicating a highly significant correlation between acquiring infection and the
development ultrasonically detectable lesions (Ziem *et al.*, 2005a).

On a global scale, anechoic lesions within the colon wall have rarely been
reported in the literature. Hypoechoic colon wall thickening to up to 8.4 mm,
depending on the severity of the disease, was reported in a study of inflammatory
bowel disease but these lesions were described as diffuse thickening of the
intestinal wall without any well-defined cystic structures (Lim *et al.*, 1994; Haber
*et al.*, 2002). Extensive hypoechoic wall thickening of the large bowel due to
diffuse infiltration of lymphoma cells was reported in intestinal Burkitt’s
lymphoma (Satomi *et al.*, 2002). In another study involving abdominal
tuberculosis, Ghazinoo and co-workers described cystic lesions with posterior wall
enhancement due to necrotic lymphadenopathy but the affected lymph nodes were
mainly located in the retroperitoneum and mesenterium (Ghazinoor *et al.*, 2004).
In a field study to investigate the extent on *Schistosoma mansoni* morbidity in a rural
area in Tanzania (Ukerewe Island, Lake Victoria); the sonographer of the present
study (NS) examined 1,253 persons by abdominal ultrasound. As part of protocol
to measure morbidity caused by intestinal schistosome infection, the
gastrointestinal tract was systematically scanned but never did the sonographer
detect any anechoic lesions in that survey. Based on these observations, it can be
concluded that ultrasound is specific in the diagnosis of the histotropic stage of *O.
bifurcum* infection and the specificity of the method should be remarkably high.

With regard to the sensitivity of ultrasound in detecting *O. bifurcum*-induced
anechoic lesions, one has to take into account the fact that ultrasonic examination
of the gastrointestinal tract is considerably hindered by the presence of gases and
faeces in the lumen. In fact, it is quite remarkable that such large number of lesions
in the colon wall is easily detectable by ultrasound without any specific bowel
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preparation. It must however be stressed that not all cystic lesions can be detected by ultrasound. We estimate that about 30 % of lesions located in the posterior wall of the colon covered by gas in the bowel lumen evades ultrasonic detection and identification. Furthermore, the limited conditions in the field set-up compared to the conditions of ultrasound departments in a well-equipped hospital affect the sensitivity of the ultrasound in our study. Alternative imaging techniques like CT or MRT scans which could be used as gold standard are in fact not available in northern Ghana. Thus, the sensitivity of the ultrasound procedures used in this study can only be roughly estimated. A number of studies on diverticulitis indicated the sensitivity of ultrasound to be between 74-97% in reaching accurate diagnosis depending on the quality of the equipment, the examination room and the experience of the investigator (Soliman et al., 2004; Parulekar et al., 1985). Despite the fact that facilities in our investigation were quite limited, we assume an analogous sensitivity of 75 – 85% in detecting anechoic lesions within the colon wall, because the cystic lesions are comparably easier to identify by ultrasound investigation than the partially discrete pathological findings in diverticulitis.

In conclusion our study demonstrates that *O. bifurcum* infection can accurately be diagnosed by ultrasound technology thanks to the fact that the histotropic stage of infection causes cystic infiltration of the colon wall. In contrast to the slowly developing pathological changes in organs caused by many parasitic infections such as schistosomiasis and bancroftian filariasis, *O. bifurcum*-induced pathological changes are detectable right at the onset of the infections (Mand et al., 2004; Mohamed-Ali et al., 1991) The high specificity and sensitivity of ultrasound in detecting the histotropic stage of infection indicates that sonography can directly provide early information about the progression of lesions following *O. bifurcum* infection and aids management and monitoring of the impact of morbidity control.

Acknowledgement
In carrying out this study, the assistance of Daniel Laar, Mohammed Awel, Moses Kolan and John Laar is gratefully appreciated. Funds were provided by The Leiden University Medical Centre (LUMC), DBL-Institute for Health Research and Development and GlaxoSmithKline.