ABC of AIDS

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GASTROINTESTINAL AND HEPATIC MANIFESTATIONS

Sexually transmitted infections of the gastrointestinal tract and liver

Symptoms	Sigmoidoscopy	Organisms
Anorectal	Proctitis or ulceration, or both	<i>Neisseria gonorrhoea</i> , Herpes simplex virus, <i>Chlamydia trachomatis</i> , <i>Treponema pallidum</i>
Anorectal and enteric	Proctocolitis	<i>Campylobacter</i> spp, <i>Shigella</i> spp, <i>Chlamydia trachomatis</i> (lymphogranuloma venereum), <i>Entamoeba histolytica</i>
Enteric	Normal	<i>Giardia lamblia</i>
Hepatitis	—	Common Hepatitis A and B viruses Rare Hepatitis C and D (δ) viruses, Epstein-Barr virus, Cytomegalovirus

Among a subpopulation of homosexual men the risk of infection with the human immunodeficiency virus (HIV) has brought about a change in sexual behaviour with a reduction in the number of partners and "safer" sexual practices. This has resulted in a reduced incidence of common sexually transmitted diseases, many of which affect the gastrointestinal tract and liver. A variety of new syndromes affecting both systems are, however, being recognised as complications of HIV infection, many of which fulfil the criteria for AIDS.

Retrosternal discomfort—dysphagia

Causes of retrosternal discomfort and dysphagia

Candidiasis
Cytomegalovirus
Herpes simplex virus

Above: oral candida. Left: barium swallow of oesophagus showing candidiasis.

Oral candidiasis may be asymptomatic or it may cause oropharyngeal discomfort and, if the oesophagus is affected, retrosternal chest pain and discomfort or difficulty in swallowing. Oral candidiasis alone does not fulfil the criteria for AIDS, but in prospective studies it indicates a poor prognosis and carries a high relative risk of later development of the full syndrome. Candidiasis is the commonest cause of oesophageal infection. Although plaques of candida can often be shown on barium swallow, oesophageal disease is best shown at endoscopy with biopsy and culture because cytomegalovirus and herpes simplex virus infection, as well as candidiasis, may cause focal or diffuse ulceration. The herpes viruses can also cause ulceration of the gastric and duodenal mucosa. Since oesophageal candidiasis is so common, a pragmatic approach in a patient with oral candida and oesophageal symptoms would be to treat him empirically for candidiasis and only to perform endoscopy if there is no response. One drawback of this approach is that biopsy or culture proved oesophageal candidiasis is required for the diagnosis of AIDS.

Diarrhoea, malabsorption, and weight loss

Causes of diarrhoea, weight loss, and malabsorption

Unknown—enteropathy
Cryptosporidium (*Isospora belli* and microsporidia)
Cytomegalovirus and herpes simplex virus
Mycobacteria
Enteric bacteria—salmonella, campylobacter
Neoplasia

Cysts of cryptosporidium. Modified Ziehl-Neelsen stain $\times 320$.

Sporocyst of *Isospora belli*.

Severe mucocutaneous herpes simplex virus infection.

Hepatitis and cholestasis

Causes of hepatitis and cholestasis

Mycobacteria
Cryptosporidium
Cytomegalovirus
Cryptococcus neoformans
Drug induced

Diarrhoea is a common symptom in patients with chronic HIV infection with and without other manifestations of AIDS. In many cases a cause is not identified. Symptomatic treatment is all there is to offer. An enteropathy with villous atrophy and malabsorption has been described, but the prevalence of this condition and its cause have yet to be determined.

Cryptosporidium is probably the commonest pathogen isolated and certainly the commonest of the protozoal causes of diarrhoea, which also include *Isospora belli* and microsporidia. Cryptosporidium is widely distributed in the animal kingdom. In immunocompetent human hosts it produces a transient diarrhoeal illness. In HIV infected hosts it can cause transient, intermittent, or persistent diarrhoea, ranging from loose stools to watery diarrhoea, with colic and severe fluid and electrolyte loss. The diagnosis can now be made without resorting to small bowel biopsy by finding the cysts in stools by a direct, modified acid fast stain or after sucrose concentration, and the diagnosis should not be discounted without examining multiple specimens.

The herpes viruses cytomegalovirus and herpes simplex virus can cause focal or diffuse ulceration of the gut, from the mouth to the anus. Most commonly herpes simplex virus causes mucocutaneous lesions at the upper and the lower ends of the gastrointestinal tract, ranging from small areas of ulceration to the more chronic, large, deep ulcers of the perianal area that are diagnostic of AIDS. Cytomegalovirus is more commonly associated with a syndrome which mimics acute inflammatory bowel disease, with abdominal pain, fever, and diarrhoea. Toxic dilatation, perforation, and haemorrhage have been described. The diagnosis is made by biopsy and culture. Histologically there is a non-specific inflammation, with dense, round (Owl's-eye) intranuclear inclusion bodies in swollen cells.

Atypical mycobacteria of the avium intracellulare complex are ubiquitous organisms with little virulence for the immunocompetent host. Disseminated infection occurs in AIDS with multiorgan disease. Gastrointestinal infection may be associated with fever, weight loss, diarrhoea, and malabsorption. Diagnosis can be made by acid fast staining of the stool or biopsy material and culture. Gut disease may mimic Whipple's disease in appearance. The small bowel shows prominent folds, with foamy macrophages stained by periodic acid Schiff, containing the organisms and filling the lamina propria. The bacteria are acid fast, unlike those of Whipple's disease. *Mycobacterium tuberculosis* infection of the bowel does occur but is less common. *Campylobacter* and *Salmonella* species infections may cause diarrhoea but the latter more commonly present as a pyrexia of undetermined origin with bacteraemia. As with other infections in patients with AIDS, relapses are common after cessation of treatment with appropriate antibiotics.

Hepatitis in patients with AIDS may present with fever, abdominal pain, hepatomegaly, and abnormal liver function tests, in particular raised alkaline phosphatase activity. In the absence of dilated bile ducts on ultrasound needle biopsy usually shows a granulomatous hepatitis, usually caused by atypical mycobacteria rather than *M. tuberculosis*. Atypical mycobacteria may be shown on acid fast staining or cultured in the absence of granulomas. *Cryptococcus neoformans* may also be implicated. The herpes viruses may also occasionally cause hepatitis as part of a disseminated infection. With the multiple therapies being used a drug induced hepatitis must always be considered in a patient with AIDS who has abnormal liver

function test results. More recently acalculous cholecystitis and cholangitis have been described with appearances on endoscopic retrograde cholangiography similar to those of primary sclerosing cholangitis with strictures and dilatation of the biliary tree. Dilatation and irregularities of the pancreatic duct have also been described. Histologically there is non-specific inflammation and ulceration. Cryptosporidium and cytomegalovirus have been shown or isolated and implicated as a cause of this syndrome. Gram negative bacteria and candida have also been cultured.

Dilated common bile duct with stricture at lower end and irregularities of extrahepatic and intrahepatic ducts.

Neoplasia and other conditions

Neoplasia and other conditions

Kaposi's sarcoma
Lymphoma
Squamous carcinoma
Hairy leukoplakia
Recalcitrant anorectal warts

The gastrointestinal tract is one of the commonest internal organs affected by Kaposi's sarcoma. If upper and lower gastrointestinal endoscopy are performed at presentation lesions will be shown in about 40% of patients. At necropsy they are present in more than 70%. However, endoscopic biopsy has a high false negative rate, with less than one third of suspicious lesions being confirmed histologically because of their predominant position deep in the submucosa. Lesions of the oropharynx, oesophagus, stomach, duodenum, colon, and rectum have been shown. The lesions have the range seen in the skin, from small telangiectatic lesions, not well shown on contrast studies and only seen at endoscopy, to larger nodular or polypoid lesions. Complications from gastrointestinal disease are unusual, but include ulceration, haemorrhage, and diarrhoea with a picture clinically and radiologically similar to acute inflammatory bowel disease. A protein losing enteropathy may also occur.

Non-Hodgkin's lymphoma may occur de novo in patients with persistent generalised lymphadenopathy or in patients with other signs and symptoms of AIDS. The tumours are of B cell origin and the survival and response to treatment is poor. Extranodal disease is common and the gastrointestinal tract is the third commonest site after the central nervous system and bone marrow. Gastrointestinal disease may be detected only at necropsy.

The recently described hairy leukoplakia presents as greyish white lesions, typically on the lateral borders of the tongue. Histologically there are keratin projections resembling hairs. Its cause is unknown, but Epstein-Barr virus has been implicated.

Recalcitrant anogenital warts are a common problem in homosexual men with chronic HIV infection, and recurrence rates with all forms of therapy are high.

There have been anecdotal reports of squamous oral and anal carcinoma in homosexual men positive for anti-HIV and the role of human papillomavirus and perhaps other viruses has yet to be elucidated.

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