EDITORIAL

Amoebic Liver Abscess with Synchronous Colitis: Lessons Learnt in Recent Times

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Entamoeba histolytica is aptly named as it causes tissue-lysing that results in amoebic colitis and liver abscess. It is one of the most important enteropathogens worldwide accounting for 40 to 100 thousand deaths annually.[1,2] The population prevalence of Entamoeba is high in our country due to crowding, poor sanitation, lower socioeconomic status, and unhygienic practices. In a study from North-East India, 13.7% of stool samples were positive for *Entamoeba histolytica* when tested using DNA dot blot technique.[3] In another study from Vellore, 8.2% of all stool samples were positive for Entamoeba cysts or trophozoites.[4]

More than 95% of patients with Entamoeba in their stools are asymptomatic. Invasive amoebiasis accounts for only 1% of all amoebic infections.[5] Amoebic liver abscess (ALA) in the most common extraintestinal presentation of invasive amoebiasis. Risk factors associated with disease severity and mortality[6,7] include young age, alcoholism, and corticosteroid use. Amoebic colitis occurs in the same frequency in men and women. However, ALA is found more commonly among men (M:F ratio >10). Testosterone has been implicated in the increased ALA risk in men, which also explains middle aged men being the most commonly affected cohort.[6] Hormonal factors and higher rates of iron deficiency anemia in women are likely protective against development of ALA.[7] Alcohol consumption confers high risk of ALA leading to hepatocellular damage.

The life cycle of the *Entamoeba histolytica* has two stages (cyst and the trophozoite) and was first described in 1928 by Clifford Dobell.[8] In most infections, the pathogenic trophozoites are restricted to the mucin layer in the intestine, where they produce new cysts. A few trophozoites invade the epithelium and lead to dissemination to extraintestinal sites like liver. The amoeba has cytolytic capabilities, creating liver abscesses with cellular debris, dead hepatocytes and liquefied cells. The lesion is surrounded by connective tissue, inflammatory cells and amoebic trophozoites. Most patients develop symptoms within 2-4 weeks of exposure.[9] Although synchronous colonic lesions in patients with amoebic liver abscess are seen in over 50% patients, symptoms of diarrhea and bleeding are uncommon. The reasons for low incidence of preceding diarrhea in these patients is unclear. Jaundice is an uncommon manifestation. There are multiple theories for jaundice which include hepatic necrosis with pressure on biliary apparatus, biliovascular fistula leading to increased bilirubin and necrosis at the margins of the abscess.[10]

In the present issue of this *Journal*, Premkumar et al[11] present their findings on 52 patients with ALA; half of their patients had simultaneous colonic involvement at colonoscopy. Most patients with colonic involvement (20 of 28 patients) had large ileo-caecal ulcers. Of these patients, 16 patients had history of intermittent bleeding per rectum; the remaining 8 patients presented with liver abscess and anemia, and gave history of bleeding per rectum on enquiry. Also, almost all their patients were men (51/52). Significant alcohol intake was more common in patients with synchronous lesions.

The large number of patients with synchronous colonic involvement in this study appear surprising at first glance, but are actually in line with previous studies from India. In a previous Indian series of patients with amoebic liver abscess, colonic involvement was seen in 58% patients.[12] Only 7% of patients had diarrhea and bleeding at presentation. The patients who had diarrhea had large confluent colonic ulcers. In another series of ALA, 77.5% patients had synchronous colonic involvement.[13] Caecum was the most commonly affected site (70%) with colonic involvement seen more commonly in patients with multiple abscesses. Small ulcerations were seen in three-fourths of patients, while large ulcerations (>3 cm) were seen in half of them. Only a quarter of the patients in this study had diarrhea at presentation, and only 5% presented with jaundice. In another series by Misra et al,[14] colonic lesions were seen in 55%. However, patients who presented with diarrhea or had history of diarrhea in preceding 2 months (28%) had more propensity for colonic lesions (90%). Also large left sided ulcers were commonly seen in elderly and those with diarrhea as presenting symptom.

The rates of synchronicity remained similar in different series. In the present series, there was unusually high prevalence of patients with jaundice (75% in patients with synchronous colonic involvement), patients with intermittent bleeding per rectum and patients needing endotherapy (24/28 patients with colonic lesions). This suggests that sicker patients were included due to a referral bias to a tertiary hepatobiliary centre.

Treatment for the patients with invasive amoebiasis include use of metronidazole with a luminal amoebicide like diloxanide furoate or paromomycin to eradicate Entamoeba cysts.[15] The clinical implication of concomitant colonic infection would be to ensure that the cysts are eradicated in these patients to prevent further spread.

Therapeutic options for ALA range

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from simple pharmacotherapy to use of interventions like aspiration or catheter placement. In a previous study of 60 patients, 82% were managed conservatively and 18% needed intervention in form of aspiration and catheter placement. Larger size of abscess with deranged liver functions were predictive of need for intervention. Patients who underwent intervention had a longer stay at the hospital. On post hoc analysis, a size of >7.7 cm predicted need for intervention.[16] Premkumar et al reported need for aspiration or catheter placement in 53% patients with concurrent colonic lesions and 41% patients without concurrent lesions.

In patients with ALA with amoebic colitis, management has remained the same over the last few decades.. There is further understanding in the pathophysiology. For many decades, it was believed that *Entamoeba histolytica* was pathogenic, and *Entamoeba dispar*, which is morphologically similar, did not cause disease in humans.[17] In the last decade, many reports of *E dispar* causing liver and intestinal lesions that were occasionally indistinguishable from those produced by *E. histolytica* have appeared;[18] this may change our thinking about management of asymptomatic cyst passers who are not always given treatment for eradicating cysts.

In the colon, trophozoites of *E. histolytica* often reside together with resident microbial flora. In patients with diarrhea and amoebic abscess, Rani et al[19] reported a reduction in *Lactobacillus* in patients with colonic infection. Also, *Bacteroides* and *Peptostreptococcus* were detected in ALA pus samples. They suggested that bacterial flora provides anaerobic conditions or low redox potential beneficial for amoebic growth. The microbiome in the colon may be altered by many causes, including alcohol and steroids; whether the increased risk of ALA in these patients can be explained by a change in microbiome is conjectural.

In conclusion, the clinician will continue to treat ALA with the same drugs and protocols used over the last few decades. It is the researcher who remains intrigued. In the near future we may find strategies for prevention, including development of vaccines for amoebiasis.

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