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# SHORT REPORT
# *Schistosoma japonicum* infection and rectal carcinoid tumour: underreported coincidence or neglected association?

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## SUMMARY

*Schistosoma japonicum* infection associated with a rectal carcinoid in an asymptomatic 44-year-old female from the Philippines is described. A systematic review of the literature could not identify similar reports, suggesting a rare coincidence. However, epidemiological data on the frequency of both conditions as well as published results of a colorectal screening programme from China indicate that underreporting of this concurrence is likely. Moreover, several studies suggest a causal link between schistosomiasis caused by *S. japonicum* and more common gastrointestinal malignancies such as colorectal carcinoma. Hence the presented case and the apparent neglect of this observation in the current literature allow speculation on a role of *S. japonicum* in the pathogenesis of rare gastrointestinal neoplasms such as carcinoid tumours as well. Future reports on similar observations could help to determine the need for systematic investigations and are strongly encouraged.

**Key words**: Infectious disease epidemiology, parasitic disease epidemiology and control.

Several parasitic diseases are known to play a role in carcinogenesis. Probably the best documented and widely known example is urogenital schistosomiasis and its association with squamous cell carcinoma of the urinary bladder [1]. Evidence that *Schistosoma japonicum* might also promote malignancy is accumulating since the first half of the 20th century. Case series followed by histopathological, and later on epidemiological, studies from endemic countries in Asia support an aetiological association with hepatocellular as well as colorectal carcinoma [2–8]. Here we report the first case of *S. japonicum* infection in association with a carcinoid tumour.

Preventive colonoscopy in an asymptomatic, 44-year-old female patient revealed a broad based, hard, submucosal nodule 50 mm above the linea dentata at the posterior wall of the rectum. Biopsies showed islets of tumour cells with a small acidophilic cytoplasm and a slightly enlarged nucleus. The tumour cells were strongly positive for chromogranin A and focally for synaptophysin. Less than 2 % of the tumour cells expressed the nuclear antigen Ki-67, indicating a low proliferative activity. Additionally the mucosa and submucosa contained multiple ovoid and in part calcified shells that contained structures consistent with miracidia. The diagnosis of a carcinoid tumour was established and concurrent schistosomiasis was suspected. The transanal local surgical, full-thickness resection of the rectum measuring $35 \times 14$ mm contained a tumour of 7 mm in diameter confined to the mucosa and submucosa with microscopically free margins. Central parts of the tumour consisted of small rather uniform cells growing in ribbons or a

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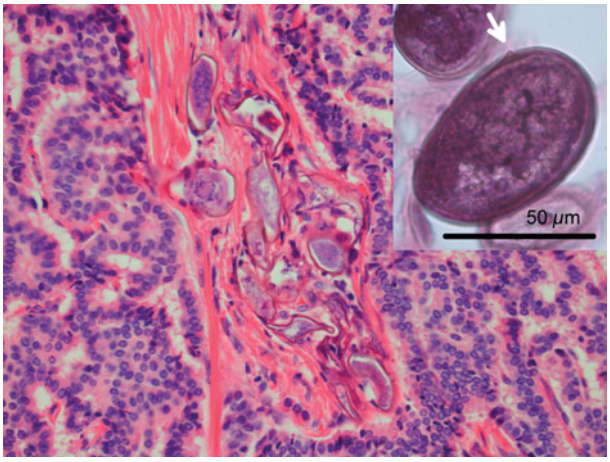


**Fig. 1.** Typical carcinoid tumour of the rectum with a cluster of collapsed and distorted eggs in the tumour stroma (haematoxylin-eosin, ×100). Inset showing egg of *S. japonicum* with arrow indicating minute lateral knob (haematoxylin-eosin, ×400).

trabecular arrangement (Fig. 1). The thick tumour stroma and the surrounding loose connective tissue contained clusters of ovoid shells and egg-like structures which were identified as eggs of *S. japonicum* on the basis of their average size of about 65 × 90 μm and a rarely demonstrable lateral knob (Fig. 1). Based on the ultimate diagnosis anti-parasitic treatment with praziquantel 60 mg/kg bodyweight per day for 3 days was advised.

Up to her 23rd birthday, before migrating to Germany, our patient lived in the province of Leyte, Philippines, and has since regularly visited her country of birth. *S. japonicum* is highly endemic in Leyte [9]. Transmission occurs when healthy skin is penetrated by cercariae during contact with fresh water. Chronic schistosomiasis is characterized by organ fibrosis due to a chronic inflammatory response to eggs that persist in host tissues and may promote carcinogenesis. Of the three most common *Schistosoma* spp. found in humans, a causal link is well established for *S. haematobium* infection and malignancy of the urogenital tract [1]. An aetiological association between *S. japonicum* infection and intestinal malignancy was controversially discussed at the beginning of the 1980s [3, 10]. Since then, several epidemiological studies found an increased risk for colorectal carcinoma in those infected, most recently in a case-control study from China [4, 6, 7]. For the other common pathogen causing intestinal schistosomiasis, *S. mansoni*, studies found no evidence for a significant role in gastrointestinal carcinogenesis [1].

We searched the PubMed database using the MESH terms 'schistosomiasis' AND ('carcinoid tumour' OR 'colorectal neoplasms') and reviewed the literature referenced within the matches of this search but could not identify a single case report of a carcinoid tumour with concurrent *S. japonicum* infection. However, one case of a rectal carcinoid tumour associated with *S. mansoni* infection from Egypt could be retrieved [11]. A second case report describing a carcinoid tumour in the sigmoid did not specify the concomitant *Schistosoma* sp. but was reported from Sudan where *S. japonicum* is not endemic [12].

To date no evidence supports a causal association of *S. japonicum* infection with intestinal carcinoid tumours. To our knowledge, this is the first report of a carcinoid tumour associated with this infection suggesting a rare and most likely coincidental finding. However, considering the global burden of 2·4 million infected people [13] and an estimated incidence rate of colorectal carcinoid tumours of 1·0–2·3/100 000 person-years in Asian individuals [14], one would expect this comorbidity to be observed more often by chance alone. As carcinoid tumours are often asymptomatic and found during routine endoscopy [15], the lack of previous reports could be explained by a lower frequency of this procedure in endemic areas. Additionally, underreporting and publication bias due to a presumed classification as coincidence is a plausible explanation for this discrepancy. We believe that these mechanisms rather than a true rarity of the association of interest are the likely reason for the scarcity of previous reports. This speculation is further fostered by the results of a large screening programme that included 198 950 individuals in a Chinese county highly endemic for *S. japonicum*. In this study, 34/75 detected colorectal malignancies were carcinoid tumours. In the same population a prevalence of schistosomiasis of 2·6% was detected. Unfortunately the report does not contain explicit information on the concurrence of these conditions [16].

Based on the presented rationale and in the light of evidence for a possible role of *S. japonicum* in the pathogenesis of colorectal and hepatocellular carcinoma, we wish to raise awareness among epidemiologists and public health officials in endemic areas of an apparent neglect of the presented concurrence of conditions and encourage future reports that could help to identify the need for systematic investigations.

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## DECLARATION OF INTEREST

None.

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