



The small liver fluke (*Dicrocoelium dendriticum*): an unusual clinical finding in chronic urticaria

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Background

Chronic urticaria is characterized by symptoms – wheals and/or angioedema – that follow a uniform course, whereby different disorders or triggers can underlie the same clinical presentation. For those affected, the disorder is associated with a significant reduction in quality of life due to the unpredictable flare-ups, unclear prognosis, intense itch, and the at times disfiguring swelling.

Nonsedating antihistamines are considered the standard symptomatic treatment [1], whereby many patients require doses that exceed the approved dose. The diagnostic work-up should classify the disorder as spontaneous or inducible and determine the etiopathogenesis as far as possible, i. e., autoimmune, autoallergy, infection-related, or due to hypersensitivity to exogenous triggers. The principle aim of the diagnostic work-up is to identify, where possible, an underlying cause, the treatment of which will halt the skin manifestations. According to current opinion, etiological research of this kind is not helpful in physical forms of urticaria. Above all, a thorough patient history as well as physical tests are recommended in these forms [2]. In other forms of urticaria, a stepwise

approach is recommended that takes into account the duration and severity of urticaria, as well as any particular indications in the patient history and special clinical features.

Particularly in the case of intermittent urticaria, investigating IgE-mediated omega-5 gliadin-induced urticaria holds promise [3]. In cases of urticaria that follow a chronic course, nonsteroidal anti-inflammatory agents should always be investigated as possible cofactors or triggers [4]. Forms of urticaria caused by acute infection are often readily apparent clinically. Verifying the effects of chronic infection or bacterial overgrowth is more challenging, as is achieving a favorable course by means of urticaria treatment. Thus, from a pragmatic standpoint, the question arises again and again as to how extensively infections, e. g., by parasites, should be investigated [5].

Case study

A 42-year-old woman presented to our specialist outpatient clinic with chronic spontaneous urticaria of 9 months' standing. The patient's history showed no indication of previous disorders or medication use. The patient, who was originally from Sri Lanka, had moved to Germany many years previously. After several inquiries, it emerged that the urticaria had appeared for the first time shortly after a visit to Sri Lanka.

Blood work, serum chemistry, and hepatitis serology were normal in the diagnostic work-up. The determination of specific IgEs for *Ascaris*, *Echinococcus*, *Anisakis*, and omega-5-gliadin also showed no pathological findings. Despite minimally elevated anti-desoxyribonucleotidase-B titers (254 U/ml, units per milliliter), no focus could be found from either a dental, an ENT, or a gynecological perspective. Abdominal ultrasound was also normal.

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Fig. 1 *Dicrocoelium dendriticum*. An egg seen in the patient's stool. (Size bar 38 μm ; the operculum is indicated by arrows)

Stool analysis with parasitology, however, was positive, showing massive infection with *Dicrocoelium dendriticum* (small liver fluke). It was possible to detect the approximately $25 \times 40\text{-}\mu\text{m}$ large eggs in the stool using microscopy (Fig. 1). Although a mild, gradual improvement of symptoms was seen following eradication of the parasite using praziquantel, full resolution of the disorder was not achieved. Stool analysis was negative already at 1 week following treatment completion. Under treatment with a double-dose antihistamine, the patient remains to date – 4 years following treatment – symptom-free.

Comment

Dicrocoelium dendriticum (also known as the lancet fluke or small liver fluke) is a bile duct parasite belonging to the class Trematoda, its main reservoirs being cattle, sheep, and other ruminants. The life cycle of the small liver fluke is extremely complex and requires snails and ants as intermediate hosts (Fig. 2). Both humans and ruminants become infected by ingesting food containing infected ants [6].

Small liver flukes live in the bile duct of the definitive host, where they produce eggs that reach the intestine via biliary secretions and are excreted. The eggs contain miracidia, which are highly resistant in the outside world, meaning that they remain infectious for several months following excretion. Snails ingest the eggs while feeding, thereby serving as the first intermediate host. The miracidia then leave the eggs and, after drilling through the gut wall, develop into sporocysts, from which they will in turn develop into cercariae. These then leave the hepatopancreas and reach the snail's lung, from where they are discharged in small balls of mucus. In order for ants to serve as the second intermediate host, they need to eat these balls of mucus coughed out by the snail. Some of the

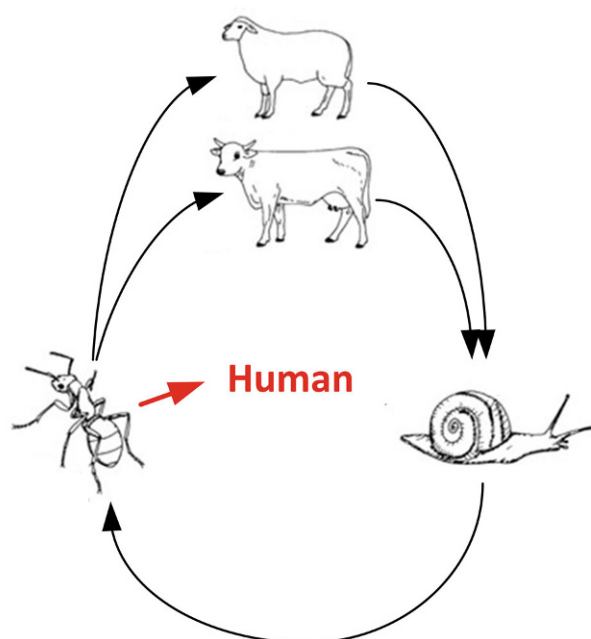


Fig. 2 The life cycle of *Dicrocoelium dendriticum* (modified from [10])

cercariae then reach the ant's subesophageal ganglion; once there, they are able to control the ant's nervous system. This causes the ant to develop mandibular spasms at lower temperatures and clamp onto leaves or blades of grass, thereby, increasing the likelihood of ingestion by ruminants. Once ingested by the definitive host, the parasite makes its way to the bile ducts of, e. g., cows or sheep, where it causes dicrocoeliosis. Although infection is essentially possible worldwide, the risk is highest in Eurasia and North Africa [7].

Mild dicrocoeliosis in humans generally follows a symptom-free course or is associated with mild abdominal or liver pain. However, cholangitis may appear. After several years, the fluke dies off and spontaneous resolution occurs. Eradication should be performed if extensive infection is detected [8], as in our patient.

Conclusion

The time course suggested that the urticaria was caused by the parasite infection and thus functioned as an indicator of small liver fluke infection. With regard to the resolution of urticaria, eradication proved to have little effect, meaning that its etiological role could not be conclusively proven. Although a mild improvement of symptoms was seen, wheal formation continued to recur in the absence of antihistamine treatment. It is likely that a functional or structural modification to mast cells and basophils takes place in the case of infection with certain pathogens in particularly predisposed individuals [9], such that the disorder persists even long after eradication of the infectious pathogens has taken place. Since eradication

of the small liver fluke should be performed in the case of extensive infection, a diagnostic work-up was retrospectively helpful.

Conflict of interest C. Blatner, E.M. Oppel, A. Wieser, T. Herzinger and F. Ruëff declare that they have no competing interests.

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