



Short communication

Halzoun, an allergic pharyngitis syndrome in Lebanon: The trematode *Dicrocoelium dendriticum* as an additional causeGeorges Khalil^{a,*}, Charles Haddad^b, Zaher K. Otrock^c, Fadel Jaber^c, Anna Farra^d^a Medical Microbiology Department, School of Medicine, Saint-Joseph University of Beirut, Lebanon^b Service de Gastro-Enterologie, Centre Hospitalier de Tonnerre 89700, Yonne, France^c Department of Pathology and Laboratory Medicine, American University of Beirut Medical Center, Beirut, Lebanon^d University Medical Center Rizk Hospital/Lebanese American University, P.O. Box: 36, Byblos, Lebanon

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ABSTRACT

Halzoun syndrome typically manifests in the form of an allergic pharyngitis following the consumption of raw or undercooked ovine liver. First described in Lebanon in 1905, it was initially attributed to *Fasciola hepatica*, while later publications have attributed it to other pathogens. There has been no definitive documentation of the pathogen causing the Lebanese Halzoun syndrome. The aim of our study was to identify the parasite responsible for the pathogenesis of the Lebanese Halzoun syndrome. 32 patients with typical clinical symptoms of Halzoun syndrome were recruited in the emergency room at our hospital from 2005 to 2007. One parasite was isolated from a patient's expectorations, and two others were isolated from pieces of a raw sheep liver retrieved from the patients' dishes. A piece of infected goat liver intended for consumption was also collected from a local butcher. All parasites were examined microscopically for identification. All patients presented with immune allergic-like symptoms of the eyes, ears, nose, or throat. All collected parasites were identified as *Dicrocoelium dendriticum*. Our study has identified *D. dendriticum*, rather than *Linguatula serrata* or *F. hepatica*, as the prime suspect in the pathogenesis of the Lebanese Halzoun syndrome.

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1. Introduction

Lebanese Halzoun is a clinical syndrome that manifests as an acute allergic edematous reaction involving the upper respiratory tract and nasopharyngeal mucosa following the consumption of raw sheep or goat liver, a known food presentation in some countries of the Middle Eastern area (Schacher et al., 1965; Drabick, 1987). Halzoun in Arabic means "small snail" (from the resemblance to a snail shell). This aspect can be seen on the surface of a liver infested by flukes, and corresponds to dilatation and ectasia of the bile duct. Local butchers can sometimes identify a heavily infected liver by surface infestation by flukes with corresponding dilatation of bile ducts.

Lebanese Halzoun was first described in the medical literature when the Lebanese physician Khoury reported the detailed clinical symptoms, signs and complications of the syndrome in 1905 (Khoury, 1905). The immature worms of *Fasciola hepatica* were

considered to be the causative agent at that time (Khoury, 1905). In 1936, Brumpt described a similar syndrome that he referred to as "buccopharyngeal distomatosis" and attributed it to *F. hepatica* or another unknown trematode (Brumpt, 1936). Since then, similar clinical syndromes, considered to be synonymous to Halzoun syndrome, were described in the literature and were attributed to different pathogens and other parasites with buccopharyngeal tropism. In 1944, on the basis of clinical cases (not detailed), Witenberg attributed Halzoun to *Limnatis nilotica* leech, without ruling out the existence of another form linked to *Clinostomum complanatum* (Trematoda) (Witenberg, 1944). Then in 1956, again on the basis of clinical cases, Watson and Kerim described two forms of Halzoun, one caused by *F. hepatica* and the other by *L. nilotica* (Watson and Kerim, 1956). In 1969, comparing Lebanese Halzoun and Marrara syndrome in Sudan, Schacher et al. identified the larva of *Linguatula serrata* as the parasite of Halzoun (Schacher et al., 1969). More recent publications have attributed Halzoun to accidental infestation by the larvae of *L. serrata*, though without any conclusive arguments (Table 1).

Despite their striking resemblance in clinical presentation, few differences exist between these food-borne diseases. For instance, expectoration of worms is rarely observed in the Lebanese Halzoun patients whereas it is a common event in Marrara syndrome. Thus, the quest to find the real pathogenic agent causing the Lebanese

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Table 1
Reports on human *Linguatula serrata* cases.

Reference	Alimentary source	Number of larvae	Country	Patients number
Unat and Sahin (1999)	Mesenteric lymph nodes	20	Turkey	1
Papadakis and Hourmouziadis (1958)	–	20 collected from the mouth and nasal discharge	Greece	1
Le Corroller and Pierre (1959)	–	Parasites collected from the nostrils following sinus surgery	Morocco	1
Khalil and Schacher (1965)	Raw liver and mesenteric lymph nodes	Numerous, collected from the mouth and the nostrils	Lebanon	4
Schacher et al. (1969)	Raw mesenteric lymph nodes and liver	Collected from the mouth, the nostrils and the throat.	Lebanon	2
Yagi et al. (1996)	Raw mesenteric lymph nodes, liver and lungs	1st case: 2 and 2nd case: 5 Many	Soudan	45
Morsy et al. (1999)	–	Numerous	Egypt	1
Maleky (2001)	–	–	Iran	1
Siavashi et al. (2002)	Undercooked sheep liver	13	Iran	3

Halzoun is both interesting and necessary. The aim of our study was to identify the parasite that is the “prime suspect” of Lebanese Halzoun syndrome.

2. Materials and methods

2.1. Patients

Patients in our study were recruited in the emergency room (ER) at Saint Louis Hospital in Jounieh, Lebanon (affiliated with Saint Georges Hospital Ajaltoun). This hospital was chosen because of its proximity to local traditional Lebanese restaurants that serve raw liver dishes. From 2005 to 2007, 32 patients with history of a recent raw/undercooked ovine liver ingestion (within few minutes to 12 h) and presenting with one or more typical Halzoun symptoms, i.e. moderate to severe pharyngitis, itchiness of throat and nose, nasal congestion and discharge and lacrimation, were included in the study. Ethical approval to conduct this study was obtained from the ethical committees at Saint Louis and Saint Georges Hospitals.

2.2. Recovery of parasites

Out of the 32 patients, parasites were retrieved from only three patients. The first yield was collected from a patient's expectorant 6 h after ER admission. The others were retrieved from the remaining pieces of raw sheep liver obtained from the actual patients' dishes at the restaurant; the first dish had 4 remaining pieces of raw liver from which 2 parasites were retrieved, and the other dish had 2 pieces of raw liver that yielded one parasite.

In addition, a piece of infected goat liver was obtained from a local butcher who had identified a heavily infected liver; 30 parasites were collected from this liver.

2.3. Staining

All recovered free parasites were stained with carmine solution (Manet and Savel, 1971; Golvan and Ambroise-Thomas, 1990). The following procedure was used: the parasite was covered in the carmine solution for at least 15 min, and then washed with hydrochloric alcohol and water. The preparation was then dehydrated by successive immersion in alcohol 70% for 1 min, pure alcohol for 5 min, methyl salicylate for 2 min, and toluene for 2 min. Finally, the preparation was fixed using Canada balsam on covered slides. The histological sections of infected goat liver were fixed in formalin 4%, and stained with haematoxylin and eosin (H & E).

3. Results

3.1. Patients

32 patients were included in this study. Parasites were isolated from only 3 patients: a 32-year-old female had a dead worm retrieved from her expectorations, and two 45- and 35-year-old males had the parasites isolated from their dishes. The mean age of patients was 35 years (range, 17–60 years), with female predominance (68%, $n = 19$).

All patients presented with immune allergic-like symptoms of the eyes, ears, nose, or throat. Throat symptoms ranging from mild itching to severe pharyngitis were observed in all cases.

Most of the cases (78%) were observed in summer and spring seasons. The origins of raw liver were 78% from sheep and 22% from goats. The entourage (persons sharing the same dish of raw liver) with symptoms suggestive of Halzoun was reported in 59.3% of the cases.

Six patients (4 women and 2 men) had severe symptoms requiring the administration of methylprednisolone (40–80 mg intramuscular or intravenous) injections. No mortalities were observed among the studied cases.

3.2. Parasite examination

The isolated parasites were examined grossly and microscopically. Identical worms were recovered from both goat liver specimens and from human sputum. With naked eye examination, the parasites measured 6–10 mm long $\times$ 1.5–2.5 mm wide. Under microscopic examination, the eggs were thick-shelled, dark brown, operculated, and measured 36–45 $\mu\text{m} \times$ 20–30 μm . The parasites appeared as small flat adult worms with the shape of a lancet (lancet fluke). The oral and ventral sucker, and the pharynx were located anteriorly (Fig. 1). The uterus lied posteriorly and the vitelline

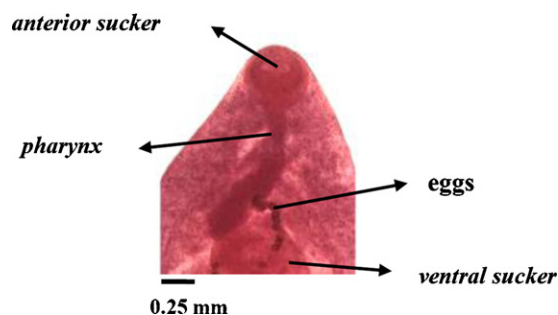


Fig. 1. Picture of the worm. Anterior part: anterior sucker and ventral sucker at 2/5 of body length (pharynx between the 2 suckers) (parasite source: piece of liver found in the patient platter).

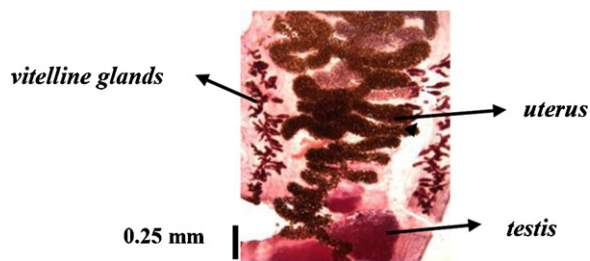


Fig. 2. Posterior part: parasite recovered in the sputum.

glands lied in the parasite mid-section (Fig. 2). The worm was identified as *Dicrocoelium dendriticum*.

4. Discussion

Lebanese Halzoun is a food-borne disease that presents as a hypersensitivity reaction of the upper respiratory tract and buccopharyngeal mucosa following the consumption of raw sheep or goat liver. Its clinical presentation, to a large extent, is similar to other food-borne diseases reported in areas where consumption of such food types is prevalent (Schacher et al., 1965; Drabick, 1987). The etiology has always been attributed to parasites; however, the identity of the exact parasite in different regions has always been debated.

If the etiology of our local Halzoun is indeed parasitical, parasites that harbour the ovine liver and qualify as suspects must be investigated and identified. Such suspects include flukes as *F. hepatica*, *D. dendriticum* and *Fasciola gigantica* (the trematodes responsible for hepato-biliary distomatosis) and linguatulids as *L. serrata*. *F. hepatica* is predominant in temperate zones while *F. gigantica* is found primarily in tropical regions (Drabick, 1987; Andrews, 1999; Otranto and Traversa, 2003; Dreyfuss et al., 2005). Cattle represent a definitive host for the hepatic trematodes, but it is only an intermediate host for the third stage larvae of *L. serrata*.

Our results, which were obtained by specific staining and microscopic observation, identified the parasites isolated from our samples as *D. dendriticum*.

D. dendriticum is devoid of spines on the teguments, so the hepatic lesions it causes are less significant than those caused by *F. hepatica* or *F. gigantica*, except in the case of massive chronic infestation (Ducommun and Pfister, 1991; Camara et al., 1996). It is therefore easier for a butcher to recognize a liver infested by *F. hepatica* than by *D. dendriticum*. Lebanese butchers sell raw liver after removing the bile duct and all other attachments. The liver is then served in the form of small cubes of 1.5–2 cm. Therefore, the possibility that larger parasites like *F. gigantica* (7 cm × 1–1.2 cm) or *F. hepatica* (2–3 cm × 0.8–1.5 cm, brown) are the cause of Lebanese Halzoun seems unlikely because of their relatively large dimensions and distinctive colours that allow their easy detection by the butcher or the consumer. The small size of *D. dendriticum* (0.5–1.5 cm × 0.15–0.25 cm) and its transparency, on the other hand, allows it to be missed (Andrews, 1999).

The ingestion of infected ovine liver can rarely cause human dicrocoeliosis. Most reported cases are spurious (causing diarrhea and transient shedding of eggs in the stool). In true infection, mature parasites can be found in the hepatobiliary system (Mas-Coma and Bargues, 1997). The immature forms of *F. hepatica* described by A. Khoury as an agent of Halzoun in 1905 may in fact be *D. dendriticum* since trematodes are frequently found together in the liver of ruminants, and the description of *D. dendriticum* came many years later due to the different generic and specific denominations it received (Manga-González et al., 2001).

L. serrata belongs to the family of the pentastomids (tongue-shaped worms) (Drabick, 1987), and is frequent in the Middle East with human cases reported from Turkey, Greece, Morocco, Sudan, Egypt and Iran (Yagi et al., 1996; Morsy et al., 1999; Maleky, 2001). It is rare in Europe; however, ocular linguatulus was reported in Austria (Koehsler et al., 2011). Common features among *L. serrata* human infections are the consumption of raw mesenteric lymph nodes and the expulsion of numerous mobile larvae of about 5–10 mm long from the mouth and nostrils (Table 1). The consumption of mesenteric lymph nodes, whether raw or cooked, is not featured in Lebanese dietary habits. Nevertheless, Halzoun syndrome continues to manifest itself occasionally after consumption of raw liver in the form of an allergic pharyngitis quite different from that encountered in Marrara syndrome that is caused by *L. serrata*.

In Lebanese Halzoun, there are often no worms or only very few non-mobile worms found in the mouth, nasal secretions or throat of patients, making it difficult to retrieve proper samples for pathogen identification. In Lebanon and the Middle East in general, better food hygiene and increased awareness about ovine hepato-biliary distomatosis over the past decade has led to a drastic decrease in the reported cases of Halzoun syndrome. In conclusion, if the etiologic agent in Halzoun syndrome is a parasite, our study has identified *D. dendriticum*, rather than *L. serrata* or *F. hepatica*, as the prime suspect in the pathogenesis of the Lebanese Halzoun syndrome. This finding needs to be confirmed in large scale studies covering many regions of the country.

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Conflict of interest

None.

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References

- Andrews, S.J., 1999. The life cycle of *Fasciola hepatica*. In: Dalton, J.P. (Ed.), Fasciolosis. CAB International Publishing, Wallingford, United Kingdom, pp. 1–29.
- Brumpt, E., 1936. Précis de parasitologie, fifth ed. Masson et Cie, Paris, pp. 572–573.
- Camara, L., Pfister, K., Aeschlimann, A., 1996. Histopathological analysis of bovine livers infested by *Dicrocoelium dendriticum*. Veterinary Research 27, 87–92.
- Drabick, J.J., 1987. Pentastomiasis. Reviews of Infectious Diseases 9, 1087–1094.
- Dreyfuss, G., Vignoles, P., Rondelaud, D., 2005. *Fasciola hepatica*: epidemiological surveillance of natural watercress beds in central France. Parasitology Research 95, 278–282.
- Ducommun, D., Pfister, K., 1991. Prevalence and distribution of *Dicrocoelium dendriticum* and *Fasciola hepatica* infections in cattle in Switzerland. Parasitology Research 77, 364–366.
- Golvan, Y.J., Ambroise-Thomas, P., 1990. Les nouvelles techniques en Parasitologie. Collection Flammarion, Paris, pp. 98–100.
- Khalil, G.M., Schacher, J.F., 1965. *Linguatula serrata* in relation to Halzoun and the Marrara syndrome. American Journal of Tropical Medicine and Hygiene 14, 736–746.
- Khouri, A., 1905. Le Halzoun. Archives de Parasitologie 9, 78–94.
- Koehsler, M., Walochnik, J., Georgopoulos, M., Prunte, C., Boeckeler, W., Auer, H., Barisani-Asenbauer, T., 2011. *Linguatula serrata* tongue worm in human eye, Austria. Emerging Infectious Diseases 17, 870–872.
- Le Corroller, Y., Pierre, J.L., 1959. On a case of human linguatulus in Morocco. Bulletin de la Société de Pathologie Exotique et de Ses Filiales 52, 730–733.
- Maleky, F., 2001. A case report of *Linguatula serrata* in human throat from Tehran, central Iran. Indian Journal of Medical Sciences 55, 439–441.
- Manet, L., Savel, J., 1971. Techniques usuelles de biologie clinique: Parasitologie. Collection Flammarion Médecine-Sciences, Flammarion, Paris, pp. 60–61.

- Manga-González, M.Y., González-Lanza, C., Cabanas, E., Campo, R., 2001. Contributions to and review of dicrocoeliosis, with special reference to the intermediate hosts of *Dicrocoelium dendriticum*. *Parasitology* 123, S91–S114.
- Mas-Coma, S., Bargues, M.D., 1997. Human liver flukes: a review. *Research and Reviews in Parasitology* 57, 145–218.
- Morsy, T.A., El-Sharkawy, I.M., Lashin, A.H., 1999. Human nasopharyngeal linguatuli-
liasis (Pentastomida) caused by *Linguatula serrata*. *Journal of the Egyptian Society of Parasitology* 29, 787–790.
- Otranto, D., Traversa, D., 2003. Dicrocoeliosis of ruminants: a little known fluke disease. *Trends in Parasitology* 19, 12–15.
- Papadakis, A.M., Hourmouziadis, A.N., 1958. Human infestation with *Linguatula serrata*: report of a case. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 52, 454–455.
- Schacher, J.F., Khalil, G.M., Salman, S., 1965. A field study of Halzoun (parasitic pharyngitis) in Lebanon. *Journal of Tropical Medicine and Hygiene* 68, 226–230.
- Schacher, J., Saab, S., Germanos, R., Boustany, N., 1969. The aetiology of Halzoun in Lebanon: recovery of *Linguatula serrata* nymphs from two patients. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 63, 854–858.
- Siavashi, M.R., Assmar, M., Vatankhah, A., 2002. Nasopharyngeal pentastomiasis (Halzoun): report of 3 cases. *Iranian Journal of Medical Sciences* 27, 191–192.
- Unat, E.K., Sahin, V., 1999. An infestation due to larvae of *Linguatula serrata*. *Cerrah-pasa Journal of Medicine* 30, 45–52.
- Watson, J.M., Kerim, R.A., 1956. Observations on forms of parasitic pharyngitis known as Halzoun in the Middle East. *Journal of Tropical Medicine and Hygiene* 59, 147–154.
- Witenberg, G., 1944. What is the cause of the parasitic laryngo-pharyngitis in the Near East (Halzoun)? *Acta Medica Orientalia* 3, 191–192.
- Yagi, H., el Bahari, S., Mohamed, H.A., Ahmed, el-R.S., Mustafa, B., Mahmoud, M., Saad, M.B., Sulaiman, S.M., el Hassan, A.M., 1996. The Marrara syndrome: a hypersensitivity reaction of the upper respiratory tract and buccopharyngeal mucosa to nymphs of *Linguatula serrata*. *Acta Tropica* 62, 127–134.