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General review

Human pentastomiasis in Sub-Saharan Africa

Les pentastomoses humaines en Afrique subsaharienne

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Abstract

Pentastomiasis is a rare zoonotic infection but it is frequently observed in Africa and Asia. Most human infections are caused by members of the *Armillifer armillatus* species. They are responsible for visceral pentastomiasis in Western and Central Africa. Humans may be infected by eating infected undercooked snake meat or by direct contact with an infected reptile. An increasing number of infections are being reported in Congo, Nigeria, and Cameroon. Despite an occasionally high number of nymphs observed in human viscera, most infections are asymptomatic and often diagnosed by accident during surgery or autopsy. The clinical presentation of pentastomiasis is quite varied and depends on infected tissues. The liver, lungs, and pleura are most frequently involved. Abdominal emergencies have been reported. Diagnostic delays always occur and diagnosis focuses on the patient's lifestyle and living environment. It is mainly based on the morphological description of the parasite's calcified cuticle, the site of the lesion, and the parasite's region of origin. Most patients do not require any treatment. Personal measures such as avoidance of contact with snake droppings are recommended to prevent transmission. Imported pentastomiasis has been observed in African migrants.

Keywords: Pentastomiasis; *Armillifer armillatus*; Central Africa; Western Africa

Résumé

La pentastomose est une zoonose rare mais fréquemment observée en Afrique et en Asie. L'espèce la plus documentée chez l'homme est *Armillifer armillatus*, responsable de pentastomose viscérale en Afrique de l'Ouest et centrale. La pentastomose à *Armillifer armillatus* est observée chez l'homme consommateur de viande de serpent infectée insuffisamment cuite ou en contact avec le reptile infecté. Le nombre croissant d'infections est le plus souvent signalé au Congo, Nigéria et Cameroun. En dépit du nombre important de nymphes qui peuvent être trouvées dans les viscères humaines, les infections sont habituellement asymptomatiques et la pentastomose est de découverte fortuite lors d'une intervention chirurgicale ou d'une autopsie. La symptomatologie clinique n'est pas spécifique et dépend des tissus infectés. Le foie, les poumons ou la plèvre sont les organes les plus impliqués. Des urgences abdominales ont été décrites, comme dans la récente découverte taxonomique au Cameroun. Le diagnostic est toujours retardé et se fonde sur une attention particulière aux habitudes de vie du patient et à son environnement. La description morphologique de la

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cuticule calcifiée, la distribution anatomique de la lésion et la provenance régionale sont les composants clés de l'orientation diagnostique. Dans la plupart des cas, aucun traitement n'est nécessaire. Pour prévenir la transmission, des mesures personnelles comme l'évitement avec les excréments de serpents doivent être proposées. Des cas de pentastomose humaine importés ont été rencontrés chez des migrants originaires d'Afrique.

Mots clés : Pentastomose ; *Armillifer armillatus* ; Afrique centrale ; Afrique de l'Ouest

1. Introduction

Pentastomiasis is an endemic zoonotic infection (porocephalosis) observed in tropical countries. It is caused by obligate parasites known as pentastomes, belonging to the Pentastomida subclass [1]. Pentastomiasis is a rare and unknown infection that is often diagnosed by accident. Nevertheless, severe presentations may occur. Visceral and nasopharyngeal pentastomiases are most frequently observed. Pentastomes are sometimes considered as a subclass of vermiform maxillopod crustaceans [2,3] or as a specific class within arthropods [4,5]. They are even sometimes considered as a distinctive phylum [1,6]. The results of recent molecular studies focusing on the classification of two species of *Linguatula* highlight the difficulties of clearly defining this group of parasites [7]. Among the four orders [1], human parasites are observed in two families of the Porocephalida order: Porocephalidae with the *Armillifer* genus responsible for visceral pentastomiasis in Western and Central Africa, and Linguatulidae or cosmopolitan linguatules whose main genus is *Linguatula*. Within these families *Armillifer armillatus* (Wyman, 1845) and *Linguatula serrata* (Frölich, 1789) are mostly responsible for human pentastomiasis [8,9].

2. Pathophysiology

Armillifer armillatus (Fig. 1) was first reported by Wyman in 1845 in Western Africa. The first human case of pentastomiasis was reported by Pruner in 1847 in Egypt [1]. The following year, Wyman identified the adult pentastome in the nasopharynx of an African rock python (*Python sebae*) (Fig. 2) [10].

L. serrata, also known as "tongueworm", most frequently occurs in South-East Asia, South America, and in the Middle East [11]. Herbivorous animals act as intermediate hosts (African wild dogs, foxes, and wolves) and harbor the parasite in their upper respiratory tract. *A. armillatus* is most frequently observed in Western and Central Africa, with the exception of a few cases reported in Malaysia. Usual hosts of *A. armillatus* are African snakes such as pythons and vipers, where the parasite is usually isolated from their lungs. Human infections caused by *Armillifer* spp. have recently been reported in China and Malaysia [12–14].

Human pentastomiasis is rarely reported in Sub-Saharan Africa. The authors of some studies reported it in 22% of autopsies performed in the Democratic Republic of Congo (DRC), 33% in Nigeria, and 8% in Cameroon [15]. Most case patients observed in Central Africa were from Nigeria and the Congo Basin [16–18] (Table 1). Most were diagnosed in northern countries in African migrants who suffered a great deal from misdiagnoses [16,19–22] (Table 2). Only one case patient was reported in Cameroon in 1985: a 34-year-old man from the Banka-Bafang region hospitalized for acute peritonitis [23]. A more recent case of pentastomiasis has been reported in Yaoundé in a 30-year-old man. The patient did not report any contact with snakes but used to live in a rural area for several years (Eastern and Central regions). He had a several-month history of refractory ascites complicated by peritonitis.

Humans may act as aberrant definitive hosts or as accidental hosts in the biological cycle of pentastomes. The biological cycle

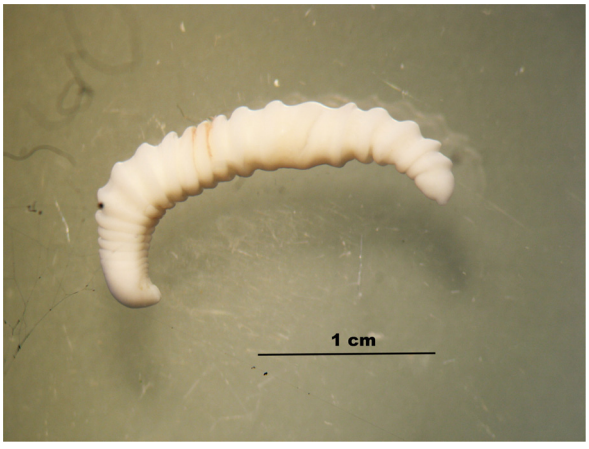

Fig. 1. *Armillifer armillatus* larva isolated from the mesentery of a Cameroonian man.
Larve du parasite Armillifer armillatus extraite du mésentère d'un homme camerounais.
Resources: personal image, Philippe Le Gall; IRD (institut de recherche pour le développement), UR BEI-072, BP1857 Yaoundé, Cameroon. 18- to 20-mm larva with 20 to 22 spiral rings.

Fig. 2. *Python sebae*; Cameroon: usual definitive host of *A. armillatus*.
Python sebae ; Cameroun : hôte définitif habituel de A. armillatus.
Resources: personal photo, Matthew Le Breton.

Table 1
Autochthonous cases of human pentastomiasis caused by *Armillifer* spp. in Africa.
Cas rapportés autochtones de pentastomose humaine à Armillifer *spp. en Afrique.*

Region of origin	Country of diagnosis	Year	Sex	Age	Diagnostic technique	Parasite	Authors
DRC	DRC	1967	M	32	X-ray	*A. armillatus*	De Coster et al. [37]
DRC	DRC	1967	F	>18	X-ray	*A. armillatus*	De Coster et al. [37]
DRC	DRC	1967	M	65	X-ray	*A. armillatus*	De Coster et al. [37]
DRC	DRC	1967	F	50	X-ray	*A. armillatus*	De Coster et al. [37]
Ghana	Ghana	1962	M	Unknown	X-ray	*A. armillatus*	Bretland [38]
Ghana	Ghana	1962	M	Unknown	X-ray	*A. armillatus*	Bretland [38]
Zimbabwe (Rhodesia)	Zimbabwe	1973	F	Unknown	Unknown	*A. armillatus*	Goldsmid and Melmed [39]
Ivory Coast	Ivory Coast	1982 (29 cases)	Unknown	Unknown	X-ray	*Armillifer* spp.	Tiendrebeogo et al. [40]
Gabon	Gabon	1984	M	72	X-ray	*A. armillatus*	Aubry [41]
Cameroon	Cameroon	1985	M	34	Laparotomy	*A. armillatus*	Herzog et al. [23]
Nigeria	Nigeria	1992	F	18	Autopsy	*A. armillatus*	Obafunwa et al. [42]
Congo	Congo	1995	M	59	Unknown	*Armillifer* spp.	Faisy et al. [18]
Central Africa	Nigeria	1996	M	50	X-ray	*A. armillatus*	Nzeh et al. [43]
Central Africa	Nigeria	1996	M	70	X-ray	*A. armillatus*	Nzeh et al. [43]
Central Africa	Nigeria	1996	F	35	X-ray	*A. armillatus*	Nzeh et al. [43]
Ivory Coast	Ivory Coast	2000	F	18	Autopsy	*A. grandis*	Yapo et al. [27]
Ghana	Ghana	2004	M	55	Laparotomy	*A. armillatus*	Dakubo et al. [44]
Ghana	Ghana	2006	F	9	Autopsy	*Armillifer* spp.	Dakubo et al. [25]
Ghana	Ghana	2006	M	32	Autopsy	*Armillifer* spp.	Dakubo et al. [25]
Ghana	Ghana	2007	M	26	Laparotomy	*Armillifer* spp.	Dakubo et al. [25]
Nigeria	Nigeria	2011	M	60	X-ray	*Armillifer* spp.	Ibinaiye et al. [45]
Nigeria	Nigeria	2011	F	57	Hepatic encephalopathy	*A. armillatus*	Adeyekun et al. [29]
Nigeria	Nigeria	2011	M	70	X-ray	*A. armillatus*	Jisieike-Onuigbo et al. [36]
Guinea	Guinea	2012	M	52	X-ray	*A. armillatus*	Bafende Aombé et al. [46]
Cameroon	Cameroon	2013	M	33	Laparotomy	*A. armillatus*	Personal data

DRC: Democratic Republic of Congo; M: male; F: female.

Table 2
Imported cases of human pentastomiasis caused by *Armillifer* spp.
Cas importés de pentastomose humaine à Armillifer *spp.*

Region of origin	Country of diagnosis	Year	Sex	Age	Diagnostic technique	Parasite	Authors
Liberia	United States	1976	M	35	X-ray	*A. armillatus*	Mapp et al. [26]
Africa	France	1982	Unknown	Unknown	X-ray	*Armillifer* spp.	Piéron et al. [47]
Eastern Africa	Japan	1987	F	Unknown	Autopsy	*A. armillatus*	Kagei and Shichiri [48]
Nigeria	Canada	1991	M	28	Autopsy	*A. armillatus*	Guardia et al. [17]
Gabon	France	1995	M	50	X-ray and renal failure	*Armillifer* spp.	Bouchaud and Matheron [21]
DRC	France	1999	M	26	Autopsy	*A. armillatus*	Lavarde and Fornes [30]
Nigeria	South Africa	2001	M	39	X-ray	*A. armillatus*	Du Plessis et al. [22]
Cameroon	France	2001	F	34	X-ray	*A. armillatus*	Touze et al. [49]
Mali	France	2005	M	Unknown	X-ray	*Armillifer* spp.	Sellier et al. [50]
Liberia	The Netherlands	2005	F	23	Laparotomy	*A. armillatus*	Tappe et al. [51]
Nigeria	Spain	2005	F	25	Laparoscopy	*Armillifer* spp.	Martin-Rabadan et al. [52]
Togo	Germany	2013	M	23	Autopsy	*A. armillatus*	Tappe et al. [16]

DRC: Democratic Republic of Congo; M: male; F: female.

and transmission of *A. armillatus* are now well-known. Adult parasites are usually isolated from the upper respiratory tract of African snakes (*Python sebae*, *P. regius*) and vipers (*Bitis arietans*, *B. gabonica*, and *B. nasicornis*) [24]. Transmission to snakes occurs by eating infected rodents. Ova are released into the environment 4 to 6 months later through respiratory secretions or feces. Vegetation and water, a source of infestation for intermediate hosts (rodents), are thus contaminated. Human contamination is accidental and occurs by direct or indirect contact with reptiles [8] (Fig. 3). Contamination occurs by eating undercooked snake meat, by direct contact with the meat (transportation, cutting, preparation), or by indirect contact with food or water contaminated by snake droppings. Snake hunting and eating is very common in various rural regions of Central

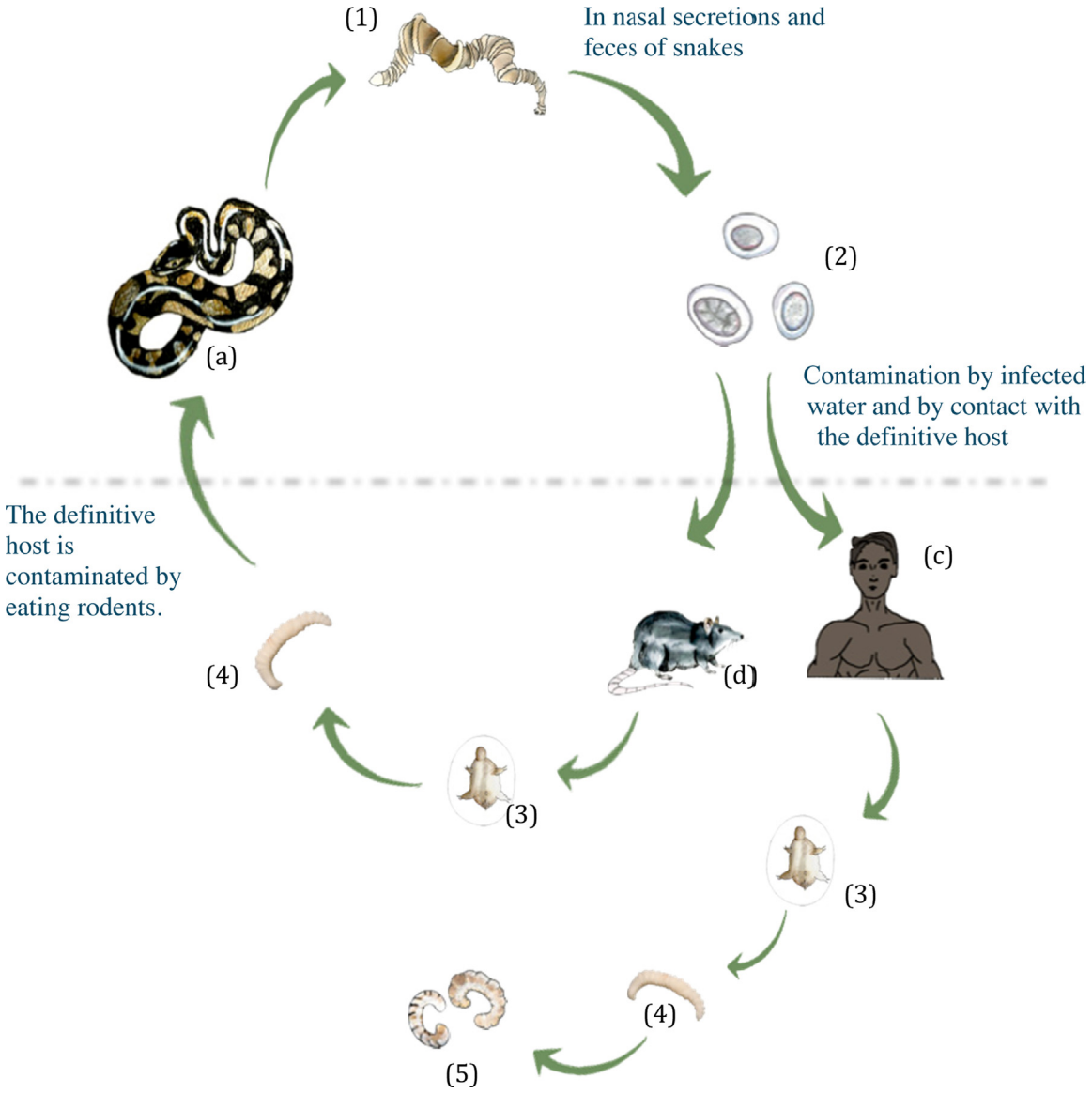

Fig. 3. Biological cycle of *Armillifer armillatus* (C. Vanhecke, E. Vanhecke): (a) definitive host: snake – *Python sebae*; (b) intermediate host: rodents; (c) accidental intermediate host: humans; (1) image of an adult *Armillifer armillatus*; (2) image of an ovum of *Armillifer* spp.; (3) image of a larva of *Armillifer armillatus* at stage 1; (4) nymph of *Armillifer armillatus* at stage 3 in the intermediate host; (5) image of a calcified nymph of *Armillifer armillatus* in the accidental intermediate host. *Cycle biologique de Armillifer armillatus (C. Vanhecke, E. Vanhecke).*

Africa, especially in the forest area of South Cameroon. Targeted species are the *Python sebae*, vipers such as *Bitis gabonica* and *Bitis nasicornis*, the *Naja melanoleuca* cobra, and some colubrid snakes.

In Cameroon, and in other African countries, snakes are also used for animistic rituals and traditional medicine. Accidental contact with snakes may then occur and individuals are faced with a repeated risk of exposure [25]. Eating snake meat, usually cooked, grilled, or with a sauce, is restricted to influential individuals or leaders of ethnic groups in Cameroon. Other members of the ethnic group thus tend to deny eating snake meat, which may represent a reporting bias when trying to identify any potential contamination.

Following ingestion, the initial stage of pentastomiasis in humans is characterized by larvae going through the intestine wall. This usually asymptomatic phase has already been observed in animals and can also occur in humans. After a few days, larvae encyst in tissues such as in the liver, spleen, mesentery, and pleura. Encysted larvae eventually grow and die within a few years. The calcified parasite may look like a horseshoe (C) on chest and abdominal x-rays (Fig. 4). In intermediate hosts, mainly rodents and accidentally in humans, larvae may hatch from the cyst and migrate again through the tissues to reach the liver, intestinal lumen, lungs, and central nervous system. This is the longest stage of their biological cycle; it may take as long as 2 years. This stage is usually symptomatic.

Human visceral pentastomiasis is rarely symptomatic and diagnosis is usually made by accident during a chest or abdomen x-ray [21,26] (calcified nymphs), an autopsy [27], or an exploratory laparotomy. Symptomatic presentations are rare and clinical symptoms are not specific. They are usually related to cystic nodules in various organs. Most patients present

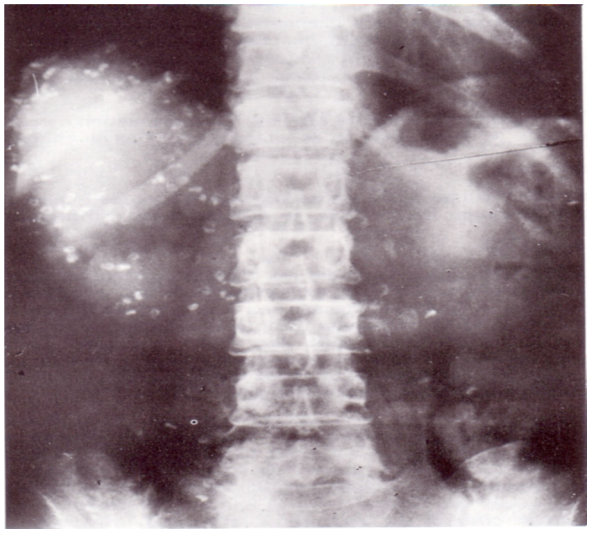

Fig. 4. X-ray of the abdomen, without any preparation, showing multiple calcified nymphs of a pentastome.
Radiographie de l'abdomen, sans préparation, avec de multiples nymphes calcifiées de pentastome.
Resources: personal image, Denis Malvy. Centre René-Labusquière (institut de médecine tropicale), université Victor-Segalen, 33000 Bordeaux.

with digestive symptoms, mainly diffuse, chronic, and isolated abdominal pain that may sometimes be associated with changes in bowel habits and vomiting [12]. Patients may also present with irritation of the upper respiratory and gastrointestinal tracts causing coughing. Liver involvement has been reported in patients presenting with pseudotumors [28] or hepatic encephalopathy [29]. Miliary lung disease presentation may also occur and must be differentiated from tuberculosis. Obstruction syndrome and peritonitis have also been described. Exploratory laparotomy and ablation of nodules helped highlight the presence of numerous pentastomes in the patient's peritoneal cavity [20]. Pentastome-induced infectious complications (digestive, pulmonary, or neuromeningeal complications, sepsis, pericarditis) or obstructions on peritoneal adherences have been observed [30,31].

3. Diagnosis

Pentastomiasis must be considered in tropical areas, and especially in Sub-Saharan Africa, in patients presenting with acute or chronic abdominal symptoms associated with eosinophilia of unknown origin. Physicians must conduct a detailed interview and enquiry about the patient's lifestyle, eating habits, and any contact with snakes such as pythons and vipers.

Molecular biology techniques, such as PCR and DNA sequencing, are currently under study for a quicker and more specific diagnosis. However, their local implementation is difficult due to their high cost and limited access [32,33].

When confronted to a confirmed pentastomiasis case, the diagnosis of the species involved is made on the basis of the most likely species of the pathogenic complex, i.e., potential ecogeographical characteristics associated with the parasite and the presence of definitive and intermediate hosts. The diagnosis is confirmed by taxonomic evaluation; macroscopic and microscopic analyses must be performed on at least one larva. Among the *Armillifer* species, *A. grandis* and *A. armillatus* (18 to 20 mm, 20 to 22 spiral rings) are present in Central Africa and taxonomic evaluations are justified by the high similarity between the two parasites. *A. grandis*, whose intermediate host is the *Bitis nasicornis* viper, seems to be smaller (9–15 mm) than *A. armillatus* and the two parasites do not have the same number of spiral rings [34]. Just like with *A. grandis*, the distinction between *A. armillatus* and *L. serrata* mainly relies on morphological features. The presence or absence of cuticular spines is one of the main differences between *L. serrata* and *A. armillatus* [31]. Similarly, *A. moniliformis*, whose intermediate host is the python, may be distinguished from *A. armillatus* by its size (12–20 mm) and number of spiral rings (26 to 30). *A. moniliformis* is mostly observed in South-East Asia [14].

4. Differential diagnosis

Other causes of abdominal calcification (x-ray and clinical symptoms) associated with eosinophilia are first considered. Misdiagnosing the disease for a malignant tumor or a lymphoproliferative disorder is one of the main reasons for diagnostic delay. Cysticercosis is usually associated with multiple muscle calcifications [22]. The presence of miliary lung disease makes it possible to be sure that there is no associated tuberculosis or endemic hemoptysis [35]. Lymph node calcifications without specificity or radiological signs of lithiasis may be differentiated by the horseshoe form of the calcified pentastome. The hepatic visceral localization must not be mistaken for a hepatocellular carcinoma or a secondary tumor localization [28].

5. Treatment

Early initiation of treatment is difficult with asymptomatic presentations or in the absence of any pathognomonic sign. There is currently no standard treatment for asymptomatic presentations as they are very hard to diagnose. Initiating treatment is not necessarily recommended as the parasite spontaneously dies after 2 years, and treating at that stage is pointless as it would be too late [19,36].

Symptomatic presentations must be treated with a radical surgical treatment [19], especially severe presentations or patients at risk of a negative outcome. Exploratory laparotomy in patients presenting with acute abdominal symptoms allows for diagnosing the parasitic disease and for removing larvae. A peritoneal lavage is also usually performed just before the end of the procedure. With regard to the last case patient reported in Yaoundé, more than a 100 nymphs of *A. armillatus* were removed from the patient's peritoneal cavity by laparotomy. Abdominal pain disappeared after surgery.

There is currently no specific standard treatment for such parasites. Symptomatic presentations are usually treated with a combination of antiparasitic treatments. A few position papers were published by Chinese teams on the treatment of pentastomiasis due to *Armillifer* spp. They reported treating patients with a monotherapy or a combination of praziquantel, albendazole,

or mebendazole. One study mentioned the use of traditional Chinese medicines in combination with praziquantel and mebendazole [12,13]. These rare observations were associated with a clinical and radiological benefit and contributed to massively eradicate the dead parasite from the patient's feces. This could act as a future composite evaluation criterion. This therapeutic strategy relying on the combination of antiparasitic treatments has the advantage of being minimally invasive. The use of a combination of praziquantel and albendazole or mebendazole should be evaluated in further studies to help design recommendations.

6. Conclusion

In Central Africa, the morbidity of pentastomiasis due to *A. armillatus* is probably overlooked because of diagnostic delays and difficulties. Further studies should be conducted on the benefits of therapeutic combinations of antiparasitic agents (praziquantel, albendazole, mebendazole). Awareness of the disease and its transmission routes must also be raised. Prophylactic measures include overcooking food (60 °C), snake meat, and animal viscera, and thoroughly washing one's hand before cooking.

Disclosure of interest

The authors declare that they have no competing interest.

Authors' contribution

C. Vanhecke wrote the article.

P. Le Gall and M. Le Breton contributed to writing the article and editing the figures and tables.

D. Malvy reviewed the article.

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