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Blastocystosis: an emerging or re-emerging potential zoonosis?

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Summary

Blastocystis sp. is an intestinal protozoa that was formerly recognised as a yeast. However, it has since been classified in the Stramenopile Kingdom. In addition to being observed in humans, the disease has been diagnosed in a wide range of animals (mammals, amphibians, birds, reptiles and arthropods). Extensive genetic heterogeneity has been demonstrated. *Blastocystis* sp. subtypes 1 to 9 were recently considered to be of zoonotic origin. While some suggested that *Blastocystis* might play a pathogenic role in intestinal disorders in humans, others reported that there was no correlation. Furthermore, amoeboid forms of *Blastocystis* might be implicated in pathogenesis. In spite of recent reports, earlier data on the prevalence of the parasite suggest that blastocystosis could have occurred sporadically or continuously in the past. It might be speculated that in cases of zoonotic genotypes producing amoeboid forms, *Blastocystis* sp. infection might rather be considered a potential re-emerging zoonosis.

Keywords

Amoeba, Blastocystis, Culture, Public health, Travel, Zoonosis.

Blastocistosi (infezione da *Blastocystis* sp.): potenziale zoonosi emergente o riemergente?

Riassunto

Blastocystis *sp. è un protozoo intestinale noto un tempo come lievito. Viene tuttavia classificato tra gli Stramenofili. E' stato isolato nell' uomo e in molti animali (mammiferi, anfibi, uccelli, rettili e artropodi); inoltre ne è stata provata una vasta eterogeneità genetica. Studi recenti hanno dimostrato l'origine zoonotica di* Blastocystis *sp. nei sottotipi da 1 a 9. Alcuni ricercatori suggeriscono che nell'uomo* Blastocystis *possa svolgere un ruolo di patogeno in disordini intestinali; altri, al contrario, che non vi sia alcuna correlazione; inoltre le ricerche hanno suggerito che le forme ameboidi di* Blastocystis *potrebbero essere implicate nella patogenesi. A differenza di quanto sostenuto da studi recenti, i dati iniziali sulla prevalenza del parassita indicano che la blastocistosi potrebbe essersi verificata , in passato, in maniera sporadica o ricorrente. In conclusione si può sostenere che nel caso di genotipi zoonotici che producono forme ameboidi di* Blastocystis *sp., l'infezione potrebbe essere considerata piuttosto una potenziale zoonosi riemergente.*

Parole chiave

Ameboide, Blastocystis, Coltura, Sanità pubblica, Viaggio, Zoonosi.

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Introduction

Blastocystis is an intestinal protozoan once recognised as yeast (2). It has recently been classified in the Kingdom Stramenopiles (1). All *Blastocystis* isolates were considered of zoonotic origin (37). Wild and domesticated animals have been demonstrated to be reservoirs for *Blastocystis* (37). Furthermore, *Blastocystis* isolates from humans and mammals, amphibians, birds, reptiles and arthropods have been reported (37). Since *Blastocystis* isolates from humans and animals have been found to be included in all *Blastocystis* sp. subtypes, it was suggested that low host specificity could be a feature of the parasite (28). Moreover, there was evidence that *Blastocystis* organisms from animals could infect humans and vice-versa (28).

Genetic variability

High genotype polymorphism has been observed among morphological identical *Blastocystis* isolates from humans and animals (37, 38). *Blastocystis* isolates from reptiles and amphibians are also included in phylogenetic tree branches (44). In addition, small subunit (ssu) rRNA gene sequence variability observed in morphologically similar human *Blastocystis* isolates might imply that the genus *Blastocystis* includes many different species (28). Since extensive genetic heterogeneity has been demonstrated, mammalian and avian isolates have been identified as *Blastocystis* sp. with a standardised subtype number in Arabic numerals, such as 1 to 9, without further subtype subclassification (6, 35, 44). Thus, *Blastocystis* organisms might adapt and survive at different temperatures (44).

No correlation has been found between the country of origin of *Blastocystis* isolates and the variety of *Blastocystis* sp. genotypes encountered in different areas of the world. Besides, different genotypes have been reported in the same country (14). Our results from genotyped *Blastocystis* isolates in faecal specimens from humans in Greece (22) were in agreement with observations that had been reported previously in that subtype 3 was the predominant genotype, whereas zoonotic genotypes were observed occasionally.

Epidemiology

Blastocystis sp. infection is reported worldwide (36). *Blastocystis* sp. infection prevalence varied widely, depending on the country. Early reports from developed countries gave lower levels of prevalence of *Blastocystis* (approximately 1.5-10%), while it seemed more prevalent (approximately 30-50%) in developing countries (36). Current data show low prevalence rates of *Blastocystis* sp. infection in Japan and Hawaii, while high prevalence rates were recorded in Argentina, Chile, Malaysia and Turkey (5, 15, 23, 27, 29, 30, 32, 33). In addition, *Blastocystis* sp. is has been detected in Romanian and Turkish parasitology laboratories (7, 10). Several reports, including some very early data, showed regions of high *Blastocystis* endemicity (46). Epidemics attributed to human *Blastocystis* were reported in the early studies, but outbreaks of infection appear to be uncommon (34, 46). Cases of clinical blastocystosis have been referred to sporadically. However, an increase in the number of cases of *Blastocystis* sp. infection recently observed both in developed and in developing countries could be due to the improved testing methods and to animal trade (3, 11, 45).

In animals, the prevalence of *Blastocystis* appeared to vary from animal to animal (37). Studies revealed that the prevalence of *Blastocystis* sp. infection is high among laboratory rats (60%), pigs (70-95%) and birds (50-100%) (37). It was also demonstrated that the prevalence of *Blastocystis* in dogs and in cattle differs from country to country (37). Furthermore, an epizootic with mortalities was reported in a primate colony (46).

Population at risk

Travellers to developing tropical countries were thought to be more prone to diarrhoea associated with *Blastocystis* (34). A high percentage of *Blastocystis* infection was found in soldiers transferred to endemic countries or regions, such as Egypt, the Middle East and Central America (34). *Blastocystis* was also highly prevalent among refugees and immigrants (36). An extremely high *Blastocystis* prevalence was noted in pre-school children

and school children in developing countries (36).

Food and animal handlers were found to be at risk of being infected by *Blastocystis* (33, 38). In addition, individuals who come into contact with animals, mainly pets, could be found to give positive results for *Blastocystis* (8). We screened stool samples from household cats from a high-income urban Greek area, for *Blastocystis* sp. infection by direct microscopy and culture using the Robinson medium. Although *Blastocystis*-like particles were observed microscopically, *Blastocystis* organisms were not been cultured (E. Papadogiannakis, E. Vassalou & C.M. Vassalos, unpublished data). This initial findings concur with the suggestion that either the culture conditions used for culturing human *Blastocystis* might not have been appropriate for growth of feline *Blastocystis* or improved sanitation could contribute to the absence of the parasite (9, 15). Thus, further molecular studies will be required to clarify this point. On the other hand, faecal specimens from primate pets that came into close contact with humans were positive for *Blastocystis* in Indonesia and in the Rift Valley in Ethiopia (16, 20). In addition, *Blastocystis* sp. isolates were detected in rural regions of developing countries and in low-income community groups (18, 38). Poor hygiene and sanitation facilities were regarded as major contributing factors (38).

Transmission

Blastocystis sp. infection could be considered to be a waterborne and foodborne disease (33, 34). Cross-transmissibility might also be speculated (27). It has been suggested that *Blastocystis* sp. infection is transmitted via the faecal-oral route (31).

The zoonotic transmission potential of *Blastocystis* sp. is based on phylogenetic analysis and other molecular approaches (37). Animals exhibiting a high prevalence of *Blastocystis* sp. infections may represent an extensive reservoir for infection of humans (28).

Morphology

The cyst is the parasite's infective form and the amoeboid form might be considered a stage in the life cycle of *Blastocystis* (37, 39). It was recently suggested that amoeboid forms could originate from vacuolar forms (39, 40).

Pathogenicity

In humans, blastocystosis has been implicated in a variety of non-specific symptoms (12). Intense abdominal disorders, together with pain, diarrhoea and constipation were reported in most cases (46). Although some suggested that the parasite might play a pathogenic role, mainly in intestinal disorders, others reported that there was no correlation (19, 36). We examined *Blastocystis* sp. isolates from human carriers by direct microscopy, Giemsa- and trichrome-stained smears and culture using the Robinson medium. Apart from viewing vacuolar organisms, we found irregular and amoeboid *Blastocystis* organisms present in symptomatic isolates (17; C.M. Vassalos & E. Vassalou, unpublished data). Thorough *in vitro* observations and further molecular analysis might be required to very the potentially pathogenic forms and their relationship with human or zoonotic genotyupes of *Blastocystis*. Our observations agreed with the suggestion that the presence of amoeboid forms in symptomatic isolates could contribute to the ambiguous pathogenicity of this parasite (40, 41).

In symptomatic human carriers, amoeboid forms of *Blastocystis* sp. can adhere to the epithelial cells lining the gut. Amoeboid *Blastocystis* cells have been detected both in patients with diarrhoea and in colonoscopy samples (17, 38, 39, 40). It could be speculated that amoeboid forms might affect gut immune homeostasis maintained by both enterocytes and different gastrointestinal immune cells (17, 43). The immune response might be elicited against carbohydrate antigens of the surface coat that most likely surrounds amoeboid forms (17, 38, 39, 40, 43). Furthermore, in active inflammation, inflammatory cell recruitment and accumulation might occur (17, 36, 43). In

addition, the occurrence of *Blastocystis* organisms in the gastrointestinal tract might modulate immune response (13).

Predisposition conditions

A number of conditions and concomitant factors might contribute to the pathogenicity of *Blastocystis* sp. infection (13, 34). In particular, alteration of intestinal barrier function, change in bowel habits, diet change, redox decrease or change in intestinal flora could explain the increased growth of *Blastocystis* (26). Although some workers have suggested that human *Blastocystis* infection could be linked to irritable bowel syndrome, others indicate that there was no correlation (19, 37, 38). Furthermore, immunosuppressed patients with *Blastocystis* infections demonstrated more severe symptoms in comparison with immuno-competent patients (37, 38). Thus, risk factors for clinical blastocystosis might comprise both host factors and different parasite strains that are shown to vary in virulence (24, 42).

Conclusions

Infection from potential pathogenic *Blastocystis* sp. resulted in a long duration of infectiousness. Contamination might occur sporadically, or even continuously, as a result of infection from a reservoir in animal hosts and from animal trade (21, 31, 45). It was suggested that a new pathogenic variant of *Blastocystis* has recently emerged in endemic countries (4). Whether there has been a true increase in blastocystosis incidence or an improvement in recognition and testing methods is uncertain. In view of the tremendous recent acceleration and expansion of global trade, human movement and travel and the growing global human and animal populations, both early and current data on the prevalence of the parasite might indicate that blastocystosis should be considered as a ubiquitous re-emerging potential zoonosis (25, 45, 46). Molecular epidemiology of *Blastoystis* sp. infections should be used to determine the frequency of zoonotic transmission both in endemic areas and in outbreak situations (35).

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