case report

Balantidium Coli ColitisRevealing a Common Variable Immunodeficiency: A Case Report

Abstract:

*Balantidium Coli*is a large protozoan parasite, measuring up to 150 micrometers, initiallyidentifiedin 1857 and laterrenamedin 1861-1862. It is an animal parasite, withitsprimaryreservoirbeingpigs (domesticpigs/wildboars), but it can alsobefound in other animal speciessuch as dogs, cats, hyenas, buffaloes, camels, monkeys, and others. Humans are an accidental host, as theyrepresent a dead-end in the parasitic life cycle. Infection by this parasite istypicallyasymptomatic or presentswithmildsymptoms. It becomespathogeniconly in cases of primary or secondaryimmunodeficiency, whereittypicallymanifests as colitis; however, urinary tract involvementisalso possible. In our case, *Balantidium Coli* infection presented multiple challenges. It is not a well-known parasite in ourregion, particularlysincepigfarmingis not practiced in Morocco. The parasite wasfound in both the urine and stool of the patient, whoexhibitedclearsigns of infectionwhichis not usualwiththis parasite. This led to the "late" discovery of Common Variable Immunodeficiency (CVID) in the patient, a primaryimmunodeficiencytypicallydiagnosedbefore the age of 4 and characterized by a deficiency in immunoglobulin production, particularlyaffecting the IgA and IgG fractions.

Introduction:

*Balantidium Coli*is a protozoan parasite measuring about 150 micrometers, withpigs as itsprimaryreservoir. Humans are accidental hosts, and contamination can occurthrough direct contact by ingesting the parasite'scyst via dirty hands or indirectly by consumingcontaminatedfood or water, the population thatismostlyaffected by thisprotozoan are farmersraisingpigs and theirfamilymembers. It is the largestpathogenicprotozoan in humans and isresponsible for a zoonosis [1]. It typically causes colitis, first described and identified by Malmstenin 1857 in two patients presentingwithdysentery. It wasinitiallynamed*Paramoecium* and waslaterrenamed*Balantidium* by Leuckartin 1861 and Stein in 1862 [2].

Common Variable Immunodeficiency (CVID) is a primaryimmunodeficiencycharacterized by a deficiency in the production of immunoglobulin G and immunoglobulin A, leading to hypogammaglobulinemia. It isusuallydiagnosedbefore the age of 4, followingrecurrent infections, particularly of the respiratory tract [3]. We report the case of a patient in whom*Balantidium Coli*colitisrevealed a Common Variable Immunodeficiency.

Clinical Case:

The patient was a 23-year-old woman, bornfrom a first-degreeconsanguineousmarriage. Shehad a history of recurrentrespiratory and digestive infections (more thanthreeepisodes per year) thatresponded to probabilisticantibiotictherapy (amoxicillin + clavulanicacid) sinceearlychildhood. Shealsohadchronicirondeficiencyanemiasince the age of 14, treatedwithironsupplementation (80 mg/day) withoutimprovement in ferritinlevels. Additionally, shehad a history of *Helicobacter pylori*gastritisdiagnosed at age 19, treatedwithamoxicillin 1 g twicedaily, clarithromycin 500 mg twicedaily, in combination withomeprazole 20 mg twicedaily for 15 days. Shehad an appendectomy at age 12 and primaryamenorrhea. The patient receivedthree doses of the Sinopharm COVID-19 vaccine.

The illnessbegan six monthsbeforeherhospitalization, with the onset of diffuse abdominal pain in the colonicregion, associatedwith mucus-bloody diarrhea, occurring 6 to 8 times per day, all evolving in a febrilecontextwithweightloss of 18 kg over six months. The condition progressedwith the appearance of vomiting, lumbar pain, hematuria, and frequent urination, prompting the patient to seek emergency care at the Ibn Sina University Hospital Center in Rabat.

On clinicalexamination, the patient wasfound to becachecticwithgrowth retardation, measuring 1.42 meterstall and weighing 27 kg, with a body mass index of 13.4. Shewasdehydrated, with a skin foldpersisting for more thantwo seconds. The patient was somnolent and confused, with a Glasgow Coma Score of 13/15, hypotensive at 91/62 mmHg, tachycardic at 100 beats per minute, and tachypneic at 27 breaths per minute, with pale conjunctiva and a temperature of 38.7°C. Pulmonaryexaminationrevealedrhonchi, and abdominal examinationrevealed a palpable spleen tip with minimal splenomegaly (15 cm liverspan) and tenderness in the colonicregionwithoutclearguarding or rigidity, with an appendectomyscar in the right iliacfossa. On rectal examination, the glovewascoveredwith mucus streakedwithblood.

The patient wasurgentlyhospitalized for an etiologicalworkup and appropriate management. The patient'slaboratoryworkuprevealedhypochromicmicrocyticanemiawith a hemoglobinlevel of 6 g/dL, moderateleukocytosis at 11,000/mm³, predominantlyneutrophils at 8,500/mm³, withmoderateeosinophilia at 620/mm³, and normal lymphocytes at 1,580/mm³ withmildthrombocytosis at 480,000/mm³. Coagulation tests were normal. The inflammatoryworkupshowed an elevated C-reactiveprotein (CRP) at 98 mg/L, withfibrinogen at 5.6 g/L. Procalcitoninwasnegative at 0.11 ng/L. The electrolyte panel showedhyponatremia at 124 mmol/L and hypokalemia at 2.8 mmol/L. Ferritinwasseverelydepleted at 3 µg/L, total proteinwasdecreased at 57 g/L, and hypoalbuminemiawasnoted at 23 g/L, withfastingblood glucose at 0.58 g/L and triglycerides at 0.28 g/L.

The patient thuspresentedwiththree major problems:

- **Severedehydration and malnutrition with probable malabsorption.**
- **A probable digestive and/or urinary infection, given the fever, digestive, and urinarysymptoms, potentially due to an intracellularbacterium, virus, or parasite (given the eosinophilia); a combination of the threeisalso possible.**
- **An immunosuppressive condition thatcouldexplain the recurrent infections as well as the profounddeterioration in the general state, such as an acquired or**

primaryimmunodeficiency, a chronicinflammatory or autoimmunedisease, an underlyingneoplastic condition, or a metabolicdisorder like cysticfibrosis.

Our prioritywas to rehydrate the patient and correct the electrolytedisturbances, alongsideantibiotictherapywithintravenousmetronidazole 500 mg three times a day. The patient underwent a QuantiFERON test, which came back negative, and a urine cytobacteriologicalexaminationrevealedleukocyturia at 130,000/mL and hematuria at 24,000/mLwithout acanthocytes, withcysticprotozoapresent in the culture. Fecalcalprotectinwasstrongly positive at 180 µg/g of stool, and the stool culture wassterile, whilethreeparasitologicalstoolexaminationsisolatedciliatedprotozoameasuringbetween 80 and 120 µm, suggesting*Balantidium coli*. Giventhisunusualfinding in ourcontext, PCR confirmation wasperformed on urine and stool, which came back positive.

Since*Balantidium coli*israrelypathogenic in humans and isthusconsidered an opportunisticpathogen, an underlying immunosuppressive condition wasinvestigated. HIV 1 and 2 serologywasperformed and wasnegative, whichwasexpectedsince an opportunistic infection wouldoccur at stages B or C (AIDS), and the patient did not presentwithlymphopenia. Cysticfibrosiswasinvestigated due to the earlyonset of recurrentrespiratory and digestive infections, with sweat chloridetestingcoming back normal at 32 mmol/L, and the search for the CFTR gene mutation wasnegative. InflammatoryBowelDisease (IBD) wasconsidered, although the patient had no erythemanodosum, oral or nasal mucosalulcerations, anal fissures, or arthralgias; ANCA and ASCA testingwasnegative, the enteroscannershowed no abnormalities, upper gastrointestinal endoscopyrevealed non-specific antrum-fundus gastritiswith*Helicobacter pylori* positive withoutulcerations or signs of malignancy, whilerectosigmoidoscopywasunremarkable, and total ileocolonoscopywas normal. The histopathologicalstudy of biopsies revealedchronicinterstitialileitis in acute vasculo-exudativeflarewithoutspecificity or malignancysigns, and non-specificinterstitialcolitiswithoutmalignancysigns. The uroscanwasalsounremarkable.

The possibility of primaryimmunodeficiencywasthenconsidered. Serumproteinelectrophoresisrevealedhypoalbuminemia at 23 g/L and profoundhypogammaglobulinemia at 2.4 g/L. Lymphocyte immunophenotypingshowed no abnormalities, and 24-hour proteinuriawasnegative at 0.11 g/24h. Quantitative measurements of immunoglobulinsrevealedseverelyreduced IgG at 1.86 g/L and IgA at 0.34 g/L, while IgM levelswere normal. The diagnosis of Common Variable Immunodeficiency (CVID) wasthereforeestablishedaccording to revised international (PAGID) criteriain 2016[15]. The patient wasplaced on therapeutichumanimmunoglobulin infusion at 0.8 g/kg during the first course, followed by 0.4/kg/month. For her*Balantidium coli* infection, shewastreatedwith doxycycline 400 mg/day on the first day, then 200 mg/day for 21 days, with good clinical and biologicalimprovement.

Discussion:

Our clinical case presentsseveralatypicalfeaturesthat are worthhighlighting. *Balantidium coli*is a large protozoan parasite, approximately 150 µm in size, commonlyfound in tropical regions, withhigherprevalence in Asia. The typicalreservoirispigs, but it can alsobefound in otherspeciessuch as dogs, cats, rats, hyenas, and monkeys [1-4]. Humans are an accidental

host, with transmission occurringeitherdirectlythrough ingestion of the parasite cyst or indirectlythroughconsumption of contaminatedfood or water [1]. The individualsmostfrequentlyaffected are pigfarmers and those in close contact withthem, as demonstrated in a studyconducted in Ghana [5].

This brings us to the first atypical aspect in the Moroccancontext: this parasite is not known to bepresenthere, and we do not have pigfarmingwhere the parasite iscommonlyfound [6-7]. Uponfurther investigation, wediscoveredthat the patient came from the Sekhirateregion, residing in a small village without running water, whichisknown for the presence of wildboarsthatcouldpotentially carry the parasite. A review of the literaturealsorevealedthatcattle can beaffected, as shown in a study on a species of buffalo in Thailand [8], as well as ostriches [4] and camels [9]. This suggests the need for an epidemiological investigation to conduct large-scale screening in variouscattle and camelfarms, screening of wildboar populations, and exploration of the groundwater for possible contamination.

It is important to note thatdifferent direct examination techniques can beused to detect*Balantidium coli*, with the best beingLugol's iodine staining [10]. However, direct examination has limitations, whichiswhy PCR has demonstratedgreateraccuracy [1, 11].

The second atypical aspectis the presence of the protozoan in the patient's urine. *Balantidium coli*isgenerallyasymptomatic or evenharmless to humans, but it can becomepathogenic in immunocompromised patients, whereittypically causes digestive symptoms, primarilycolitis [1-12]. However, in our patient, the parasite was not onlyfound in the urine but alsoshowedsignificantclinical and biological impact. This prompted us to search for similar cases in the literature, wherewefoundtwo reports: the first involving a pregnantwoman in Ethiopia [13], and the second in an Iranian patient withbladder cancer [14]. Notably, all three cases involvedwomen, eventhough the carriage of *Balantidium coli* shows a slight male predominanceaccording to the Ghana study [5]. It appearsthaturinarylocalizationis more common in females.

The thirdatypical aspectis the latediagnosis of Common Variable Immunodeficiency (CVID), whichis the mostcommonprimaryimmunodeficiencydisorder. This condition is more familiar to pediatricianssinceitisgenerallydiagnosedbefore the age of four [3]. This delay in diagnosis can beattributed to the limitedaccess to healthcare, due in part to the significantshortage of doctors in Morocco, as well as the lack of awareness about CVID amonggeneralpractitioners, highlighting the need for specialized training.

Conclusion:

*Balantidium coli*is a protozoan parasite,primarilyhosted by pigs. Humans serve as an accidental host. This parasite israrelypathogenic in humans, requiring an immunosuppressive condition to becomeharmful, which classifies it as an opportunisticpathogen. Whenpathogenic, *Balantidium coli*typically causes colitis but can also have urological manifestations. The key takeawayisalways to consider an underlying immunosuppressive condition, whetherprimary or acquired, as thisparasitosismaybe indicative of such a state.

Disclaimer (Artificial intelligence)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

References:

[1]- Microbiology of WaterborneDiseases (Second Edition), Microbiological Aspects and Risks 2014, Pages 277-286, Microbiology of WaterborneDiseases, ChapterFifteen - Balantidium coli, Rachel M. Chalmers, Head of Cryptosporidium Reference Unit, Public Health Wales, Singleton Hospital, Swansea, UK, https://doi.org/10.1016/B978-0-12-415846-7.00015-9

[2]-Balantidiasis, Updated: Aug 25, 2023, Author: Subhash Chandra Parija, MD, MBBS, PhD, DSc, FRCPath; Chief Editor: PranatharthiHaranChandrasekar, MBBS, MD, https://emedicine.medscape.com/article/213077-overview?form=fpf

[3]- Revue Francophone des Laboratoires Volume 2023, Issue 549, February 2023, Pages 38-46, Les déficits immunitaires communs variables : définition, physiopathologie et diagnostic biologiqueCommon variable immunodeficiency, definition, frequency and diagnosis Emma Chambery a, Marie-Nathalie Kolopp-Sarda a b, Christophe Malcus c, https://doi.org/10.1016/S1773-035X(23)00025-4

[4]- Source: National Center for Emerging and ZoonoticInfectiousDiseases (NCEZID), Division of ParasiticDiseases and Malaria, Last Reviewed: June 6, 2019, https://www.cdc.gov/dpdx/balantidiasis/index.html

[5]- Aninagyei et al. BMC Infect Dis (2021) 21:1047, RESEARCH ARTICLE Prevalence and riskfactors of humanBalantidium coli infection and its association withhaematological and biochemicalparameters in Ga West Municipality, Ghana Enoch Aninagyei1* , Salifu Nanga2, Desmond Omane Acheampong3, Rita Mensah4, Mercy Nelly Boadu5, HenriettaTerko Kwansa□Bentum1 and ClementOkraku Tettey1, https://doi.org/10.1186/s12879-021-06731-2

[6]-Veterinary World, EISSN: 2231-0916 Available at www.veterinaryworld.org/Vol.14/April-2021/33.pdf RESEARCH ARTICLE Open Access Prevalence of Balantidium coli (Malmsten, 1857) infection in swinereared in South Italy: A widespreadneglectedzoonosis Filippo Giarratana1 , Luca Nalbone1 , Ettore Napoli1 , Vincenzo Lanzo2 and Antonio Panebianco1 1. Department of Veterinary Science, University of Messina, Polo Universitariodell'Annunziata, 98168 Messina, Italy; 2. Freelance Veterinary Professional, 89024 Polistena (RC), Italy. Correspondingauthor: Luca Nalbone,

[7]- Pathogens Article Prevalence of Swine Gastrointestinal Parasites in Two Free-Range FarmsfromNord-WestRegion of Romania Mihai-HoriaBăie¸s 1 , ZsoltBoros 1 , Călin Mircea

Gherman 1,* , Marina Spînu 2 , Attila Mathe 3 , Stefan Pataky 3 , MenelaosLefkaditis 4 and Vasile Cozma 1,5 1 Department of Parasitology and ParasiticDiseases, Faculty of VeterinaryMedicine, University of Agricultural Sciences and VeterinaryMedicine of Cluj-Napoca, Mănă¸stur Street 3-5, 400372 Cluj-Napoca, Romania 2 Department of InfectiousDiseases, Faculty of VeterinaryMedicine, University of Agricultural Sciences and VeterinaryMedicine of Cluj-Napoca, Mănă¸stur Street 3-5, 400372 Cluj-Napoca, Romania 3 Agricultural Research and Development Station of Turda, Agriculturii Street 27, 401100 Turda, Romania 4 Laboratory of Microbiology and Parasitology, Department of VeterinaryMedicine, School of Health Sciences, University of Thessaly, 43100 Karditsa, Greece 5 Academy of Agricultural and Forestry Sciences Gheorghe Ionescu-Sise¸sti (A.S.A.S.), Mărăs,ti Boulevard 61, 011464 Bucharest, Romania, https://doi.org/10.3390/pathogens11090954

[8]-Veterinary World, EISSN: 2231-0916 Available at www.veterinaryworld.org/Vol.13/August-2020/8.pdf RESEARCH ARTICLE Open Access Gastrointestinal parasite infections in fighting bulls in South ThailandDomechaiKaewnoi, RatchakulWiriyaprom, SaowakonIndoung and RuttayapornNgasamanFaculty of Veterinary Science, Prince of SongklaUniversity, Hatyai, Songkhla, Thailand. Correspondingauthor: RuttayapornNgasaman

[9]- Sazmand et al. Parasites Vectors (2019) 12:610 https://doi.org/10.1186/s13071-019-3863-3 REVIEW Zoonotic parasites of dromedarycamels: so important, soignoredAlireza Sazmand1* , Anja Joachim2 and Domenico Otranto1,3

[10]-Veterinary World, EISSN: 2231-0916 Available at www.veterinaryworld.org/Vol.14/April-2021/9.pdf RESEARCH ARTICLE Open Access Comparisonbetween five coprologicalmethods for the diagnosis of Balantidium coli cysts in fecalsamplesfrompigs Juan Carlos Pinilla1 , Andrea Isabel Pinilla2 and Angel Alberto Florez1 1. Department of VeterinaryMedicine, Faculty of Exact, Natural and Agricultural Sciences, University of Santander, Bucaramanga, Colombia; 2. Department of Microbiology, Faculty of Health, IndustrialUniversity of Santander, Bucaramanga, Colombia.

[11]- Identification of ZoonoticBalantioides coli in Pigs by Polymerase Chain Reaction-Restriction Fragment LengthPolymorphism (PCR-RFLP) and Its Distribution in Korea by Jae-Won Byun 1,Jung-Hyun Park 2,Bo-Youn Moon 1,Kichan Lee 1,Wan-Kyu Lee 2ORCID,Dongmi Kwak 3ORCID andSeung-Hun Lee 2,

[12]- Korean J Parasitol Vol. 58, No. 1: 47-49, February 2020 ⍰ CASE REPORT https://doi.org/10.3347/kjp.2020.58.1.47 •Received 11 December 2019, revised 6 February 2020, accepted 12 February 2020.) © 2020, Korean Society for Parasitology and Tropical Medicine This is an Open Access article distributedunder the terms of the Creative Commons Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0) whichpermitsunrestricted non-commercial use, distribution, and reproduction in any medium, provided the original workisproperlycited. DysenteryCaused by Balantidium coli in China Peixia Yu*, JianRongRong, Yan Zhang, Jingjing Du Department of ClinicalLaboratoryMedicine, Shanxi Bethune Hospital & Shanxi Academy of Medical Sciences, Taiyuan, 030009, Shanxi, PR China

[13]-Almaw A, Berhan A, Solomon Y, Malkamu B, Eyayu T, Workineh L, Mekete G, Yayehrad AT. Balantidium coli; Rare and AccidentalFinding in the Urine of PregnantWoman: Case Report. Int Med Case Rep J. 2022 Mar 22;15:105-109. doi: 10.2147/IMCRJ.S355536. PMID: 35345500; PMCID: PMC8957295.

[14]-DOI: 10.1002/ccr3.7494 CASE REPORT Uninvitedguest, Balantidium coli in urine in a patient withbladder cancer: A case report and review of the literatureFarnaz Farmani1 | Neda Soleimani1,2 | Mohammad Razeghi1 | Amir Zamani1 | Sahand Mohammadzadeh1,2 | Davoud Soleimani3

[15]-La Revue de Médecine Interne Volume 42, Issue 7, July 2021, Pages 465-472Les déficits immunitaires communs variables (DICV) : partie 1 : évolution des critères diagnostiques et des connaissances génétiquesCommon variable immunodeficiencydisorders: Updated diagnostic criteria and geneticsAuthor links open overlay panel C. Fieschi a b, J.-F. Viallard c d ; https://doi.org/10.1016/j.revmed.2021.03.328