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РЕЗЮМЕ

УСОВЕРШЕНСТВОВАНИЕ ЭТИОЛОГИЧЕСКОЙ ДИАГНОСТИКИ ЦЕРЕБРАЛЬНОГО ТОКСОПЛАЗМОЗА У ВИЧ-ИНФИЦИРОВАННЫХ ЛИЦ

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Целью работы явилось определение диагностической ценности параллельного определения в крови и спинномозговой жидкости индекса авидности иммуноглобулинов класса IgG к *Toxoplasma gondii* методом трехстадийного твердофазного иммуноферментного анализа с применением антигена *T. gondii*, белок-диссоциирующего агента и моноклональных антител против IgG человека у ВИЧ-инфицированных лиц с очаговым поражением головного мозга.

Результаты исследования показали, что проведение иммуноферментного анализа прямым и диссоциированным методами позволяет выявлять специфические интрацеллюлярные и сывороточные иммуноглобулины, что и предлагается в целях усовершенствования диагностики церебрального токсоплазмоза у ВИЧ-инфицированных лиц. Высокая информативная способность тест-системы для определения индекса авидности IgG антител к *T. gondii* определяет возможность ее использования в алгоритме диагностики этиологического фактора нейроинфекции у ВИЧ-инфицированных.

რეზიუმე

ცერებრალური ტოქსოპლაზმოზის ეთიოლოგიური დიაგნოსტიკის სრულყოფა აივ-ით ინფიცირებულ პირებში

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კვლევის მიზანს წარმოადგენდა სისხლში და ზურგის ტვინის სითხეში IgG კლასის იმუნოგლობულინების ავიდობის ინდექსის განსაზღვრა *Toxoplasma gondii* მიმართ სამსტადიური მყარფაზური იმუნოფერმენტული ანალიზის მეთოდის მეშვეობით ანტიგენ *T. gondii*-ის, ცილა დისოცირებელი აგენტის და ადამიანის IgG საწინააღმდეგო აგენტის გამოყენებით პაციენტებში აივ-ინფექციით და თავის ტვინის კეროვანი დაზიანებით.

კვლევის შედეგებმა აჩვენა, რომ იმუნოფერმენტული ანალიზი, ჩატარებული პირდაპირი და დისოცირებული მეთოდით, იძლევა სპეციფიკური, ინტერპრეტაციური იმუნოგლობულინების გამოვლენის შესაძლებლობას, რაც ემსახურება აივ-ით ინფიცირებულ პირებში ცერებრალური ტოქსოპლაზმოზის დიაგნოსტიკის სრულყოფას. *T. gondii*-ის მიმართ ანტისხეულების IgG ავიდობის ინდექსის განსაზღვრის ტესტ-სისტემის მაღალი ინფორმატიულობა უზრუნველყოფს აივ-ით ინფიცირებულ პირებში ნეიროინფექციის ეთიოლოგიური ფაქტორის დიაგნოსტიკაში მის გამოყენებას.

VISCERAL GNATHOSTOMIASIS WITH SIMULTANEOUS DAMAGE OF THE UPPER AND LOWER PARTS OF THE GASTROINTESTINAL TRACT

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Gnathostomiasis is a parasitic infection caused by the third stage of the larvae of *Gnathostoma* species nematodes, which are observed predominantly in tropical and subtropical countries. This food zoonosis is endemic in areas where raw freshwater fish and shellfish are consumed, especially in Thailand and Southeast Asia, Japan and Latin America (Mexico). Previously, the disease was rarely found outside the endemic regions, but during the last decades, the number of cases registered and observed in countries where it is not endemic has increased. The reasons for this are the distribution of tourism, the change in food habits, the violation of the technologies of cooking and marinating fish [1,2,3,4,9]. We report a unique case of visceral gnathostomiasis with simultaneous damage of the upper and lower parts of the gastrointestinal tract.

Case report. The patient, a 28-yr-old white female came to the Clinical of the National Medical University (Kyiv, Ukraine). She complained about the inability to eat solid food (she eats only liquid food "Fortisip"), feeling of heaviness in the abdomen

after each food intake, regurgitation, and heartburn, periodic nausea, and vomiting. She noticed on and off the loose stool.

According to the patient, her parents and the medical documentation the disease began 14 years ago (in 2003) 2 weeks after a trip to Thailand where she consumed raw freshwater fish as sushi. At that time, she complained of mild fever, spasmodic abdominal pain, lack of appetite, bloating, diarrhea. Acute enterocolitis was diagnosed, and she was treated symptomatically. In spite of this, she had only some improvement but she did not return for follow up visit. Several times per week she has experienced mild cramping abdominal pain that is followed by watery bowel movements since that time.

After two and half years (in 2006) she noticed migratory swellings under the skin around the chest and abdomen associated with edema and pruritus. The patient came to Emergency Room of the Moscow Clinic. The white blood cell count was 11,300 mm³ with a differential count of 60% PMNs, 20% lymphocytes, 3% monocytes, eosinophils 15%, basophils 1%. The

hemoglobin and hematocrit were 12.3 mg/dl and 37%, respectively, and the platelet count was 400,000. However, over the next 2 months of treatment with antihistamines and steroids, the patient continued to have these issues.

Six months later the patient had a segmental resection of the bowel due to bowel obstruction. The pathologist described eosinophilic infiltration of the mucosa and submucosa, neuropathy, and degeneration of sympathetic and sensory nerve fibers.

Since that time she did not visit any physician for follow up. In 2016, in addition to the previous symptoms the signs indicating pronounced gastroparesis were noted: constant regurgitation and vomiting, heartburn, eructation, heaviness in the abdomen after each food intake, inability to eat solid food. So the patient visited the Clinical of the National Medical University. Scintigraphy and radiological investigations showed severe gastroparesis, moderate gastroesophageal reflux, colon atony. The upper endoscopy and colonoscopy performed and biopsy showed larval worms of *Gnathostoma* in specimens from different parts of the gastrointestinal tract. Visceral gnathostomiasis was diagnosed, and it was treated with albendazole 400 mg twice daily for 21 days.

However, the patient went to Australia and did not return to follow up to our clinic and, unfortunately, the connection with her was lost.

Differential diagnosis. One of the rare causes of gastrointestinal damage associated with eosinophilic gastroenteritis and characterized by symptoms of abdominal pain, diarrhea, nausea and vomiting, weight loss and abdominal distension, malabsorption syndrome. The diagnostic criteria are eosinophilic infiltration of the wall of affected bowel with the mandatory exclusion of other causes of eosinophilic infiltration, such as parasites (helminths), medications, systemic connective tissue diseases [16]. Occasionally, the disease can be presented with obstruction of gastric outlet or even may manifest itself as an acute bowel obstruction, that can be the reason for surgical interventions.

Chronic intestinal pseudo-obstruction (CIPO) is a syndrome that develops as a result of changes in intestinal motility, which leads to clinical manifestations resembling intestinal obstruction, but in the absence of any mechanical obstructive process [13]. The causes of chronic intestinal pseudo-obstruction are primary lesions of intestinal muscle fibers (insufficiency of alpha-actin, family or sporadic visceral myopathy, autoimmune leiomyositis) or secondary (systemic lupus erythematosus, polymyositis, amyloidosis, progressive muscle dystrophy), some medications (neuroleptics) [12,13]. The neuropathic variant of CIPO can occur as a result of central nervous system diseases (Parkinson's disease, tumors, stroke, encephalitis) or disorders of peripheral nerve fibers which innervate different gastrointestinal segments (diabetic neuropathy, Hirschsprung's disease, Chagas disease, paraneoplastic syndrome, autoimmune diseases, amyloidosis). The rare causes of CIPO are mitochondrial diseases – the mesenchymopathic variant of CIPO (loss of interstitial cells of the Cajal). Among the infectious and helminthic causes of CIPO are neuroborreliosis [14], capillariasis [15].

Also according to current international clinical guidelines [10,11], the main causes of gastroparesis are diabetes mellitus, thyroid dysfunction, neurological diseases (for example, Parkinson's disease), previous stomach surgery and autoimmune diseases (most commonly systemic sclerosis). In some cases, gastroparesis may occur as a result of a viral infection, iatrogenically after the use of narcotic analgesics and anticholinergics. The rare causes of gastroparesis are amyloidosis, paraneoplastic diseases, damage to the muscular layer of the stomach, mesenteric ischemia.

The history of the disease and a set of laboratory and instrumental examinations which our patient have done over last 14 years, including the histological investigations, allow us to exclude the main and rare causes of gastroparesis described above. Regarding the administration of certain medications that could be the cause of the clinical picture, the abolition of these drugs for a long time did not lead to an improvement. Also, when managing patients with gastroparesis, it is recommended to exclude rumination syndrome, anorexia nervosa and bulimia [10]. The consultation of a psychiatrist and appropriate treatment excluded the possibility of a psychiatric origin of gastroparesis.

The diagnosis visceral gnathostomiasis was made by the history of the disease, the epidemiological history of trip to the endemic region, the consumption of raw freshwater fish, the causal relationship of the clinical manifestation of the disease after the tourist visit to Thailand, swellings under the skin, peripheral eosinophilia, positive biopsy investigations on *Gnathostoma*, the presence of eosinophilic infiltration of the intestinal mucosa and the degeneration of the sympathetic and sensory nerve fibers.

Humans are casual and atypical hosts of *Gnathostoma* spp, which does not support the reproductive cycle of helminth. After entering of the third stage larvae of *Gnathostoma* into the human stomach with infected fish, they penetrate through the wall of the stomach and migrate throughout the body, resulting in mechanical damage of human tissues and releasing of secretory proteins, including hyaluronidases, hemolysins, and metalloproteinases. Gnathostomiasis can be presented as four clinical varieties: (1) cutaneous form with intermittent migratory swellings; (2) a visceral form with a damage of the liver or the gastrointestinal tract; (3) neurognathostomiasis; (4) oculargnathostomiasis. Cutaneous form is the most common manifestation of larvae invasion [2,3]. Visceral form is the rarest variant [5-8]. Also, we did not find among the databases the cases of damaging of both upper and lower parts of the gastrointestinal tract with visceral and sensory neuropathy, as in this case described. Albendazole and ivermectin, which are prescribed at least for 21 days are used for the treatment of confirmed gnathostomiasis, but data on the long-term management of patients with chronic visceral gnathostomiasis, unfortunately, were not found [3,5,8].

Thus, we report the rare and atypical case of damaging of the gastrointestinal tract as a result of visceral gnathostomiasis. Visceral forms of this helminthiasis are detected and diagnosed extremely rare, therefore the management of such patients requires an individual and balanced approach since it is almost impossible to predict the consequences of any medical interventions.

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SUMMARY

VISCERAL GNATHOSTOMIASIS WITH SIMULTANEOUS DAMAGE OF THE UPPER AND LOWER PARTS OF THE GASTROINTESTINAL TRACT

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In this article, we described a rare atypical clinical case of tropical helminthiasis – a visceral gnathostomiasis with simultaneous damage of the upper and lower parts of the gastrointestinal tract. The visceral form is the rarest variant and among the literary data, only single cases of this form are described in the world. Therefore the management of such patients requires an individual and balanced approach since it is almost impossible to predict the consequences of any medical interventions. This determines the clinical uniqueness of this case and requires further research of clinical guidelines for the management of such injuries.

Keywords: gnathostomiasis, gastroparesis, chronic intestinal pseudo-obstruction.

РЕЗЮМЕ

КЛИНИЧЕСКИЙ СЛУЧАЙ ВИСЦЕРАЛЬНОГО ГНАТОСТОМОЗА С ОДНОВРЕМЕННЫМ ПОВРЕЖДЕНИЕМ ВЕРХНИХ И НИЖНИХ ЧАСТЕЙ ЖЕЛУДОЧНО-КИШЕЧНОГО ТРАКТА

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В статье описан редкий и атипичный клинический случай тропического гельминтоза – висцерального гнатостомоза с одновременным повреждением верхних и нижних частей желудочно-кишечного тракта. Висцеральная форма является самым редким вариантом. В литературных данных описаны только отдельные случаи этой формы гнатостомоза. Ведение таких пациентов требует индивидуального и сбалансированного подхода, поскольку практически невозможно предсказать последствия любых медицинских вмешательств. Это определяет клиническую уникальность этого случая и требует дальнейшего изучения и разработки соответствующих клинических руководств и рекомендаций.

რეზიუმე

ვისცერული გნატოსტომოზის კლინიკური შემთხვევა კუჭ-ნაწლავის ტრაქტის ზედა და ქვედა ნაწილების ერთდროული დაზიანებით

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¹ა. ბოგომოლცის სახ. ეროვნული სამედიცინო უნივერსიტეტი, შინაგანი მედიცინის კათედრა №1, კიევი, უკრაინა; ²სამედიცინო უნივერსიტეტი, სკოლა ყველა წმინდანის, ფარმაკოლოგიის კათედრა, როზო, დომინიკის თანამეგობრობა

სტატიაში აღწერილია ტროპიკული ჰელმინთოზის იშვიათი და ატიპიური შემთხვევა - ვისცერული გნატოსტომოზი კუჭ-ნაწლავის ტრაქტის ზედა და ქვედა ნაწილების ერთდროული დაზიანებით. ვისცერული ფორმა წარმოადგენს ყველაზე იშვიათ ვარიანტს, და მსოფლიო ლიტერატურაში გნატოსტომოზის ამ ფორმის მხოლოდ ცალკეული შემთხვევებია აღწერილი. ასეთი პაციენტების მართვა მოითხოვს ინდივიდუალურ და დაბალანსებულ მიდგომებს, რამდენადაც, პრაქტიკულად შეუძლებელია წინასწარ განისაზღვროს ამა თუ იმ სამედიცინო ჩარევის შედეგი, რაც მეტყველებს ამ შემთხვევის კლინიკურ უნიკალურობაზე და მოითხოვს შემდგომ შესწავლასა და განვითარებას შესაბამისი კლინიკური რეკომენდაციების გამომუშავებით.