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Amebiasis - E.Histolytica – A Catalyst Of The Beginning Of Tumor And Other Complications

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Abstract: ***In 2007 we drew attention to the fact that an increasing number of patients were seeking care in the The target organs of the lesion were uterus, liver, intestines, eyes, prostate, brain, heart, breast, and other organs. For the first time in the period from 2007 to 2009 we conducted a study of more than 1,250 patients in the region Akwa Ibom, Ikot Abasi and have found out that the main reason of the defeat was E.histolytica. (1, 2).***

In the period from 2009 to 2014 we continued to study amebiasis and have come to a series of conclusions. Amebiasis can not be asymptomatic without clinical manifestations.Trofozoit-erythrophage E.histolytica causes serious complications. It forms chronic, weakly flowing course of disease, leading to the depletion of the body which is the cause of the wide range of secondary diseases and represents a high risk to the health of patients. We examined the patients from different regions of the world: Nigeria, Cape Verde, Israel, South Africa, Senegal, Mozambique, Namibia, Russia, Ukraine, Portugal, the United States and other countries. We are convinced that doctors in different countries and regions do not understand or do not represent that along with dangerous infections as AIDS, malaria and schistosomiasis, amebiasis is the most hidden and poorly understood infectious disease which affects rapidly a large number of people without a certain incubation period. It causes a lot of complications which may occur in any period of patient's life.

I. INTRODUCTION

The protozoal infection remains a major cause of high morbidity of the population. It is well described by experts of different countries of the world and there are a great number of drugs for the treatment of this disease. (3)

We studied two protozoal diseases - malaria and amebiasis. Malaria is usually an acute infectious, well described process with not always clinically flowing picture. The methods of its diagnostics and treatment are well established. That is why we did the emphasis on the study of the epidemiology, clinic, diagnostics, treatment and prevention of amebiasis. The main cause of this disease is the penetration of E.histolytica cysts into the body. The aims of our research are to develop a simplified method of diagnostics of amebiasis, to work out the simplest methods of treatment until the full recovery of the patient and, certainly, the prevention of amebiasis. Moreover, the long-term consequences of the damage of the human body by cysts and by mobile trophozoites - erythrophage E.histolytica have not been studied yet. It is still believed that there is asymptomatic carrier morbidity of E.histolytica but our team of specialists does not support this opinion.

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II. EPIDEMIOLOGY OF AMEBIASIS

Epidemiology of infection by E.histolytica cysts, as a cause of the defeat of the human body was described by many authors. (10,11,12,13,14) The prolong existence of cysts in natural foci contributes to the rapid spread of amoebiasis around the world. In most African countries water is the main source of infection. In countries with hot humid climate such as Nigeria, Cameroon, Mozambique, amebiasis is widespread throughout the country. In hot and dry countries with open sources of water used by the local population, the largest number of patients with amebiasis is observed. (Libya, Cape Verde, South Africa). Eating of vegetables, fruits without heat treatment promotes the penetration of cysts into the intestine and the development of the disease. The serving staff of restaurants, shops, local market traders in most cases is the source of amebiasis infection. Patients with chronic form of amebiasis complicated by the lesions of uterus, prostate, lung, amebomas of intestine are a constant source of amebiasis infection. (15).

III. MATERIALS AND METHODS

Since March 2007 the investigation of the main causes of morbidity of the factory workers and the local population in the area of the plant, a state of Akwa Ibom, has been started in the Nigeria hospital of Aluminium Plant Alscon. We also conducted the constant surveillance of foreign experts. The patients from different regions of Nigeria and from other parts of Africa such as Cape Verde, Senegal, South Africa, Mozambique, Libya, Zimbabwe, Angola, Cameroon and the patients from the ECOWAS countries were examined. Besides we conducted laboratory screening of residents of Tver (Russia) in a laboratory of the city Hospital N1. We examined patients of all ages, from 1 to 90 years. Patients from schools, kindergartens, shops, markets and patients of gynecological and surgical clinics, restaurant staff were included into our study. During the period from 2007 to the present time we examined 6520 patients from Central Africa, South of Africa (3020 males, 3500 females) and 450 persons from Russia (Tver, Russia). Most of them (5410 pers.) were examined for cyst carrier morbidity, although some of them had uncertain clinical manifestations of the disease.

IV. LABORATORY DIAGNOSTICS

The simplest form of diagnostics of amebiasis is microscopic analysis of feces. (5, 6, 7). In a container with two standard container spoons of stool we add 5 ml. of saline. After shaking one drop of medication is applied to a glass slide and is covered with a cover slip. The presence of mobile trophozoites is estimated and the number of cysts is counted. We investigated the presence of mobile trophozoites in fresh stool samples and after passing some hours or days. When the container is stored at room temperature, moving trophozoites can be found in stool for 3 days, in two weeks cysts are reduced in size and then disappear. The conclusion on the extent of the body damage is made according to the presence of living trophozoites and the amount of cysts in the 10 fields of view.

The presence of 1 to 10 cysts is denoted by one plus (+), the presence of 10 to 30 cysts - by two pluses (++) and 30 or more cysts - by three pluses (+++). But this is not a criterion for assessing of the severity of the disease. Only on the basis of clinical and other research methods one can judge about the state of health of the patient affected with E.histolytica. (8) If E.histolytica cysts in stool are detected in males of the genital age it is recommended to examine the urine and sperm on the presence of E.histolytica cysts. It is also recommended to study the samples microscopically after the prostate massage, no less than in the 10 fields of view, without the saline dilution. The count of cysts is carried out in the same manner as in case of stool analyses. Females, especially with gynecological problems, are required thrice microscopy of the smears from the walls of the vagina and cervix for the presence of cysts and mobile trophozoites of E.histolytica.

V. ADDITIONAL METHODS OF RESEARCH

The complete blood analysis was carried out in all patients if E.histolytica was observed in their stool. In patients with a clinical picture of anemia, multiple uterine fibroma and hemorrhoidal hemorrhages the values of red blood (hemoglobin, erythrocytes) were significantly reduced.

The gastroscopic and colonoscopic investigations were conducted if they were indicated. In most cases, the mucous of rectum and sigmoid were injured by multiple, deep and bleeding ulcers with purulent contents. On colonoscopy in the dome of the cecum one can see the submucosal, yellowish, multiple, grainy formations in size from 0.5 cm to 3 cm. resembling caviar. In different parts of the colon one can detect single amebic polyps. In case of the prolonged and incorrect treatment of amebiasis the commissure are formed and the obstruction of the affected area may occur in future. Histological examination and removal of polyps are recommended. (16) On histological examination it is necessary to differentiate malignant adenocarcinoma from adenocarcinoma with chronic current amebiasis caused by E.histolytica. It is necessary to investigate the biopsy specimens for the presence of cysts and trophozoites of E. histolytica. At present the importance of social screening colonoscopy and polypectomy is recognized, because colorectal cancer ranks the third place in cancer morbidity and mortality in the world. The patients with intraepithelial neoplasia and highly differentiate intramucous carcinoma have favorable prognosis in case of removal of the polyp in time and subsequently annual monitoring of the large intestine. (V.I. Nikishaev, A.R.Paty. I.N.Tumak, I.A.Kolyada). At present we believe that the damage of the colon by E.histolytica cysts and trophozoites is one of the main triggers of amebomes, precancerous adenocarcinomas of the intestine and other organs infected by live trophozoites-erythrophage E.histolytica such as uterus, prostate, organs of sight, mammary glands, all organs with the smooth muscular fibers.

Ultrasonic investigation and echocardiography are indicated to all patients with amebiasis. Ultrasonic examination of the uterus and the prostate should be

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conducted for all patients of the childbearing age. Mammography is recommended for women to detect amebome of the mammary glands.

VI. PATHOLOGY-ANATOMY STUDY OF AMEBOME OF UTERUS

The post-mortem study of remote amebome of the uterus was conducted in 31 patients. Histological picture of fibromas has the same microscopic picture. (15, 16, 17, 18)

The tumor is composed of the smooth muscular fibers intertwined in different directions. The nuclei of muscular cells have rod-shaped form with rounded ends. Stroma is fibrous as the narrow layers. In some places the layers of fibrous tissue are wider, hyalinized. There are large foci of fibrosis and hyalinosis, large thick-walled vessels, foci of necrosis of tumor tissue, some cysts without epithelial lining. A similar picture is observed in biptatach obtained from the remoted amebome of the prostate. (20, 21)

We consider erroneous the opinion that the movable trophozoite-erythrophage E.histolytica migrates into the body through the blood flow for two reasons. Both malaria and E.histolytica relates to a class of protozoal infections. Clinically, the release of the malaria plasmodium into the blood is accompanied by a number of clinical symptoms one of which is a high temperature caused by the reaction of body to foreign proteins. It does not happen in the case of amebiasis. In most cases the damage of the body by E.histolytica takes place without temperature syndrome. After study of the anatomy structure of the smooth muscle fibers we came to the conclusion that the trophozoite-erythrophage advanced to full-plethoric target organs in the interstitial space of smooth muscular fibers of the vessels. Electron microscopic studies have shown that there is no membrane and protoplasmic continuity between individual fibers of the muscular syncytium. They are separated from each other by thin (200-500 Å) slits. Without causing septic reaction of the body to E.histolytica and reaching the target organ, Trophfozoit- erythrophage continues to move and causes mechanical, toxic damage of the smooth muscle cell. In contrast to the multi-core fibers of the skeletal muscles that can not be divided after the completion of differentiation, the smooth muscular fibers have only one nucleus and are able to divide throughout the whole life of the body. (22) The damage of the tissue by trophozoite-erythrophage triggers the abnormal division of the smooth muscles, changing the trajectory of the growth of the smooth muscular cells from longitudinal to sickle - ring, forming konglamerat-amebome,. It eventually begins to germinate by the large thick-walled deformed vessels and is gradually transformed from benign amebome into adenocarcinoma.

VII. TREATMENT OF AMEBIASIS AND ITS COMPLICATIONS

Tinidazole was the main drug indicated for the treatment of uncomplicated forms of amebiasis in patients aged from 7 to 90 years. One tablet contains 500 mg of Tinidazole. From one to four tablets per day were administered depending on the age and weight of the patient. It is recommended to take 4 tablets once a day after meal for 5-10 days. Children under 7 years are assigned 5 ml. of syrup-suspension of Metronidazole three times a day for 5-10 days depending on the clinical course of amebiasis. After 15 days of treatment the reanalysis of feces is assigned. If the cysts are detected again the second course of treatment is assigned until the complete recovery. It is necessary to control the level of yeasts in feces analyses, which increases after taking antiamebic drugs. The main representative of these yeasts is Candida Albicans. Fluconazole is antifungal drug and is also administered, 1 capsule (150 mg) once a day. The course of treatment is 5-10 days.

The disappearance of cysts in fecal specimens is not considered as the full recovery of the patient. The patient is assigned quarterly examination of stool for a year and then the subsequent examination of feces every six months of life.

The treatment of complicated amebiasis is well described in the medical literature. The clinical picture of amebiasis must be primarily differentiated from other acute abdominal pathologies (ulcerative colitis, Crohn's disease). Differentiated diagnostics of the pain in the right iliac region in amoebiasis and appendicitis is based on the analysis of feces only. Detection of trophozoites and cysts in the stool of the patient is a contraindication to surgery. Surgery is recommended in case of massive hemorrhage or peritonitis only. The treatment of amoebic abscesses of the liver, lungs and brain are usually carried out surgically. (9) Single and multiple amebomes of the uterus, prostate, breast and bowel polyps require mandatory surgical treatment to prevent degeneration of the benign process into malignant.

Amoebiasis of the skin is treated by the local treatment of the affected area by 5% iodine solution until complete recovery, with the obligatory antiamebic course of treatment.

Amebic damage of the eyeball is treated surgically and the repeated course of anti-relapse treatment by Tinidazole is indicated.

If amebome is detected in any organ of the patient the surgical operation is necessary in order to save the physiological functions of the organ.

VIII. RESULTS

It was noticed that among 6520 examined inhabitants of Africa there were no E. histolytica cysts or their living forms in feces of 1450 persons (22.3%) only. Among the inhabitants of Tver the number of such individuals was significantly greater, there were 330 patients out of 450 examined which accounted for 73.4% ($p < 0,01$). The obtained data on the one hand support the general statement that amoebiasis is more common in the countries with hot climate. However, on the other hand the overall incidence of identification of amebiasis is much higher than that indicated in literature (1), it is about 10%. It turned out that in general E. histolytica infestation of the population living in a temperate climate is rather high. Indeed, cysts or trophozoites were found in feces of 26.6% examined residents.

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All examined individuals (5190 patients) in feces of which cysts and trophozoites have been found could be divided into 2 groups. The first group included 4022 patients, who had cysts in their feces only, i.e. they were cyst carriers. On the whole it was available in 57.7% regardless the place they lived. Most of them had not any complaints.

It turned out that the incidence of cyst carrier morbidity was different and depended on the place the patients lived. Thus, among 98 examined residents of Tver (Russia) the cyst carrier morbidity corresponding to one + was in 70 examined residents (71.5%), corresponding to ++ - in 20 examined residents (20.4%) and corresponding to +++ - in 8 examined persons (8.2%). The different picture was available in 3924 inhabitants of Africa. On this continent cyst carrier morbidity corresponding to + was detected in 1350 (34.4%); ++ in 1525 (38.9%) and +++ in 1049 (26.8%). The presented data clearly show that among the inhabitants of Africa cyst carrier morbidity occurs rather often with the dominance of the high degree of contamination of feces.

Among 4022 cyst carriers the case-histories of 453 individuals were carefully studied and special attention was paid to any complaints during the last 6 months related mainly to the gastrointestinal tract: abdominal pain, lumbar area, diarrhea, with the presence of blood and mucus in the stool, malaise, and sometimes fever. Among these 453 investigated people only 233 (51.5%) were monitored during the last 6 months. It should be noted that only 163 (70%) of those 233 patients went to the doctor but amebiasis was not diagnosed and all were treated for bacillary dysentery.

A different situation was observed in examined individuals in whose feces trophozoites have been found. Nobody of 22 residents of the city Tver felt themselves completely healthy. In most cases, they had general, uncertain complaints: malaise, weight loss, disability, poor appetite, decreased interest to environmental life, etc. And only 8 examined patients had more specific complaints: abdominal pains in the ileocecal region, sometimes unstable stool with mucus and blood. These data provided the basis for the differential diagnosis between bacterial dysentery and amebic colitis (amebic dysentery). The survey allowed in all cases to put the diagnosis last mentioned. The application of Tinidazole (2 g once a day) for 5 days in all cases gave excellent results.

The situation in Africa was as follows. From 1139 surveyed patients with trophozoites in feces 450 individuals (39.5%) had not any complaints and they considered themselves healthy. 386 observed persons (33.9%) had indefinite nature of the complaints, but no pathology was found. However, it should be noted that among these individuals there was quite common unexplained loss of weight sometimes to exhaustion (73; 19.0%). In 303 persons (26.6%) there was a fairly clear objective pathology, which in the most cases corresponds to the certain nosology: amebic colitis was diagnosed in 206 patients (68.0%), liver abscess - in 26, dermal damages of hands and legs like resistant erythema and pruritus - in 15 (5.0%), ameboma uterus - in 6 (2.0%), different eye diseases – in 4 (1.4%), prostatitis – in 7 (2.4%), brain abscess – in 1 (0.4%). In 38 observed patients (12.6%) amebiasis was diagnosed in combination with other infectious disease (AIDS, malaria, filariasis, ascoridosis, strongyloidosis, syphilis, tuberculosis, etc.). It changes the clinical picture of amebiasis, and made it difficult to diagnose. However, there is no doubt that the combination of amebiasis with other infectious (parasitic) pathology impaired the general condition of the patient and made it difficult to treat. Specific treatment in all cases gave a positive effect.

As a result of the conducted research the methodology of the most economical diagnostics of amebiasis in the developing countries with highly informative and simplified monitoring of morbidity in any region of the world was worked out. A formula of the cyst counting on microscopic examination in the10 fields of view was recommended. The problem of benign tumors of various organs of uterus, prostate, breast, eye, polyps of intestine with their transformation in carcinoma was studied. The most economical way of amebiasis treatment with the drug Tinidazole was developed. It was recommended the regimen of treatment and the medicinal prevention of damages of the body caused by Candida Albicans as a result of antiprotozoal therapy of amebiasis.

IX. CONCLUSIONS

Conclusions made by the authors as a result of clinical investigations and studies of the scientific literature, once again prove that the defeat of the human body by E.histolytica cysts can not be called amebiasis “carrier morbidity". The defeat of the body by E.histolytica leads to the disease with a different symptomatic picture, with the defeat of organs and tissues where there are the smooth muscular fibers. Persistence of trophozoite - erythrophage in the body leads to a number of serious complications such as anemia, abscess formation, the formation of amebomes in multiple target organs of the uterus, prostate, breast, eyeball, skin, single and multiple polyps of the colon with a tendency to degeneration in cancer, heart failure, impaired fertility and deep vascular lesions. The tissue damage by trophozoite-erythrophage launches pathological division of smooth musculature by changing the growth trajectory of the longitudinal smooth muscular cells in sickle - ring, forming conglomerate-amebome, which eventually begins to grow with large, deformed, thick-walled vessels and gradually degenerates from benign ameboma in adenocarcinoma.

On the base of the clinical observations and the study of literature data, we came to the conclusions about the possible ways of passage of trophozoite-erythrophage in the intercellular space of smooth musculature of the target organs, without clinical manifestations in patients. It is necessary to continue the study of the process of the spread of trophozoite-erythrophage in the human body by means of post-mortem - histological examination of biopsy samples from the target organs, having the smooth muscular fibers. The obligatory surgical treatment of amebomes of uterus, prostate, breast and intestinal polyps should be performed. In the case of ulcerative lesions of the sigmoid and rectum the conservative treatment should be primarily recommended until the complete disappearance of trophozoites- erythrophages and cysts in the analyses of fecal specimens, and scrapings from the affected

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surfaces. Surgical treatment is recommended if it is indicated in cases of bleeding, perforation, fistula formation.

Simple diagnostics and monitoring of the effective treatment of patients, led to conclusions- recommendations for the control of amebiasis in patients of all ages and pregnant women. It does not depend on the country they live in: Africa, Europe, Asia and other countries. During the year, it is necessary to investigate the stool thrice in 6 months in order to identify and to cure E.histolytica to the complete disappearance of cysts from the body.

Based on this work, we can conclude that the Entamoeba histolytica is today a real danger to the health and lives of our people. It causes a number of serious poorly differentiated complications which lead to misdiagnoses and thus incorrect treatment especially in such branches of medicine as gynecology, urology, oncology, gastroenterology, neurology and many others.

We would like to recommend doctors of all medical institutions in the world to pay attention to this kind of pathology, and during routine medical check-ups to pay more careful attention to the condition of the gastrointestinal tract of the patients. The heads of maternity hospitals and antenatal clinics are recommended to conduct more thorough medical examinations of women.

Epidemiologists need to develop a number of international programs against Entamoeba histolytica. It is necessary for military doctors to study carefully epidemiology, clinic and pathogenesis of the disease, because Entamoeba histolytica can be used as a biological weapon, leading to the female and probably male infertility, and a large number of unexplored consequences of the lesions caused by this type of protozoal infection. It is also recommended to explore and to develop the methods of disinfection of water and food processing, to search new medicines and disinfectants. A mass propaganda campaign against Entamoeba histolytica should be organized on the level of WHO.

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