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CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF NEUROBRUCELLOSIS ACCORDING TO THE INFORMATION OF SAMARKAND MUNICIPAL INFECTIOUS DISEASES HOSPITAL

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Brucellosis is a particularly dangerous and socially significant infection that causes considerable economic damage and leads to a high level of patients' disability (Vershilova P. A., 1961, Beklemishev N. D., 1965).

Brucellosis is a global problem for medical and veterinary health services (Corbel M. J., 1997, Boschiroli M. L., 2001).

According to the information of WHO Joint Expert Committee on Brucellosis (1986), this disease is registered among animals in 155 countries around the world.

Mostly Brucellosis is spread in the Mediterranean countries, Asia Minor, South and South-East Asia, Africa, Central and South America (Sauret I. M. E., 2002; Ergonul O. E. A., 2004; Karabay O. E. A., 2004; Getinkaua Z. E. A., 2005; Alim A., Tomul Z. D., 2005; Onishchenko G. G., 2005)

These indices are ten times higher in countries of Central Asia. The registered cases of this disease here are compounded 116 cases per 1 million people in Kazakhstan and 362 in Kyrgyzstan. In Uzbekistan, there are 18 cases per 1 million people. In the Russian Federation there are 4.1 cases per 1 million people, Greece – 21 cases, Germany and the United Kingdom – 0.3 cases.

Key words: neurobrucellosis; neuritis; plexitis.

Chronic brucellosis is rather widespread infectious autoimmune disease. Nowadays the problem of brucellosis is considered as quite actual for the countries with the developed cattle-breeding sector in the agriculture. 80 % of cases the acute brucellosis become chronic and 35 % of the patients become disable. Mostly there fall ill with this disease young employable people, that cause damage to social and economic sphere and in its turn it presents another actual aspect of this problem. On the basis of pathogenesis of the chronic brucellosis underlie intracellular parasitizing of brucellas with anti-lysozyme activity.

Analyzing literature information of Russian scientists about the chronic brucellosis for the last 20 years, we haven't found any reference about neurobrucellosis.

Neurobrucellosis – zoonotic infection disease caused by gram-negative bacterium of Brucella family and characterized by affection of all areas of nervous system: central, peripheral and vegetative.

Actuality of the problem of neurobrucellosis is defined with such peculiarities as clinical presentation changes of the modern brucellosis, differing from the uncertainty of symptoms. All this requires the searching of modern methods of investigation which let diagnose neurobrucellosis promptly and spend appropriate therapy, which considerably will improve the patient's life quality and let continue their workability.

Based on different scientists' opinions, Neurobrucellosis is observed in 5–10 % patients (Yetkin M. A., 2006) and it is considered as rare, but serious complication of this infection. According to classification neurobrucellosis is divided into areas which it can affect: CNS lesion (meningitis, encephalitis, myelitis, vasculitis of cerebrum vessels, vertebral and basilar insufficiency, hypertensial, diencephalic hypothalamic syndromes and etc.), PNS (neuritis, radiculitis, plexitis, solar plexitis, radicular syndrome and etc.), ANS (vasoneurosis, atmospheric sensitivity, microcirculation disturbance, intestine atony and etc.) and psychobrucellosis (asthenoneurotic syndrome, depressive syndrome, hallucinosis and etc.)

Clinical picture may remind acute meningitis, encephalomeningitis, and in some cases – paresis or dysfunction of cerebral nerve. Damage of big peripheral nerve tube may cause a strong neuralgia.

Objective of investigation: to give characteristic of clinical and epidemiological manifestations of patients with chronic brucellosis with nerve system lesion.

Materials and methods

It was conducted retrospective analyses of epidemiological situation on the brucellosis in Samarkand region on the basis of official statistical information of incidence of brucellosis in Samarkand city for the period from 2008 to 2018 years.

From patients with diagnosis of chronic brucellosis which had been hospitalized in RCIH (Regional Clinical Infection Hospital) for the period from January of 2018 to February 2018 year, there were selected 54 patients with nerve system lesion. To diagnose brucellosis there was used the clinical classification by K. Djalilov (1987).

For verifying brucellosis there was used Write's tests (as positive there was accounted titre 1:150) and Hedelson's (positive and distinctly positive result).

Clinical examination of patients included thorough collection of anamnesis, including epidemiological.

Examination included complete blood count with leucoformula, bacteriological blood inoculation, in case of need there was conducted CT and neuropathologist's consultation.

Examination Results

During analyzing perennial dynamics (from 2008 to 2018) of patients' incidence there was determined that the highest level of incidence was observed in Nurabad,

Khushrabad and Bulungur districts. Present comparative analysis of examined patients with brucellosis has shown evident tendency to increasing of brucellosis incidence in the territory of such districts as Nurabad, Khushrabad, Bulungur, Urgut and Pastdargom.

During investigation of the absolute rate of incidence in Samarkand region for all period there was revealed that the peak of incidence fell in 2018 year, what corresponds to 13.8 % of cases, besides the lowest rate 5.5 % was observed in 2008. Thus it was revealed that from 2009 there had been observed an increase of brucellosis incidence (in 2009-6.9 %), then a certain fall of this rate to 6.6 % of cases (2010) and then again considerable increase to 13.8 % of cases in 2018 (Fig. 1).

Among the infection ways there dominates contact one (48.2 %), alimentary way of contagion is composed 33.7 %, and in 18.1 % of patients the infection way hasn't been identified.

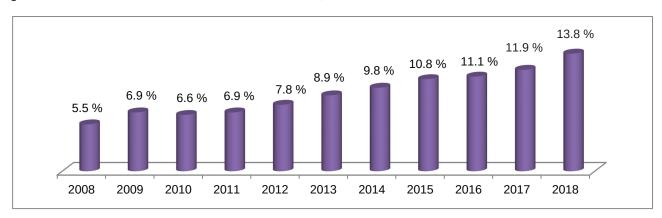


Figure 1. Dynamics of Brucellosis incidence in Samarkand region for the period from 2008 to 2018.

It was revealed that increase of the brucellosis incidence begins from May, and decrease of the disease is observed from July, that is most probably connects with biological cycles of animals (lambing time, division) and spending principal agricultural works.

An age characteristic of patients with chronic form of brucellosis is presented in the Figure 2. Analysis of age structure of patients has shown predominant visit of employable people to doctor: till 14 years -4%, 14–17 years -7.7%, 20–25 years -17.7%, 25–35 years -21.2%, 35–40 years -22.3%, 40–50 years -11.3%, older 50 years -10.1%.

Majority of patients was males -58.3 %, another part of patients were females -41.7 % (Fig. 3).

Organs lesion of the patients with chronic brucellosis form was registered with different frequency, so the changes

of the cardiovascular system is 24 % of cases; locomotive system is observed in 60.2 % of cases, nerve system 13.2 %, urogenital system in 3.6 % cases. In some cases there are observed combined lesion of the organs and system.

Taking into consideration patients' complaints, clinical manifestations of nerve system lesion variate in considerable range from 2 % to 95 % and can be accompanied with such syndromes as CNS injury (meningitis, encephalitis) PNS (neuritis, radiculitis), ANS (vegetative vascular dystonia) and psychobrucellosis (asthenoneurotic syndrome, depressive syndrome, hallucinosis and etc.) (Table 1). Grave injury of nerve system is observed in 2–8 % cases (Zavalishin I. A.).

 $3.7\,\%$ of patients suffered from Meningitis of brucellosis etiology.

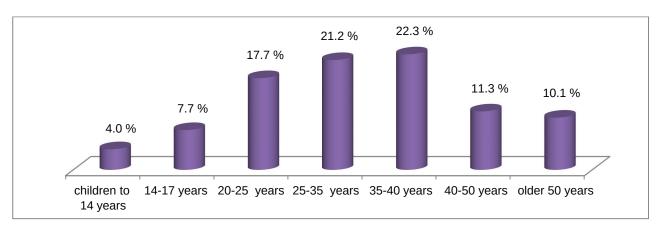


Figure 2. Age patients' distribution.

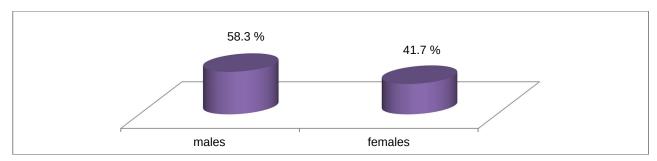


Figure 3. Gender patients' distribution.

Table 1
The main clinical manifestations in patients with neurobrucellosis

Nº	Clinical sign	Absolute	%
1	Meningitis	2	3.7
2	Encephalitis	1	1.8
3	Radiculitis	41	75.9
4	Polyradiculitis	11	20.3
5	Neuritis of facial nerve	23	42.5
6	Neuritis of vestibular-cochlear nerve	19	35.0
7	Neuritis of optic nerve	7	12.9
8	Malfunction of vegetative nerve system	51	94.4
9	Functional disorders of nerve system	28	51.8
10	Psychosis	6	11.1

Clinical syndrome of brucellosis meningitis: muscular rigidity of occiput, Kerninig and Brudzinskiy's symptoms, painful point on the face, head and neck, essentially through vessels, sometimes it is observed cranial nerves lesion (in the first place facial and auditory). In cerebral liquid there

was found pleocytosis, albumen increase, xanthochromia, not rarely it is observed decrease of blood sugar and cloride content, but substance of potassium, calcium, and inorganic phosphor usually increase.

Both early and late forms of brucellosis encephalitis are characterized by indispensable involvement of brain layers and characterized by cranial nerves, often there are involved auditory, facial and optic nerves, but it is described also concurrent defeat of oculomotor, with trigeminal, wandering and sublingual nerves. All forms of Brucellosis lesion of central nervous system is accompanied with polymorphism what confirms diffusivity of pathologic process. Meningoencephalitis clinically is manifested by paresis of extremities of spastic type and sensory abnormality of referred character. Meningo-encephalitis was detected in 1.8 % of patients.

Clinical presentation of Brucellosis radiculitis was detected in 75.9 % of patients and characterized by acute and badly localized pains in lumbosacral area which last for hours, days, or weeks.

Mostly pains are progressing gradually, increasing by degrees and almost all pains involve area of lumbosacral roots. It's very often observed allergic syndrome, with painful points. Usually objective sensory abnormalities aren't acute,

typical extended pain, in spite of their high intensity, they often haven't exact localization: patients try to find painful place themselves, but it doesn't turn out well, usually the patients tell that "it aches all extremity". It is characterized by volatility of pains.

Poliradiculitis was observed in 20.3 % patients; it wasn't always symmetrical and it didn't always involve all extremities. Polyradiculitis was preceded by rich vegetative symptomatology: cyanosis, fall of temperature, strength of hyperhidrosis of distal parts of limbs, sometimes was observed hydrops, arthropaty, which combined with lesion of vertebral, extremities' joints and etc.

Clinical symptomatology of neuritis of facial nerve in all examined patients is characterized by presence of smoothing of nasolabial fold, with drooping of eyelid and corner of the mouth, sensation of weak burning, tingling, weakness of facial muscles, disorder of taste, excessive saliva production. This symptom was observed in 42.5 % of cases.

Neuritis of vestibulocochlear nerve is often met (35 %) in patients with neurobrucellosis and was characterized by hearing loss, usually bilateral. Loss of hearing mostly is the only manifestation of chronic brucellosis after acute form.

According to different informative sources in half of patients with chronic brucellosis hearing loss is observed. So that neuritis of vestibulocochlear nerve – important diagnostic sign of chronic brucellosis.

Principal manifestation of optic nerve lesion – loss of vision (partial or total), or sudden appearance of erased or blurring vision, besides patients feel painful sense in defected eye (colors are seemed blurring in comparison with another eye). In many cases it only affects one eye, and patients may not aware about losing the colored vision, until the doctor asks them to close or cover healthy eye. According to informative sources describing brucellosis neuritis, it is proved that 92 % of patients feel the pain in the eye, which in a fact preceded visual lost of this eye in 39.5 % of cases.

Neuritis of optic nerve mostly affects young people at the age from 18 to 45 years, on an average females and there was registered 12.9 % of patients.

Lesion of vegetative nervous system is observed almost in all patients with brucellosis (94.4 %) and manifested acute

sweat or skin dryness, its peeling, atrophy, acrocyanosis, hair shedding, fragility of nails, pressure drop, weight loss, emaciation, osteoporosis, fibrosis of muscles and elasticity diminution.

During brucellosis it is rather often may observe functional disorders of nerve system and it was detected in 51.8 % of patients. Functional disorders of nerve system are met mainly in the initial stage of the disease and it is manifested in form of emotional instability, irritability, distraction, anorexia, insomnia with headache, asthenia, sluggishness, memory loss, apathy.

During brucellosis psychosis are described by many scientists. Mental disorder can be appeared in different phase of disease. In the present group of examined patients the psychosis were manifested in form of visual and ear hallucinations, delirium, euphoria, psychomotor stimulation and it was diagnosed in 11.1 % patients.

Conclusions

- 1. Taking into consideration existence of epizootic nidus of brucellosis neat cattle and small cattle, epidemic situation in Samarkand region is unstable. It is typical alternation of periods of disease increasing with peak in 2009, and decreasing to minimum in 2010. From 2011 in the region there was observed gradual increase of brucellosis disease, which has been continuing to actual time.
- Nerve system lesion can be manifested in different stages of disease and be the first clinical manifestation of brucellosis. Clinical presentation of brucellosis is characterized by multiformity of symptoms and remitting disease course. Mainly there fall ill people connecting with livestock farming, and people who don't use pasteurized milk, so that it is necessary to treat more careful to patients with neurologic manifestation, who live or have come from precinctive location on brucellosis, not to avoid missing diagnose: neurobrucellosis. Taking into account variety of clinical form, mechanisms, lying on basis those or other manifestations of neurobrucellosis, making up plan of treatment of the patient it is necessary to take into consideration the disease form, process stage, totality and character of nidus lesion, existence of concomitant pathology, allergy anamnesis, patient age - that is therapy must be severely differential, which would rise patient's life quality.

Literature

- 1. Earhart K. Risk factors for brucellosis in Samarqand Region, Uzbekistan / K. Earhart // International Journal of Infectious Diseases. $-2009.-Vol.\ 13,\ N\ 6.-P.\ 749-753.$
- 2. Желудков М.М. Состояние эпидемиологической ситуации по бруцеллезу в России / М.М. Желудков, А.Е. Цирельсон, О.С. Ходарцев // Материалы III Ежегодного Всероссийского Конгресса по инфекционным болезням (Москва, 28-30 марта 2011 г.). Инфекционные болезни. 2011. Т 9, приложение № 1. С. 129.
- 3. Абуова Г.Н. Состояние заболеваемости зоонозными инфекциями в Южно-Казахстанской области на современном этапе / Г.Н. Абуова, М.О. Карымсакова, Г.К. Насырова // Центрально-Азиатский научно-практический журнал по общественному здравоохранению. 2011. № 4. С. 36-40.
- 4. Акказиева Б.А. Страновое исследование по Таджикистану: Системы здравоохранения в отслеживании НИЗ. Характерные

- особенности системы здравоохранения в области НИЗ / Б.А. Акказиева // ВОЗ. – Душанбе, 2013. – С. 53.
- 5. Трудный пациент: энцефаломиелит бруцеллезной этиологии / Г.Н. Абуова, Ф.А. Бердалиева, Т.А. Кусеинов и др. // Южно-Казахстанская государственная фармацевтическая академия, ГИБ, ШГССМП, г. Шымкент, Казахстан. 2014.
- 6. Холмуратов У.К. Клинико-эпидемиологические аспекты течения бруцеллёза за последние годы по Самаркандской области / У.К. Холмуратов, Ш.А. Рустамова, Н.А. Ярмухаммедова // Вопросы науки и образования. 2019. 33(83).
- 7. Ярмухамедова Н.А. Функциональные изменения со стороны сердечно-сосудистой системы у больных с хроническими формами бруцеллёза / Н.А. Ярмухамедова, Н.С. Якубова, О.С. Тиркашев и др. // Достижения науки и образования. 2020. № 4(58).

References

- 1. Earhart, K. (2009). Risk factors for brucellosis in Samarqand Region, Uzbekistan. *International Journal of Infectious Diseases*, 6 (13), 749-753.
- 2. Zheludkov, M.M., Tsyrelson, A.E., & Khodartsev, O.S. (2011). State of epidemiology situation of brucellosis in Russia. *Materials of III of Annual All-russian Congress on infectious diseases (Moscow, March, 28-30, 2011). Infectious Diseases*, 1 (9), 129 [in Russian].
- 3. Abuova, H.N., Karymsakova, M.O., Nasyrova, H.K. (2011). State of morbidity zoonotic infections in the South-Kazakhstan area on the modern stage. *Centrally Asian Scientifically Practical Magazine on a Community Health Care*, 4, 36-40 [in Russian].
- 4. Akkaziyeva, B.A. (2013). Research on Tadjikistan: Systems of health protection in watching NIZ. Characteristic features of the system of health protection in area of NIZ. *WHO*, *Dushanbe* [in Russian].
- 5. Abuova, H.N., Berdaliyeva, F.A., Kuseunov, T.A., Muminov, A.K., Yavrov, M.Yu., & Onishchenko, E.M. (2014). Difficult patient: encephalomyelitis of brucellosis etiology. *South-Kazakhstan State Pharmaceutical Academy,* Shymkent, Kazakhstan [in Russian].
- 6. Kholmuratov, U.K., Rustamova, Sh.A., & Yarmukhammedova, N.A. (2019). Clinical and epidemiology aspects of brucellosis flow in the last few years on the Samarkand region. *Questions of Science and Education*, 33(83) [in Russian].
- 7. Yarmukhamedova, N.A., Yakubova, N.S., Tirkashev, O.S., Uzakova, G.Z., & Achilova, M.M. (2020). Functional changes from the side of the cardiovascular system for patients with the chronic forms of brucellosis. *Achievements of Science and Education*, 4 (58) [in Russian].

КЛІНІЧНІ ТА ЕПІДЕМІОЛОГІЧНІ АСПЕКТИ НЕЙРОБРУЦЕЛЬОЗУ ЗА ДАНИМИ САМАРКАНДСЬКОЇ МУНІЦИПАЛЬНОЇ ІНФЕКЦІЙНОЇ ЛІКАРНІ

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РЕЗЮМЕ. Бруцельоз є особливо небезпечною і соціально значущою інфекцією, яка завдає значного економічного збитку і призводить до високого рівня нездатності пацієнтів. Бруцельоз – загальна проблема для медицини і ветеринарії. Згідно з інформацією міжвідомчої експертної комісії з бруцельозу ВООЗ (1986), ця хвороба реєструється серед тварин у 155 країнах.

Здебільшого бруцельоз розповсюджений у Середземномор'ї, Малій Азії, Південній і Південно-Східній Азії, Африці, Центральній і Південній Америці. Рівень захворюваності в десятки разів вищий у країнах Центральної Азії і становить зокрема 116 випадків на 1 млн населення в Казахстані, 362 — у Киргизстані. 18 — в Узбекистані, 4,1 — у Російській Федерації, 21 — у Греції, 0,3 — у Німеччині та Великобританії.

Ключові слова: нейробруцельоз, неврит, плексит.

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