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CLINICAL ASPECTS, DIAGNOSIS, AND TREATMENT OF GOAT-
SHEEP TYPE BRUCELLOSIS IN THE GENERALIZATION
STAGE OF INFECTION WITH FOCAL LESIONS

By

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CLINICAL ASPECTS, DIAGNOSIS, AND TREATMENT OF GOAT-SHEEP
TYPE BRUCELLOSIS IN THE GENERALIZATION
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L. V. Yarovoy

The clinical features of brucellosis have still not been adequately elucidated in the literature as to pathogenic stages. The generalization stage with focal lesion is far from complete in most studies, as individual clinical forms of the disease, which to a considerable extent is explained by the difficulties in diagnosing its early clinical stages (K. V. Bunin, 1960). In the classification of the clinical forms of brucellosis, we adhere to the pathogenic scheme proposed by G. P. Rudnev (1955) and A. F. Bilibin (1947). Our first report (L. V. Yarovoy, 1961) was devoted to an analysis of the course of brucellosis during the generalization stage of the infection.

Under observation were 320 patients with brucellosis in the generalization stage with focal lesions (199 men, 121 women). Seven persons were 14 years old or younger, 306 were from 15 to 59, and 7 were 60 or older. According to the anamnesis, 72.9% of the patients were infected from sheep, 1.9% from goats, 19.9% from cows. Of those 111, 4.4% had contact with various agricultural animals. The sources of

infection were not established in 3.9% of the patients. The clinical-epidemiologic and bacteriologic examinations showed that all those infected had brucellosis of the goat-sheep type (in Stavropol kray, migration of brucellae to cows is prevalent). The clinical-epidemiologic diagnosis of all patients was confirmed by laboratory tests (Table 1).

TABLE 1

Wright's, Huddelson's and Burnet's
Tests in Brucellosis Patients in
in the Generalization Stage
with Focal Lesions

Laboratory investigation	Frequency of Positive Reactions, %		
	in unvaccinated persons	in vaccinated persons	total
Wright's tests . . .	76,3	75	75,9
Huddelson's test . .	89,2	84,3	87,8
Burnet's cutireaction	62,9	63,8	65

Cultures of goat-sheep type brucellae were separated from the blood of 105 (32.8%) of the patients (including from 28 previously vaccinated). Prophylactic vaccinations against brucellosis with live vaccine were given to 92 (28.75%) of the persons before the disease. Of these, 10 became ill in the first two months and 34 a year after vaccination. Therefore, 47.8% of those vaccinated were infected with brucellosis during the period of low strength of immunity.

Focal lesions occurred in the patients after the onset of the disease: from the 5-7th through the 14th day of the disease in 5% of the patients, from the 15th day through the 3rd month of disease in 81.5%, from the 3rd to the 6th month of disease in 9.7%, from the 6th to the 10th month in 1.8%, about 2 years in 2% of the patients. The pathogenic stages of the disease (generalization stage and generalization stage with focal lesions) do not correspond to the hypothetical division in time in acute, subchronic, and chronic brucellosis.

Of those infected, 0.6% had the mildest course of brucellosis, 27.5% had mild, 53.4% had average severity, 16.9% had severe, and 1.6% had a severe course. We did not detect any difference in the severity of the course of brucellosis between those vaccinated and those not vaccinated.

TABLE 2

Comparative Data on the Frequency of General Symptoms of Brucellosis in the Generalization Stage and Generalization Stage with Focal Lesions

Symptoms	Frequency of symptoms, %	
	in generalization stage	in generalization stage with focal lesions
Fleeting pains in joints, muscles, loin	70.9	89.4
Headache	54.5	70
Asthenia	72.7	66.3
Sweating	70.9	92.8
Chills	70.9	68.1
Temperature: a) high	61.8	54.1
b) subfebrile	31.8	37.8
c) normal	6.4	8.1
Polymicroadenitis	66.4	84.7
Bilatation of heart	10	24.4
Dullness of heart tones	46.4	69.1
Systolic apex murmur	14.5	17.8
Hypotonia	48.2	46.2
Bronchitis	13.6	11.3
Hepatomegaly	50.9	86.3
Splenomegaly:		
a) determinable by percussion	35.5	20.3
b) " " palpation	30.9	35
Anorexia	21.8	32.5
Diarrhea	4.5	0.9
Constipation	6.4	1.3
Skin eruptions	10.9	5.9

A study of the fever in the generalization stage with local lesions showed that at this stage, like in the generalization stage, a normal and subfebrile temperature is characteristic for the mild course of brucellosis, high temperature for average and severe courses. Subfebrile temperature was observed in the average-severe course of brucellosis in 41.5% of the patients and in 7.4% of the patients with a severe course. Subfebrile temperature was noted only in 10% of the patients with average-severe brucellosis in the generalization stage.

As is known, recurrence of fever in any type of brucellosis and constancy (often with several waves) of prolonged subfebricity is characteristic for this disease.

Fleeting pains in the joints, muscles, and loin, headache, sweating, polymicroadenitis, dullness of the heart tones, hepatomegaly, and anorexia occur more often in the generalization stage with focal lesions than in just the generalization stage. The other symptoms are found just as often in one stage as the other (Table 2).

As an analysis of the observations showed, the occurrence of focal inflammatory processes during transition from the generalization stage to that with focal lesions sharply distinguish these stages from each other and make it possible to differentiate them easily. All patients complained of persistent pains at sites of focal lesions. Most frequently affected in brucellosis are the locomotor apparatus (76.6%) and nervous system (63.4%), more rarely the internal organs (17.2%) and urogenital system (10.9%), but any organs and systems of the human organism can be affected (Table 3).

TABLE 3

Clinical Forms of Focal
Lesions in Brucellosis
During the Generalization
Stage with Focal Lesions

Clinical Form of Brucellosis	Frequency of forms, %		
	in unvaccinated persons	in vaccinated persons	total
Clinically combined . .	58	61.9	59
Locomotor . . .	26.3	20.7	24.7
Nervous . . .	14	9.8	12.8
Visceral . . .	1.3	3.3	1.9
Urogenital . . .	0.4	4.4	1.6

Different combinations of focal affections with the involvement of the locomotor apparatus and nervous system, locomotor apparatus and internal organs, and more rarely of the locomotor apparatus, nervous

system, and internal organs are possible in the clinically combined forms. Still more rarely found are other combinations of lesions, when the urogenital system, endocrine glands, and other organs are affected.

We will cite brief data on affection of various organs and systems in brucellosis in the generalization stage with focal lesions.

Locomotor apparatus. Upon examining 320 patients we found lesion of the locomotor apparatus in 245 (76.6%). More than 400 joints were affected in these patients; more than 430 other pathological changes of the locomotor apparatus were noted. The character of the lesions is as follows: synovitis in 49.6% of the patients; arthritis in 39.1%; bursitis in 7%; peri-arthritis in 0.8%; para-arthritis in 0.4%; peri-ostitis in 0.8%; and myositis in 2.3% of the patients. The joints can be divided in the following manner by the frequency of affection (in descending order): knee, shoulder, talocrural, radiocarpal, cubital, hip, sacroiliac, metacarpophalangeal and phalangeal, vertebral, etc. Suppurative arthritis was not noted in the patients. Sacroiliitis, which is given a diagnosis value since it is not found in other diseases, was observed in 11% of the patients. The more complex the articular structure, the greater its functional load, the more often it was affected. For example, synovitis and arthritis of the right shoulder joint were observed more often.

Nervous system. We observed lesions of the nervous system in 203 (63.4%) of the patients (Table 4).

Two of the patients with meningo-encephalitis died; one of them still had brucellar endocarditis. As regards the peripheral nervous system, we most frequently encountered funiculitis of the lumbosacral region. In most patients (80% of 203) lesions of the nervous system were combined with lesions of other organs and systems.

TABLE 4

Composite Data on Lesions of
the Nervous System in Brucel-
losis in the Generalization
Stage with Focal Lesions

Forms of lesions of the nervous system	Number of patients			
	un- vacci- nated	vacci- nated	total absolute number	%
Meningo-enceph- alitis	3	0	3	1,5
Meningitides	3	0	3	1,5
Funiculitis	92	48	140	69
Radiculitis	27	2	29	14,2
Ischio-radiculitis	9	4	13	6,4
Neuritis	7	7	14	6,9
Shoulder plexitis	1	0	1	0,5
			203	100%

Most frequently involved along with the nervous system was the locomotor apparatus (almost 70% of all patients), more rarely the internal organs (15%) and the urogenital system (10%); the endocrine glands and visual organs were affected considerably more rarely. Only 41 of the 203 persons had just neurobrucellosis.

Lesion of the visual organs (uveitis, iritis, choroido-iritis, conjunctivitis, inflammatory exophthalmos) was observed in 5 (1.6%) of the patients. The psyche of the patients as a rule changed during the disease. The generalization stage was characterized by euphoria, more rarely by depression, adynamia and even a condition resembling the typhoid state. The generalization stage with focal lesions was characterized by asthenia of the psyche against a general depressed background, a tendency toward "drift into the disease", emotional instability, egocentricity. Acute psychosis was observed in one patient.

Internal organs. Lesion of the internal organs was established in 56 (17.5%) of those examined; visceral form of brucellosis in 6 (1.9%); in the remaining 49, lesions of the internal organs was accompanied by lesions of other organs and systems (locomotor apparatus in 16, locomotor apparatus and nervous system in 18, nervous system in 9,

etc.). The data on the character of the lesions of the internal organs are shown in Table 5.

TABLE 5

Composite Data on Affection of Internal Organs at the Generalization Stage with Focal Lesions

Character of lesions	Number of patients		
	Unvaccinated	Vaccinated	Total
Bronchopneumonia	9	6	15
Endocarditis	5	1	6
Myocarditis	18	2	20
Myocardiodystrophy	4	4	8
Allergic changes of the vessels with expressed functional disorders	1	2	3
Interstitial hepatitis	3	0	3
Peritonitis	0	1	1

Brucellar bronchopneumonia was frequently not determined by percussion or roentgenologically, but on auscultation sonorous moist rales were easily heard. Other clinical signs of brucellosis were evident in these patients, and focal lesions of the locomotor apparatus and nervous system were identified.

Evident pathologic changes in the cardiovascular system were observed in 37 patients (11%). Deserving of particular attention is brucellar endocarditis which occurred as a type of acute septic endocarditis and was accompanied by demonstrations of brucellar sepsis—bronchopneumonia, focal glomerulonephritis, and petechial eruption. In two patients we observed a combined affection of the aortic valves and ostium arteriosum cordis; in two others, lesion of the aortic valves. One of these patients had a rupture in the wall of the base of the aorta (with formation of an aneurysm in the transverse vein of the heart), only the mitral valves were affected in two patients. Persistent treatment with antibiotics (levomycetin, biomycin, streptomycin, oxytetracycline for intramuscular injection) and with other substances

did not yield an effect in acute brucellar endocarditis. During the first 6-9 months of the disease, all patients died. The duration of the disease from the onset of endocarditis until death was 3-5 months. We observed three patients with brucellar endocarditis during consultations, therefore when processing the results we did not take into account their treatment so as not to artificially inflate the per cent of mortality. In sporadic patients we found brucellar hepatitis, which was distinguished by a rather torpid course, and peritonitis.

Urogenital system. Fugacious cystitis was found in 1.5% of the men and 7.4% of the women. We assume that in most cases this was non-specific cystitis. Focal glomerulonephritis was observed only in 6 patients suffering from endocarditis. We did not observed isolated lesions of the kidneys. In 30 (15%) of the 199 men we found lesions of the sexual organs: orchitis in 27 (13.5%) patients, orchiepididymitis in 2 (1%), and epididymitis in 1 (0.5%) patient. In one patient, orchitis quickly terminated with atrophic sclerosis of the testis.

Of the 121 female patients with brucellosis in the generalization stage with focal lesions, the sexual organs were affected in 5 (4.13%); 2 patients had endometritis (one of them had a spontaneous abortion), 1 had salpingo-oophoritis, 1 had adnexitis, and 1 had colpitis.

Of the 35 male and female patients with affection of the urogenital system, focal lesions just of the sexual organs were found in 5 patients and affections of other organs and systems were observed in the remaining 20 (clinically combined forms according to G. P. Rudnev).

The clinical features of brucellosis in the generalization stage with focal lesions were so unique and characteristic that in 94.7% of the patients brucellosis was suspected by the doctors when the patients first arrived for medical help. In 5.3% of the patients a differential diagnosis was made with rheumatic polyarthrititis, typhoid fever,

influenza, Q fever, typhus, pulmonary tuberculosis, radiculitis, and orchitis of nonbrucellar etiology.

In order to compare and differentiate goat-sheep type brucellosis from the bovine-type, we later studied the clinical features of the bovine-type of brucellosis in man. Having examined 8 patients in a bacteriologically confirmed focus of the bovine type and then having continued a study of the bovine-type of brucellosis in another 30 patients, we arrived at the conclusion that the bovine-type of brucellosis in man can be clinically differentiated from *Br. melitensis*.

The bovine-type of brucellosis begins gradually, unnoticeably. Persistent arthralgia or focal lesions of the peripheral nervous system occur at a subfebrile or normal temperature. It is usually not possible to detect clinically the early stage of the disease, i.e., the generalization stage. The course of the disease is sluggish, without a distinct development of symptoms. The objective signs of the disease are scarce, there are many subjective complaints; in one of the patients with bovine-type brucellosis we observed encephalitis, which occurred at a low subfebrile temperature. Consideration of the epizootic and epidemiologic data helps in differentiating the types of brucellosis.

Upon migration of the goat-sheep type to cows and infection of man from them, the clinical aspects are more evident, the generalization stage occurs typically, in conformity with the clinical characteristics of the goat-sheep type. Fever was observed in many of the patients.

Treatment. Synthomycin or levomycetin was used in 115 patients, streptomycin intramuscularly in 51 (including 38 patients who received streptomycin in combination with synthomycin or levomycetin, or with biomycin), tetracycline and oxytetracycline intramuscularly in 24

patients, brucellosis vaccine based on G. P. Rudnev's method in 67 (including 54 patients who received it in combination with antibiotics), the same based on Sepp's method in 6, intracutaneously in 6 patients. Symptomatic treatment was carried out with 25 patients. Four patients received perorally cyanophytin (an extract of blue-green algae from Lake Tambukan, having antibiotic and biostimulating action; suggested by A. L. Shinkarenko, M. I. Mamaychuk, and L. D. Suntsova). The course of antibiotics consisted of 3, more rarely 4-10 day cycles. The first cycle of treatment with streptomycin lasted 15-20 days; we used average daily doses. The duration of the first interval was 5-7 days, the second and third intervals were from 10 days to 2-3 weeks. Vaccinotherapy was carried out by the usual method.

In the combined treatment with vaccine and antibiotics, the latter were used as one or two cycles; the first cycle was performed at the start of treatment, the second during the period of vaccinotherapy. In addition to specific treatment, the patients received pathogenic and symptomatic drugs; analgesics (pyramidon, analgin, novocaine, sometimes promedol as indicated) were given to 166 patients, physiotherapeutic procedures were carried out on 168 patients, massage on 13, and retransfusion of blood in fractional doses with 20 patients. The patients also received vitamins C, B₁, B₁₂, etc.

The immediate results of treating the patients who were admitted with brucellosis in the generalization stage with focal lesions were as follows: compensation of the pathologic process occurred in 38.8% of the patients, subcompensation in 56.4%, no improvement in 2.7%, and deterioration and death ensued in 2.1% of the patients. Among the patients admitted with the generalization stage of brucellosis, compensation of the process was noted in 58.8% and subcompensation in 42.2%.

We followed up the remote results of treatment after the generalization stage in 84 persons and after the generalization stage with focal lesions in 148 persons. Twenty-eight persons were under observation up to 1 year, 38 up to 2 years, 59 up to 3 years, 92 up to 6 years, and 15 up to 9 years. Complete recovery was noted in 31% of the patients that were admitted with brucellosis in the generalization stage with focal lesions and in 43.2% of the patients who were admitted with the disease in the generalization stage; aftereffects remained in 69 and 56.8% of the patients respectively.

No drop in workability requiring disablement was observed later in patients who entered for treatment with brucellosis in the generalization stage. In 31% of the persons with aftereffects of brucellosis, which were noted after the generalization stage with focal lesions, the workability was lowered and they were officially invalided, including 1/6 of all patients relegated to invalids of the I-II groups.

The immediate results of intravenous vaccinotherapy and the combined therapy of vaccine with antibiotics in patients at the generalization stage with focal lesions were better than on treatment with antibiotics alone. With vaccinotherapy and combined vaccino- and antibiotic therapy, compensation of the pathologic process ensued in 47.2% of the patients, subcompensation in 51.7%, deterioration and death in 1.1% of the patients. With antibiotic treatment we observed the same results in respectively 35.3, 62.1, and 2.6% of the patients.

Hemocultures of brucellae of the goat-sheep type were obtained from 22 patients before treatment, from 44 during treatment (22 persons received antibiotics, 3 vaccine, 13 vaccine in combination with antibiotics, and 6 patients received symptomatic substances). Hemocultures were taken in 39 persons after completion of treatment (16

persons received antibiotics, 6 vaccine, 12 vaccine together with antibiotics, and 5 persons received symptomatic treatment).

The generalization stage with focal lesions is the period of maximal development of pathologic processes in brucellosis and determines the further course and outcome of the disease. The results of specific treatment at this period are worse than in the generalization stage. Therefore, the main diagnostic and therapeutic work as to brucellosis patients at places where goat-sheep brucellosis is widespread should be carried out as early as possible, i.e., still in the generalization stage of the process. In this manner disability and fatality from brucellosis can be reduced to a minimum.

Conclusions

1. In brucellosis of the goat-sheep type in man, the occurrence of local inflammatory lesions of various organs and systems is a characteristic clinical feature which enables us to distinguish easily the generalization stage with focal lesion from the preceding generalization stage.

2. In goat-sheep type of brucellosis, a clinically combined form was encountered in 59% of the patients, locomotor form in 24.7%, nerve form in 12.8%, visceral in 1.9%, and urogenital in 1.6% of the patients.

3. Diagnosis of brucellosis as to pathogenic stages of the disease makes it possible to glean a more accurate idea of the patient and a better administration of treatment, since it is to a considerably greater degree determined by the specific pathogenic stage than by its duration. A hypothetical division in time into acute, subchronic, and chronic brucellosis does not correspond to the pathogenic stages of the disease.

4. In order to maintain the principle of individualized treatment of a patient with brucellosis in the generalization stage with focal lesions, we must take into account, in addition to the severity of the disease, all focal lesions, their localization and character in the patients.

The generalization stage with focal lesions is the period of maximal development of pathologic processes in brucellosis and determines the further course and outcome of the disease. Therefore, the basic diagnostic and therapeutic work in the habitat of goat-sheep brucellosis should be done at the generalization stage.

5. In the overwhelming majority of cases, brucellosis of the goat-sheep type in man occurs as a cyclic bacteremic disease in which compensation, and then recovery can ensue at any stage of the disease. Brucellar sepsis very rarely occurs. The clinical picture and the outcome of brucellar endocarditis give us grounds to consider this variety of brucellosis to be a particular phenomenon of acute sepsis.

6. The immediate results of intravenous vaccinothrapy as well as of combined treatment with vaccine and antibiotics in brucellosis in the generalization stage with focal lesions were better than the results of antibiotic treatment, whereas a better effect is obtained in the generalization stage with antibiotics than with treatment with vaccine and its combination with antibiotics.

The bacteriostatic action of the antibiotics used in brucellar infection in the generalization stage with focal lesions is inadequate; this is determined, on one hand, by the need for repeated treatment and, on the other, by the possibility of bacterimia after completing the antibiotic treatment.

7. In addition to specific agents (antibiotics and vaccine), pathogenetic therapy is widely used in brucellosis at the generalization

stage with focal lesions: analgesics, physiotherapeutic procedures, massage, hemo- and vitaminotherapy.

8. Brucellosis in those vaccinated occurs the same as in the unvaccinated, the reason for which is the greater sensibilization of those vaccinated to brucellosis.

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