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CLINICAL FEATURES AND TREATMENT OF BRUCELLOSIS OF THE
GOAT-SHEEP TYPE IN THE STAGE OF FOCAL LESIONS

By

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CLINICAL FEATURES AND TREATMENT OF BRUCELLOSIS OF THE
GOAT-SHEEP TYPE IN THE STAGE OF FOCAL LESIONS

L. V. Yarovoy

The stage of focal lesions in brucellosis is pathogenically characterized by the fact that bacteremia is stopped as a consequence of the sharply increased specific protective reactions of the organism, and focal inflammatory processes in individual organs and systems continue. In spite of the fact that individual authors distinguish and differentiate this stage of brucellosis as an independent stage of the disease, we have not found in the literature available to us, investigations with a detailed treatment of factual material of observations of such patients.

We had under observation 102 patients (46 men and 56 women) suffering from brucellosis of the goat-sheep type in the stage of focal lesions; most of the patients were between 20 and 60 years of age. Twenty-two persons subcutaneously received prophylactic vaccinations of live brucellar vaccine of the bovine type BA before the onset of the disease. Of these, 10 became sick a year after prophylactic vaccination and 5 in the first 2 months from time of vaccination, i.e., they were infected during the period of low strength of postvaccinal

immunity. Seven of those vaccinated became ill from the 3rd to the 10th month after vaccination: this is the period of maximal strength of postvaccinal immunity. One hundred patients were sent for hospital treatment with the diagnosis of "brucellosis," and two in connection with the concomitant disease, dysentery. When comparing the severity of the course of brucellosis in the stage of focal lesions and in the generalization stage with focal lesions (320 patients examined) it was found that at the stage of focal lesions most patients (69.6%) had a mild course of the disease, whereas in the preceding stage of the disease (generalization with focal lesions) mild forms were found in 28.1% of the patients. An average-severe course of brucellosis was noted half as many times in the stage of focal lesions as in the preceding stage of the disease (27.5 and 53.4% respectively), and a severe course in one-sixth as many (2.9 and 18.5% respectively). These data indicate a more mild course of brucellosis in the stage of focal lesions. The generalization stage with focal lesion represents a period of maximal development of pathologic processes in the organism.

Comparative data on the frequency of individual symptoms of brucellosis by stages of the disease are shown in Table 1.

We see from Table 1 that in the stage of focal lesions we rather frequently find a number of signs which are also characteristic for the preceding stage. At the same time a number of symptoms are observed less often in the stage of focal lesions than in the generalization stage with focal lesions. This fact is of considerable differential diagnostic importance. Consideration of the temperature reaction deserves special attention. In brucellosis at the stage of focal lesions, during periods of exacerbation, the temperature of 22% of the patients was normal, subfebrile in 52.7%, and only in 25.3% of the patients did we observe short-lived temperature rises.

TABLE 1

Comparative Data on the Frequency of Brucellosis
Symptoms as to Pathogenic Stages of the Disease

Symptoms of brucellosis	Frequency of symptoms by stages (in %)		
	Generaliza- tion stage (110 pa- tients)	Generalization stage with fo- cal lesions (220 patients)	Stage of fo- cal lesions (102 pa- tients)
Fleeting pains in joints, muscles, and loin	70,9	89,4	75,5
Headache	54,5	70	50,9
Asthenia	72,7	66,3	34,3
Sweatiness	70,9	92,8	44,1
Chills	70,9	68,1	9,8
Temperature			
high	61,8	54,1	25,3
subfebrile	31,8	37,8	52,7
normal	6,4	8,1	22
Polymicroadenitis	66,4	84,7	59,8
Dilatation of heart	10	24,4	8,8
Dullness of tones	46,4	69,1	11,7
Systolic apex murmur	14,5	17,8	12,7
Hypotonia	48,2	46,2	3,9
Bronchitis	13,6	11,3	4,9
Hepatomegaly	50,9	86,3	38,2
Splenomegaly			
by percussion	35,5	20,3	19,6
by palpation	30,9	35	8,8
Anorexia	21,8	32,5	9,8
Diarrhea	4,5	0,9	1,9
Constipation	6,4	1,3	2,9
Skin eruptions	10,9	5,9	2,9

A latent or explicit wavelike fever regardless of the characteristics of the temperature curve is characteristic for the preceding stages of brucellosis; in the generalization stage fever was observed in 61.8% of the patients and in 54.1% in the generalization stage with focal lesions. A normal temperature was encountered three to four times more frequently in the stage of focal lesions than in the preceding stages (22 and 6.4-8.1% respectively).

In a differential diagnosis of stages of brucellosis, it is also necessary to take into account that hematogenic generalization of *Br. melitensis*, which is characteristic for the generalization stage with focal lesions, is absent in the stage of focal lesions. Blood cultures of all those we examined bacteriologically yielded negative results. The occurrence of new focal lesions, observable in the generalization

stage with focal lesions, is not characteristic for the stage of focal lesions.

Data on the clinical forms of focal lesions based on Rudnev's classification, are shown in Table 2.

A neural form of brucellosis is encountered more often in the stage of focal lesions than in the preceding stage of the disease. Since we don't have the opportunity to give detailed characteristics of the affection of various organs and systems, we will attempt to hit only the highlights characteristic for this stage. Comparative data on the frequency of focal lesions of individual systems by stages of brucellosis are shown in Table 3.

We see from Table 3 that inflammatory changes in the nervous systems are most frequently found in the stage of focal lesions (in 78.4%, which is 15% more often than in the generalization stage with focal lesions). According to our data, lesions of the locomotor apparatus, which in the generalization stage with focal lesions were the main ones and were found in 76.6% of the patients, in the stage of focal lesions were noted in 60.8%. Inflammatory changes of the nervous system, internal organs, and visual organs occur more torpidly and longer than lesions of the locomotor apparatus. The latter pass more quickly. This fact can explain the relatively greater frequency of lesions of the nervous system in the stage of focal lesions than of the locomotor apparatus. The character of the changes of the locomotor apparatus and the nervous system is similar in both stages. We most frequently observed in the locomotor apparatus synovitis (56 patients), less often bursitis (18), arthritis (15), para-arthritis (3), periostitis (3), tendovaginitis (1), myositis (8). The prevalence of synovitis, fugacity, and the serous character of arthritis give us grounds to share the opinion of A. L. Myasnikov that lesions of the locomotor

TABLE 2

Comparative Data on the Clinical Forms of Focal Lesions by Pathogenic Stages

Name of clinical forms of brucellosis by G. P. Rudnev's classification	Frequency of forms of brucellosis in stage of focal lesions			Frequency of clinical forms in generalization stage with focal lesions (mg)		Check of reliability of differences in indexes				Conclusion on reliability of the existence of a difference in indexes
	Number of patients			total	%	m ₁	m ₂	M ₁ -M ₂	$2\sqrt{\frac{m_1^2+m_2^2}{n}}$	
	unvaccinated	vaccinated								
Clinically combined	41	14	55	53.9	59	±4.9	±2.7	5.1	11	Doesn't exist
Locomotor	15	2	17	16.7	24.7	±3.6	±2.4	8	8.6	"
Neural	20	5	25	24.5	12.8	±4.2	±3.5	11.7	10.8	Exists
Visceral	4	1	5	4.9	1.9	±2.1	±0.7	-3	4.8	Doesn't exist
Urogenital					1.6					

TABLE 3

Comparative Data on Frequency of Focal Lesions of Individual Systems by Stages of Brucellosis

Name of system	Number of patients										Check of the reliability of the existence of differences in indexes							
	In stage of focal lesions in generalization stage with focal lesions (320)																	
	In stage of focal lesions (102)																	
	un- vacci- nated	vacci- nated	total	%	total	unvacci- nated	vacci- nated	total	%	m ₁	m ₂	M ₁ -M ₂	$2\sqrt{\frac{m_1^2+m_2^2}{n}}$					
Locomotor apparatus	48	14	62	60,8	173	72	245	76,6	±4,8	±2,3	15,8	10,6						
Nervous system	61	19	80	78,4	142	61	203	63,4	±4,07	±3,6	-15,0	10,8						
Internal organs	13	2	15	14,7	39	16	55	17,2	±3,5	±2,0	2,5	8,0						
Urogenital system	5	3	8	7,8	22	13	35	10,9	±2,7	±1,7	3,1	6,2						
Visual organs	3		3	2,9	4	1	5	1,6	±1,6	±0,7	-1,3	3,4						

apparatus in brucellosis bear an allergic character in most patients.

Data on the forms of affections of the nervous system in brucellosis patients in the stage of focal lesions are given in Table 4.

TABLE 4

Data on the Affection of the Nervous System in
Brucellosis at the Stage of Focal Lesions

Form and localization of lesions of nervous system	Number of patients			%
	unvacci- nated	vacci- nated	total	
Encephalitis	1	—	1	1,25
Arachnoencephalitis, cervical and lumbar funiculitis	1	—	1	1,25
Encephalomyeloradiculo- neuritis	1	—	1	1,25
Funiculides:	52	17	69	86,25
of the lower chest division	2	3	5	6,25
of the lower chest and lumbo- sacral division	5	1	6	7,5
of the lumbar division	1	—	1	1,25
of the lumbosacral division	42	13	55	68,75
of the cervical and lumbosacral division	2	—	2	2,5
Lumbosacral radiculitis	2	—	2	2,5
Ischioradiculitis and funiculitis	1	1	2	2,5
Neuritis of the right cubital nerve and lumbosacral funiculitis	1	—	1	1,25
Evident vegetative neurosis	2	1	3	3,75
Total ...	61	19	80	100

Of the 102 examined, lesions of the internal organs were found in 15: 8 with hepatitis, 1 with splenitis, and 6 with disorders of the cardiovascular system (1 with myocarditis, 5 with evident allergic changes of the vessels). A number of special characteristics of lesions of the internal organs were noted during this stage. In contrast to the preceding stage, in the period of focal lesions we do not find brucellar bronchopneumonia and endocarditis and, as an exception, myocarditis occurs. Hepatitides were most often observed. According to the clinical demonstration they were dissimilar. Along with the easily diagnosable cases in which hepato- and splenomegaly occur, we encountered hepatitides with effaced symptoms—with negligible enlargement of the liver, slightly expressed painful symptoms and others.

Syndromes caused by hyperergic affection of the vessels, characteristic for brucellosis, dominated in patients during the stage of focal lesions. Changes in the urogenital system were noted in the same number of men as in the preceding stage (about 15% of the number of men examined). Orchitis and epididymitis were most frequently observed. Adnexitis was detected in 2 of the 56 women examined. Glomerulonephritis was absent in the examinees.

Lesions of various organs and systems were usually found not isolatedly, but in different combinations; the nervous system and locomotor apparatus were most frequently involved in the pathologic process.

As a result of studying certain indexes of the blood picture as to stages of the disease, we detected a number of shifts occurring in the stage of focal lesions, namely an increase to the norm of the percent of hemoglobin, normalization of the leukocyte formula (in $\frac{1}{4}$ of the patients) and of the ESR (in 90% of the patients). These positive shifts agree with the clinical picture and show that the infectious process subsides. In the generalization stage with focal lesions and in the stage of focal lesions, as compared with the generalization stage, we more rarely encountered hypo- and aneosinophilia (75.4% in the I stage, 69.7% in the II, and 58.8% in the III), the number of patients with a normal level of eosinophils increases (13.6% in the I stage, 19% in the II, and 22.6% in the III) as well as eosinophilia (10.9% in the I stage, 11.3% in the II, and 18.6% in the III). These changes to a certain extent are a reflection of allergic rearrangement occurring in the organism during the course of the infectious process; in a number of cases they can be considered as a indexes of normergy.

Upon admittance to the clinic, 10 of the 102 patients had negative Wright, Huddelson, and Burnet reactions. The presence of positive reactions to brucellosis in these patients in the preceding stage was

established by studying the medical documentation. The results of the serological examinations and of the allergy test are shown in Table 5 by stages of the disease.

Wright's reaction in the stage of focal lesions was negative in 62.7% of the patients and its titers were reduced in comparison with the preceding stage. The same can be said about Huddelson's reaction. In the latest instructions for laboratory diagnosis it is recommended to set up the Huddelson's reaction with 0.04-0.02-0.01 ml of serum and not to take 0.08 ml for the experiment. Agglutination with 0.04 ml of serum, which is hypothetically equivalent to Wright's reaction in a titer of 1 : 100, is to be considered "doubtful." On the basis of the data of examining patients in the stage of focal lesions, when the possibilities of laboratory proof of diagnosis are sharply reduced (see Table 5), we consider it advisable to evaluate Huddelson's reaction with 0.04 ml of serum as slightly positive and not as doubtful, and with 0.08 ml of serum as doubtful.

We used antibiotics in the treatment of our patients. Synthomycin and levomycin were given to 47 patients (of them, 7 in combination with streptomycin), preparations of the tetracycline series in 2 patients (1 oxytetracycline intramuscularly and the other, biomycin perorally). Thirty-four patients received one cycle of antibiotics, 11 had two cycles, and 4 patients had three cycles. In the stage of focal lesion, the three-cycle treatment with antibiotics had no advantages over the one- and two-cycle treatments. According to our data the effectiveness of antibiotics at this stage of brucellosis was considerably lower than in generalization of the infection. Vaccinotherapy was carried out with 13 patients, of which 7 were treated by G. P. Rudnev's method (2 of them received vaccine in combination with levomycin), 5 were treated intracutaneously, and 1 patient treated by

Sepp's method. Forty patients received symptomatic treatment. All patients received analgesics (analgin, pyramidon, promedol); 84 underwent physiotherapeutic procedures (quartz lamps, sunlamps, diathermy, etc.), massage, vitamins; 9 patients received retransfusions in fractional doses. The clinical demonstrations of brucellosis and the results of treatment of persons who received prophylactic vaccinations before the disease and of those unvaccinated were practically the same. The results of treating patients in the stage of focal lesions are shown in Table 6, and comparative data on the results of treatment by stages of the disease are shown in Table 7.

TABLE 5

Indexes of Wright's and Huddelson's Reactions and Burnet's Test by Stages of the Disease

Name of reaction and test	Results of reaction	Indexes in % by stages		
		Generalization stage (110 patients)	Generalization stage with focal lesions (300 patients)	Stage of focal lesions (102 patients)
Wright's reaction	Negative	19,1	24,4	62,7
	Positive in titers of			
	1:100	20	18,3	12,7
	1:200	13,6	14	17,7
	1:400	25,5	23	5,9
	1:800 and higher	21,8	20,3	1
		60,9	57,3	24,6
Huddelson's reaction	Negative	11,8	12,7	34,1
	Positive in titers of			
	1:100			7,8
	1:200	14,6	17,7	31,4
	1:400	73,6	69,6	23,4
		88,2	87,3	60,8
Burnet's reaction	Negative	19,1	37,3	27,5
	Positive, size of infiltrates in cm			
	to 2	11,8	10	20,6
	2-4	40	29,7	32,3
	4-6	20,9	18	15,7
	6-8	8,2	5	3,9
		69,1	52,7	51,9

We see from the data of Table 7 that the immediate results of treatment in the generalization stage were better than in subsequent stages of the disease. In the generalization stage with focal lesions there occurs the highest stress of the morbid processes in the organism, whereas in the stage of focal lesions localization of the infection

TABLE 6

Results of Treatment of Brucellosis Patients
in Stage of Focal Lesions

Method of treatment	Number of pa- tients	Results of treatment					
		Compensation		Subcompensation		Without improvement	
		un- vacci- nated	vacci- nated	unvacci- nated	vacci- nated	unvacci- nated	vacci- nated
Synthomycin, levo- mycetin	47	12	5	20	7	2	1
Oxytetracycline i.m.	1	0	0	1	0	0	0
Biomycin	1	0	0	0	1	0	0
Vaccine by Rudnev's method	7	1	1	4	1	0	0
Vaccine i.v.	5	1	0	4	0	0	0
Vaccine by Sepp's method Symptomatic	1 40	0 8	0 2	1 25	0 4	0 1	0 0
Total...	102	30		68		4	

TABLE 7

Comparative Data on the Results of Treating
Patients with Brucellosis by Pathogenic
Stages of the Disease (in %)

Results of treatment	Generaliza- tion stage (110 pa- tients)	Generalization stage with fo- cal lesions (320 patients)	Stage of fo- cal lesions (102 pa- tients)
Compensation	58.8	38.8	29.4
Subcompensation	42.2	56.4	66.7
Without improvement	—	2.7	3.9
Deterioration and death	—	2.1	—

ensues, bacteremia is stopped owing to the sharply increased specific phylactic reactions of the organism, and clinical manifestations of the disease subside. Thus the course of the infectious process in the stage of focal lesions fosters a more rapid onset of improvement, i.e., subcompensation. Therefore, therapeutic measures in the stage of focal lesions more quickly lead to abatement of the pathologic processes (subcompensation) than in the generalization stage with focal lesions. A complete, persistent compensation by using analogous specific substances (antibiotics, vaccine) in the stage of focal lesions is achieved even in a slightly smaller per cent of cases than in the generalization stage with focal lesions (respectively 29.4 and 38.8%).

Remote results of treatment after the stage of focal lesions were studied in 34 patients. Duration of observation: 2 years for 3 persons, 3 years for 13 patients, from 3 to 6 years for 12, and more than 6 years for 6 persons. Complete recovery was established in 2 persons, aftereffects remained in the other 32. Most patients (18) had aftereffects in the form of lumbosacral funiculitis and radiculitis (3), arthralgia and the vegetative syndrome, less frequently found were splenomegaly (2), hepatitis (1), ischialgia (1), spondylosis (1), loss of sight (1), residual phenomena of encephalomyeloradiculoneuritis (1). Work performance was appreciably lowered in most of those examined. Remote results of treatment after the stage of focal lesions were considerably worse than after the generalization stage (complete recovery was observed in 43.2% of the patients and there were no aftereffects of brucellosis such that would require official disablement) and after the generalization stage with focal lesions (31% of the patients recovered without aftereffects).

Conclusions

1. The stage of focal lesions in brucellosis of the goat-sheep type can be differentiated by clinical demonstrations from the preceding stage—the generalization stage with focal lesions.

2. Inflammatory changes of the nervous system, internal organs, and visual organs in brucellosis in most cases occur over a longer time than changes of the locomotor apparatus. Therefore, at the stage of focal lesions, changes of the nervous system are found more often (in 78.4% of the patients) than disorders of the locomotor apparatus (60.8%). The character of the changes of the locomotor apparatus and the nervous system in both stages is identical.

3. Hepatitides and allergic changes of the vessels are most frequently found in the internal organs in the stage of focal lesions. In contrast to the preceding stage, in this stage brucellar bronchopneumonia and endocarditis are not noted and, as an exception, myocarditis occurs.

4. Lesions of various organs and systems in most cases are encountered not isolatedly, but in various combinations, whereby the nervous system and locomotor apparatus are most often involved in the process.

5. In the stage of focal lesions, the per cent of hemoglobin in the blood increases, the leukocyte formula (in $\frac{1}{4}$ of the patients) and the ESR (in 90%) are normalized. These shifts agree with the clinical picture and show that the infectious process abates.

6. In the generalization stage with focal lesions and in the stage of focal lesions, as compared with the generalization stage, we more rarely find hypo- and aneosinophilia; the number of patients with a normal content of eosinophils and eosinophilia increases. These changes are to a certain extent a reflection of the allergic rearrangement of the organism occurring during the course of the infectious process, and in a number of cases are indexes of normergy.

7. Laboratory diagnosis of brucellosis at the stage of focal lesions is difficult. Ten of the 102 patients had negative Wright's, Huddelson's reactions and Burnet's test.

8. The immediate results of treating patients in the stage of focal lesions by using analogous specific and symptomatic agents were better than in the generalization stage with focal lesions and appreciably worse than in the generalization stage.

9. The remote results of treating patients with brucellosis after the stage of focal lesions were appreciably worse than in patients who

began treatment in preceding stages.

10. The most frequent aftereffects of brucellosis after the stage of focal lesions were chronic lumbosacral funiculitis and radiculitis, arthralgia, and the vegetative syndrome; less often encountered were splenomegaly, hepatitis, decrease in visual acuity, residual phenomena of encephalomyeloradiculonephritis, etc.

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