ClinicSearch

International Journal of Clinical Therapeutics

Andrey M. Dmitrovskiy

Open Access

Research Article

Clinical Manifestations of Diseases Caused by Y.Pseudotuberculosis and Y.Enterocolitica (Yersinioses)

Dmitrovskiy A.M.[1*], Ospanbekova N.K.[2], Syzdykov M.S.[1], Maukayeva S.B.[3], Kamytbekova K.Zh.[4], Iskakova F.A.[5], Ryabushko Ye.A.[1]

[1] National Science Center for Extremely Dangerous Infections.

[2] Kazakh-Russian medical university.

[3] Semey medical university.

[4] Kazak-Turkish International University.

[5] Kazakh National University.

***Corresponding Author:** Andrey M. Dmitrovskiy, M.D, DoS, Prof., National Center for Extremely Dangerous Infections, Central Reference Laboratory, 14 Zhahanger St, 050054, Almaty, Kazakhstan.

Received date: September 12, 2022; Accepted date: September 14, 2022; Published date: January 10, 2023

Citation: Dmitrovskiy A.M., Ospanbekova N.K., Syzdykov M.S., Maukayeva S.B., Kamytbekova K.Zh., et al. (2022). Clinical Manifestations of Diseases Caused by Y.Pseudotuberculosis and Y.Enterocolitica (Yersinioses). *International Journal of Clinical Therapeutics*. 2(1); **DOI:** 10.31579/2834-5010/006

Abstract

Yersinioses are typical representatives of zoonotic infectious diseases. Yersinioses are widespread without clearly delimited endemic territories. Yersinias (except Y.pestis) have neither specific hosts nor specific vectors, they can survive and reproduce in an abiotic environment – soil, rotting plant remains, etc. (which allows some authors to attribute them to sapronoses).

Yersinia, under certain conditions, can survive, persist and even multiply in the environment (soil, water, feed), which, therefore, can act as a reservoir of infection through which pathogens can be transmitted from a sick host to a healthy one, maintaining stable circulation in both natural and anthropogenic ecosystems.

Yersinia were isolated from almost all possible animals – mammals, birds, fish, reptiles and amphibians, from blood-sucking vectors (fleas, ticks) in different climatic and geographical zones. However, they are more "tied" to a humid and cool climate, or give rise to morbidity among hosts and humans in the cold and wet season – winter-spring, and are more often found at this time in rodents and farm animals.

The source of Yersinioses for humans are

- farm animals – indirectly (through animal products), less often – with direct contact;

- synanthropic rodents, more often indirectly (through contaminated vegetables and fruits, salads, other foods consumed without thermal processing), rarely – with direct contact;

- abiotic environmental factors (contaminated storage of meat and vegetables, water, soil);

- but also a sick person (more often with close contact, for example, mother–child, children in closed institutions, nosocomial infections, etc., as well as sexually).

According to the mechanism of infection, one or another clinical form of Yersinioses develops [1,2,3,4].

Keywords: pseudotuberculosis; yersiniosis; zoonoses; clinical manifestation; classification; clinical forms

Introduction

Various clinical syndromes caused by *Yersinia* are often described, and the syndromes seem to be completely different and unrelated to each other. All this leads to immersion in the syndrome diagnosis, which in our opinion is only the first stage of the diagnosis of infectious diseases, the first, but not the only one.

The task of modern medical science, in particular in the field of infectious diseases, in our opinion, is to build a system of ideas about infectious

diseases, a system of harmonious connections of clinical manifestations with the pathogenesis of the course of an infectious disease, when instead of disparate and, at first glance, unrelated syndromes, we see clear relationships and patterns. “Behind the trees we can see the forest”.

All these points prompted us to write this article.

Yersinia is gram-negative rods, no different from other representatives of the *Enterobacteriaceae family*, mobile (at lower temperatures – 22ºC), have a typical endotoxin, periodically they detect exotoxin-like substances (capsule).

Such properties of these pathogens as psychrophilicity (i.e., the ability to exist and reproduce at low temperatures, including at +4 ºC, - refrigerator conditions), as well as oligocarbophilicity and oligonitrophilicity (i.e., minimal requirements for organic carbon and nitrogen for their vital activity, which practically makes it possible to use for accumulation microbes in ordinary or buffered saline solution, determine the ecology of Yersinioses [5,6].

The causative agents of Yersinioses (unlike Y. pestis) have a relatively weak virulence for humans and mammals, which for a long time allowed them to be classified as conditionally pathogenic flora and still does not make it possible to find a laboratory model for a deadly infection.

However, the concept of virulence of a microorganism is a relative concept and mediated by the sensitivity (infectious) of the macroorganism. Under certain conditions of temporary or permanent immunosuppression, infection can occur very easily from an insignificant infecting dose[7].We distinguish several phases of the infectious process [8,9]:

- introduction of the pathogen and its primary adaptation corresponding to the incubation period in the clinic;

- primary focality with regional manifestations, corresponding in the clinic to the initial period (first wave) of the disease (1-3 days), the development of inflammatory processes in the "place of the entrance gate" of infection – primary focal manifestations, however, Yersinioses is characterized by the involvement of lymphoid cells and organs in the pathological process, and above all - regional lymph nodes (this particular we designate the symptom complex as "regional manifestations"), while from them, as well as from the primary focus of infection, it is possible, as a rule, to isolate the pathogen;

- generalization (hematogenous dissemination), which begins and proceeds somewhat delayed, but parallel to the phase of primary focality, leading, with unfavorable development of the process, to the phase of –

- secondary focality (parenchymal dissemination) at the site of fixation of the pathogen by cells of the reticular-endothelial system, corresponding in the clinic to the second wave of the infectious process (end of I – beginning of II weeks – 5-12 days of illness).

This is the dynamics of the infectious process – the dynamics of the spread of the pathogen itself in the patient's body.

However, this dynamics is based on a toxic process, manifested in the form of a so–called systemic post-aggression oscillatory reaction (SPAOR), which determines the described wave-like dynamics of pathogenesis and clinical manifestations of yersiniosis, this reaction concerns almost all body systems, including immune systems - cellular and humoral [10,11].

The SPAOR consists of phases:

- immediate depression lasting several hours and practically detected only in the experiment and the is more pronounced the if the initial dose of the infection is greater;

- activation, for example, of the cellular immune system, manifested in the clinic by initial (1-3 days of illness) neutrophil leukocytosis;

- oppression, which develops after activation according to the law of negative feedback inherent in all biological processes, and manifests itself to a greater extent, the greater the activation, precisely due to the suppression of the cellular immunity system in the middle – end of the first week of the disease and develops after hematogenic – parenchymal dissemination of the pathogen, secondary foci in parenchymal organs, and in there is an increasing leukopenia in the blood due to neutropenia.

In the case of the development of an exorbitant (exceeding the physiological parameters of the cellular immunity system) activation, it is followed by its complete depletion, which practically represents an infectious–toxic shock (ITSH).

Thus, the intensity of toxic (endotoxin) manifestations determines the generalization, the development of secondary foci, in fact, septic complications.

The allergic component also plays a significant role in pathogenesis, and such syndromes as generalized spotty-papular rash, polyadenopathy (in 25-33% of patients), arthralgia, as well as purulent necrotic tonsillitis and abdominal syndromes develop precisely on a sensitized background, as manifestations of infectious allergies. In the phase of secondary focality during the 2nd, 3rd and subsequent waves, in some cases, manifestations of infectious and allergic syndromes (polyarthritis, myocarditis, Reiter's, Crohn's syndromes, erythema nodosum, etc.) begin to prevail.

Material and methods.

For more than 40 years we have been dealing with the problems of clinical manifestations of diseases caused by representatives of the genus *Yersinia*.

Historically, clinically and epidemiologically, the Plague stands apart in this group. However, the most "old" representative of the genus is *Y.pseudotuberculosis* (discovered in 1884), which was considered a rare disease for a long time after the discovery of the pathogen. However, in the 60s of the 20th century, the situation changed and the registration of cases of both infection caused by Y.pseudotuberculosis and, later, Y.enterocolitica, as well as other "new" *Yersinia*, began to increase rapidly. From this we can conclude that this group of microorganisms is quite actively developing and new pathogens / infectious diseases are appearing before our eyes, actively filling the niche of the human population.

We analyzed the clinical course of infection caused by *Y.pseudotuberculosis* (Pseudotuberculosis) i and infection caused by *Y.enterocolitica* (Yersiniosis or Intestinal Yersiniosis) mainly admitted to the Infectious diseases Hospital in Almaty city. Thus, the selection of patients imposes certain restrictions:

- hospitalized patients, therefore, the disease was quite severe for them;

- to the clinic of infectious diseases [12], which means that many syndromes, on the one hand, such as Crohn's disease, acute terminal ileitis / appendicitis, on the other hand, such as pneumonia or rheumatism, fell into other clinics and fell out of our field of vision.

Nevertheless, additional studies conducted by us in the relevant clinics allow us to conclude that our studies have sufficiently covered the spectrum of clinical manifestations and, therefore, the objectivity of ideas about diseases caused by *Y.pseudotuberculosis* and *Y.enterocolitica* (Yersinioses).

Discussion

Clinical manifestations of Yersinioses]13].

The onset is usually acute, with a sudden, chilling increase in temperature, the appearance of general intoxication and local manifestations.

There are three main variants of the onset of Yersinioses:

a) with a general febrile (primary generalized) syndrome – in 36.1- 41.4% of patients (fever, accompanied by chills and the development of general

intoxication, enlargement of the liver and spleen (hepatolienal syndrome), without pronounced local symptoms);

b) with lesions of the digestive system – in 31.6 – 36.6% (less pronounced temperature reaction and general intoxication, the development of dyspeptic phenomena – nausea, vomiting, abdominal pain, diarrhea);

c) with lesions of the respiratory system in 27.0 – 27.2% of patients (development against the background of fever and general intoxication – sore throat and catarrhal inflammation of the upper respiratory tract mucosa).

There are other more rare variants of the onset of Yersinioses – with lesions of the mucous membrane of the genital tract, skin, conjunctiva of the eyes (depending on the mechanism of infection).

According to the duration, the course of Yersinioses is conditionally divided into acute (1-2 months); subacute (3-5 months) and chronic (6 or more months) [14].

According to the severity of the course of Yersinioses, it is divided into mild, moderate and severe.

The division of Yersinioses into clinical forms, their relationship with the phases of the infectious process and the mechanism of infection is given in Table 1.

	Groups of forms	*Primary focal (with regional manifestations)*	*Generalized*	*Secondary-focal (with regional manifestations)*
Localization of the entrance gate" of infection (infection through…)	Skin	*Cutaneous*	Secondary-generalized	Hepatitis Pneumonic Meningoencephalitic Mixed Septic other poorly differentiated forms
	Gastrointestinal tract	*Intestinal* **Abdominal**		
	Respiratory tract	**Acute respiratory** *Purulent tonsillitis*		
	Sexual pathways	**Genital**		
	Unknown immunosup-pression)	Not manifested	**Primary-generalized**	
Clinical periods	Incubation	Initial (1-3 days)	Full swing	Aggravations and Complications
Phases of the infectious process	Implementation and initial adaptation	Primary-focal and regional manifestations	Generalization (hematogenic dissemination)	Secondary-focal and regional manifestations

Table 1: Clinical - pathogenetic classification of Yersinioses [15].

Primary focal forms.

Cutaneous form (develops in isolated patients, or under certain conditions of outbreak - cutting and working with sick animals - contact wound infection). It is characterized by an inflammatory lesion of the skin, manifested by diffuse hyperemia and edema resembling erythematous erysipelas. Unlike erysipelas, the formation of bubbles is uncharacteristic. Abscesses, phlegmons, regional lymphadenitis, liver enlargement may occur [16].

Acute respiratory form (observed in 11-14% of patients). The leading syndrome in this case is acute inflammation of the mucous membrane of the upper respiratory tract, as well as fever and intoxication [17].

We separate also **Purulent Tonsillitis form** (in 4-7% of patients). It is characterized by the development of purulent or necrotic lesions of the tonsils against the background of damage to the upper respiratory tract and general intoxication. The liver is often enlarged, the heart suffers [17].

Intestinal (gastrointestinal) form (develops in 19-25%). It proceeds with a predominant lesion of the gastrointestinal tract in the form of various combinations of gastritis, enteritis and colitis syndromes. General intoxication and temperature reaction are less pronounced than in other forms. Dehydration may occur, especially in children.

We separate also **Abdominal form** (patients of which, as a rule, are admitted to surgical hospitals). It is characterized by a combination of syndromes of acute appendicitis, terminal ileitis and mesenteric adenitis.

Genital form (with lesions of the genital tract) develop quite often, but as a rule they are not diagnosed. They are manifested in women in the form of colpitis, adnexitis, and urethritis; in men in the form of urethritis and prostatitis. It is often the cause of infertility, miscarriages, intrauterine infection.

Primary generalized (or Febril) form (is in 30-35% of patients). It is characterized by all signs of acute generalized infectious disease – fever, hepatolienal syndrome, general intoxication, in the absence of local symptoms of both primary and, at least for some time, secondary foci. Corresponds to the stage of generalization of the infectious process, from which the disease immediately begins, due, apparently, to a certain degree of immunosuppression.

Secondary-focal forms.

Pneumonic form (about 7% of patients). It is characterized by the development of pneumonia (usually after Purulent Tonsillitis or Acute Respiratory forms), which is the leading sign of the diseas [18].

Hepatitis form (11-13% of patients), usually after Intestinal or Abdominal forms. It is characterized by the development of acute parenchymal hepatitis, jaundice, liver enlargement. [19,20]

Meningoencephalitic form (1-2%). The phenomena of serous or mixed meningitis and encephalitis develop, as a rule, it proceeds benign, but in rare cases, it can lead the patient to death [21,22].

Mixed form is indicated by us with the development of two different secondary foci.

Septic form (2-6% of patients). It is characterized by the development of several secondary foci at once, the defeat of many organs and systems, and a progressive acyclic course]23].

There are other poorly differentiated secondary forms with lesions of the kidneys [24], joints, lymph nodes, the development of abscesses of different localization, etc.[25].

Conclusion

Clinical diagnosis presents certain difficulties due to the significant “polyfocality” and variety of clinical manifestations. However, it is this "polyvisceral ity", the combination of several sometimes completely different syndromes, the desire to make several diagnoses to the patient, that is precisely the first of the signs that make it possible to suspect Yersinioses. They are characterized not so much by some pathognomonic signs (which are not present), as by their combinations.

One of the most characteristic is the combination of generalized exanthema (more often of a spotty-papular nature) and generalized polyadenopathy. This combination is extremely characteristic, almost pathognomonic for Yersinioses.

Fever, enlargement of the liver, less often of the spleen, damage to the gastrointestinal tract, respiratory system, cardiovascular, urinary and reproductive systems are also typical.

Thus, the clinical diagnosis of Yersinioses is based on a characteristic combination of a number of signs.

Some help can be provided by the dynamics of changes in the peripheral blood picture, which is characterized by a tendency to neutrophilic leukocytosis in the initial period (1 wave – 1-3 days), radically changing from the end of the first week (5-7 days – the beginning of the second wave) to a tendency to leukopenia, neutropenia and relative lymphocytosis.

Suspicion of Yersinioses should be caused by cases of a typical syndrome (exanthema – polyadenopathy – fever – intoxication – damage of liver – intestines – tonsils), however, even in such cases, laboratory - etiological confirmation of the diagnosis is necessary.

On the other hand, all the syndromes described above should be examined for Yersinioses.

References

1. Dmitrovskaya T.I., Dmitrovskiy A.M. (1989). Yersinioses in Kazakhstan- Alma-Ata, 1984.- 144 p.
2. Dmitrovskiy A.M., Dovgal G.D. Disease caused by Y. enterocolitica in farm animals// Problems of infectious diseases- Alma-Ata, - pp. 79-82.
3. Syzdykov M.S., Dmitrovskiy A.M., Rashat B.S., Cirelson L.E., Okapov N.K. et al. (1998). Yersinioses – ecology, epidemiology, epizootology and the basics of the organization of preventive work: Guidelines- Almaty- 12 p.
4. Stepanov V.M., Dmitrovskiy A.M., Ospanov K.S., Merker V.A., Karimova G.A., et al. (2003). Methodological recommendations on epidemiology, epizootology, prevention, clinic, treatment and laboratory diagnosis of Yersinioses- Astana, - 47 p.
5. Stepanov V.M., Bezrukova L.S., Arkhangelskaya N.P., Dmitrovskaya T.I., Dmitrovskiy A.M. et al. (1979). Some properties of the causative agent of Pseudotuberculosis isolated from people in Alma-Ata//Abstracts of the X Scientific Conference of Anti-plague institutions of Central Asia and Kazakhstan- Alma-Ata- pp. 205-207
6. Bezrukova L.S., Stepanov V.M., Arkhangelskaya N.P., Dmitrovskaya T.I., Dmitrovskiy A.M. et al. (1979). Properties of causative agent of Pseudotuberculosis and Intestinal Yersiniosis isolated in humans // Healthcare of Kazakhstan- N 8. - pp. 51-53.
7. Stepanov V.M., Bezrukova L.S., Dmitrovskiy A.M. (1991). Microbial landscape of *Yersinia* as a prognostic criterion for assessing the health of the population // In the book: Modern problems of assessing the driving factors of public health- Almaty - pp. 164-168.
8. Dmitrovskaya T.I., Dmitrovskiy A.M. (1985). Forms of the course of Yersinioses infection // Healthcare of Kazakhstan- N 8.- pp.51-54.
9. Dmitrovskiy A.M. (1985). Yersinioses (Pseudotuberculosis and Yersiniosis) clinical and pathogenetic classification // Materials of the IV Joint Congress of Hygienists, Epidemiologists, Microbiologists, Parasitologists and Infectious Disease specialists of Kazakhstan. - Shymkent, - pp. 146-148.
10. Isin Zh.M., Tugambayev T.I., Dmitrovskiy A.M., Suleymenov B.M. (1987). The role of endotoxin in the pathogenesis of Yersinioses and Plague infection// Bacterial toxins- Moscow, - pp. 51-54.
11. Shishkina T.S., Dmitrovskiy A.M., Isin Zh.M., Tugambayev T.I. (1992). Oscillatory reaction of humoral-cellular immunity during experimental infection with pathogens of the genus *Yersinia*// Organization of surveillance in case of Plague and measures of its prevention: Materials of the interstate scientific and practical conference.- Alma-Ata, Vol. III.- pp. 464-466.
12. Dmitrovskiy A.M., Karabekov A.Zh., Stepanov V.M., Bezrukova L.S., Syzdykov M.S. et al. (2001). Yersinioses in the clinic of infectious diseases // "Issues of tuberculosis and other infectious diseases": Proceedings of the Kazakh State Medical University, Almaty, -Part III.- pp. 75-80.
13. Dmitrovskiy A.M., Syzdykov M.S., Rashat B.S., Cirelson L.E., Okapov N.K. et al. (1999). Yersiniosis – clinical manifestations, treatment and the basics of the organization of medical care: Guidelines- Almaty, - 14 p.
14. Dmitrovskiy A.M., Dmitrovskaya T.I., Stepanov V.M., Bezrukova L.S. (1985). Outcomes and consequences of Pseudotuberculosis and Yersiniosis// Materials of the Congress of Infectious Diseases- Tashkent, - pp. 75-77.
15. Dmitrovskiy A.M., Dovgal G.D. (1983). Three cases of the cutaneous form of Yersiniosis // Clinical medicine- - N 4.- pp. 77-78.
16. Dmitrovskiy A.M. (1985). Pseudotuberculosis and Yersiniosis with respiratory damage. I. Acute Respiratory and Purulent Tonsillitis forms // Proceedings of the XII Inter-republican Conference of Anti-plague institutions of Central Asia and Kazakhstan- Alma-Ata, - pp. 253-255.
17. Dmitrovskiy A.M. (1985). Pseudotuberculosis and Yersiniosis with respiratory damage. II. Pneumonic forms // Proceedings of the XII Inter-republican Conference of Anti-plague institutions of Central Asia and Kazakhstan- Alma-Ata, - pp. 255-257.
18. Dmitrovskaya T.I., Dmitrovskiy A.M. (1985). Pathology of the liver in Yersinioses//Successes of hepatology-Riga-N 11.-pp.65-71.
19. Dmitrovskaya T.I., Dmitrovskiy A.M. (1991). Hepatitis of Pseudotuberculosis etiology // Problems of infectious and non-infectious pathology of the hepatobiliary system. - Ashgabat, - pp. 138-139.
20. Dmitrovsky A.M., Dobritsa V.P., Nekrasova L.E., Meka-Mechenko T.V., Kugach I.V. et al. (1998). Clinical manifestations and classification of Yersinioses// Nederlands Tijdschrift Voor Medische Microbologie: Materials of 7th International Congress on Yersinia-Nijmegen, - Supp. lI.-Vol. 6 June- P.37.
21. Dmitrovsky A.M., Nekrasova L.E., Meka-Mechenko T.V., Ryabushko Ye.A., Kuzmin Yu.A. et al. (1996). Fatal case of Pseudotuberculosis in humans// Ecological aspects of epizootology and epidemiology of plague and other particularly dangerous infections: Materials of the scientific conference- Almaty, - pp.15-16.

22. Dmitrovskaya T.I., Dmitrovskiy A.M., Kuchina N.N. (1980). Septic form of Yersinioses// Septic diseases: Materials of the plenum of the Scientific Council of the USSR Academy of Medical Sciences- Tbilisi, - pp. 159-161.
23. Dmitrovsky A.M., Nekrasova L.E., Meka-Mechenko T.V., Kugach I.V., Turegeldieva D.A. (1998). Pseudotuberculosis meningoencephalitis//Nederlands Tijdschrift Voor Medische Microbologie: Materials of 7th International Congress on Yersinia-Nijmegen - Supp. lI.-Vol. 6 June- P.38.
24. Turegeldieva D.A., Nekrasova L.E., Meka-Mechenko T.V., Dmitrovsky A.M., Dernovaya V.F. (1998). *Yersinia* in the pathology of the urinary system//New organizational and therapeutic and diagnostic technologies in medicine: Proceedings of the Conference of young medical scientists- Almaty- pp. 64-65.
25. Dmitrovsky A.M., Ogay Ye.A., Abentayeva B.A., Tynybekov A.S. et al. (2002). Outcomes of Yersinioses in children // In the dook: *Infectious diseases*- Almaty, pp. 48-51.