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GROUP FOOD POISONING DUE TO PASTEURELLA PSEUDOTUBERCULOSIS

Acta Gastroentero Belg. 29:341-50, 1966 P. Desmet and E. Vanussel

Introduction

Pseudotuberculous pasteurellosis has been known since 1883; Malassez and Vignal described the agent that causes this disease; but the disease as such was not properly described until 1889 by Pfeiffer. This was a rodent disease which involved only veterinary medicine until Saisawa (Tokyo) in 1909 reported a complete observation of deadly septicemia in man, caused by the bacillus of Malassez and Vignal.

During the following years, a number of similar observations were published, including those by Lorey in Germany (1911), by Roman in 1916 and by Neugebauer in Czechoslovakia (1933), by Paul and Weltmann in Austria (1934), by Dujardin-Beaumetz in France (1938), by Topping in the United States, by Machiavello in Brazil, by Moss and Battle in 1941, and by Mason and Meyer in the United States in 1948.

The listing of these few cases, which have been described in medical literature, seems to prove that this disease is extremely rare in man; it seems that the disease is found primarily among animals, both domestic and wild, and that it is found all over the world.

In 1910, however, Albrecht in Austria reported another form of human pseudotuberculosis. This was a localized form, described under the name of suppurative follicular enteritis. This observation, like all of the others, was forgotten so that, in 1953, there was still doubt as to the precise etiology of this follicular enteritis.

At last, Masshoff and Knapp in Germany demonstrated that the bacillus of Malassez and Vignal was the causal agent of this disease. Since then, hundreds of similar cases have been diagnosed, particularly in France and Germany, so that the disease has now been pretty well identified.

What are we dealing with, as a matter of fact, when we speak of pseudotuberculous pasteurellosis?

Recalling the first observations of Saisawa and Albrecht, we distinguish two forms: the generalized or septico-typhoidic form, which most frequently is deadly, and the localized or benign form, in other words, mesenteric adenitis.

1. Mesenteric Adenitis

We can only briefly sketch the very thorough studies devoted to this subject recently by Masshoff and Knapp in Germany, by Girard and Mollaret in France, and by Daniels in Holland. In passing we might note that a number of

articles have been published on this subject in Belgium, particularly by Callens and Van de Voorde (1961) and by Bruynoghe and Wauters (1964).

The symptomatology here is the same as that of the classical mesenteric adenopathies: most frequently we are dealing here with the appendicular syndrome which does not enable us to judge the nature of the lesions; only laparotomy or serological tests can tell us something about that.

The discovery of adenites in the process of abscess formation, sometimes even pseudotumoral, without any attack on the appendix, although often involving the small intestine, is the determining factor in the laboratory research intended to bring out the role the agent of pseudotuberculosis pasteurellosis plays in causing this disease. This is why we remove some ganglions, during the operation, in order to make culture seedings and this is also why we determine, in the serum, the agglutinins titer with respect to various strains of pseudotuberculosis pasteurella, from I to V.

We must note, however, that we can find some particularities, enabling us to outline our diagnosis, already during the clinical stage. First of all, we are dealing here with young or adolescent subjects, mostly male. We note the absence of any contration, the paraumbilical seat of the pain, and the perception of a mass corresponding to the adenopathy. In the medical history, we can often find evidence of contact with animals. Finally, the disease occurs mostly during the cold seasons.

This disease is always benign and recovery is either spontaneous or comes due to the effect of streptomycin, or it comes after surgical intervention. This surgical intervention is necessary in cases with uncertain etiology and in case of complications (peritonitis, invagination).

2. The Septicotyphoidic Form

On the basis of a personal observation in 1964, we would now like to go into detail in discussing the pathogenicity and pathology of this very serious form.

Observation. V. P. Joseph, born on 7 September 1964 [sic], a man 49 years old, a joiner by profession, came to our clinic. At that time he had a very definite [open] icterus; he had fever with almost daily chills. He complained of headaches and said that he felt sick. He was anorexic and felt pain in the right hypochondrium and in the epigastrium.

Clinical examination revealed some additional important features; we found a hypertrophied right-hand amygdala, without any acute inflammation, a submaxillary ganglion on the right side, the size of a pea, a number of small axiliary ganglions, and finally a slightly squamous polymorphous erythema, on the level of the inside of the shank in the region of the triangle of Scarpa. The liver was sensitive to pressure and protruded beyond the right-

hand costal edge by 1-2 cm.

The disease began around 5 August of that year; on that date, our patient, along with 16 other people, had eaten the leftovers from a wedding dinner the day before. The leftovers had been kept overnight in the cellar of the farm house.

About 24-36 hours after having eaten this meal, everyone of the 17 people here revealed the signs of acute gastro-enteritis, with nausea, vomiting, stomach pains, diarrhea, and fever. We must note that none of the participants in the wedding dinner - that is those others who did not eat the leftovers from the wedding feast -- revealed any sickness whatever and that another four individuals who did not eat the leftovers did not have any trouble. About five days later almost all of them recovered, either spontaneously or as the result of the usual treatment for gastro-enteritis, although a certain asthenia did persist for several days and in some cases for several weeks.

But the history of our patient was much longer. After this short period of gastro-enteritis the patient did not recover completely and complained of headaches with rachialgias, lumbalgias, and pains in the arms and legs and, finally, sometimes nighttime perspiration.

On 17 August he felt quite sick and took his temperature for the first time; he found that his temperature was 38.5° C. Then, every evening around 1700 hours, he felt a similar surge of fever; this situation continued for about 5 weeks.

The icterus appeared on 19 August; during the further development of the disease, he came up with bloody sputum and melena. During the fever period, which came before his admission to our clinic, he was given various antibiotics (Madribon, Terramycin, Sigmamycin) and we gave him Palliopen and Ambrasynth, without any results, however.

We must note, however, that the administration of Bactocilline 1200 for 3 days was followed by a drop in temperature. Unfortunately, for reasons which we do not know, the administration of this substance was suspended and not resumed, in spite of a new surge of fever (figure 1).

This is the medical history background at the time we admitted the patient on 7 September, in other words, one month after the beginning of the symptoms.

In view of this very strange clinical picture, the differential diagnosis appeared to be particularly delicate. We contemplated the possibility of salmonellosis, with vesicular localization and with localization also in the bile ducts (cholecystitis with cholangitis), an abscess of the liver, and infectious hepatitis (microbial or parasitary).

The radiological examination of the thorax and of the abdomen

revealed only an enlarged liver. The biological study revealed the following: leucocytosis: 25,000; accelerated sedimentation: 50 mm (Linzmeyer); bilirubinemia: 2.8 mg%; alkaline phosphatases: 7.1 U. Bessey-Lowry; COT: 140 U; GPT: 190 U; flocculation test: slight right-hand deviation; hypergammaglobulinemia: 31.4%; urobilinuria: positive.

These results correspond to those obtained in hepatitis. But the etiological problem had not been solved as yet.

Two blood cultures, taken on 15 and 22 September, remained sterile; the same happened in the case of coproculture (22 September), bile culture (16 September), and urine culture (28 September). There was no eosinophilia. The serological results of 19 August were just as disappointing.

Salmonella typhi O: 1/20.
Salmonella typhi H: 1/20.
Salmonella paratyphi A O: negative.
Salmonella paratyphi A H: negative.
Salmonella paratyphi B O: 1/160.
Salmonella paratyphi B H: negative.
Salmonella typhimurium H: negative.
Brucella abortus Bang: negative.
Brucella melitensis: negative.

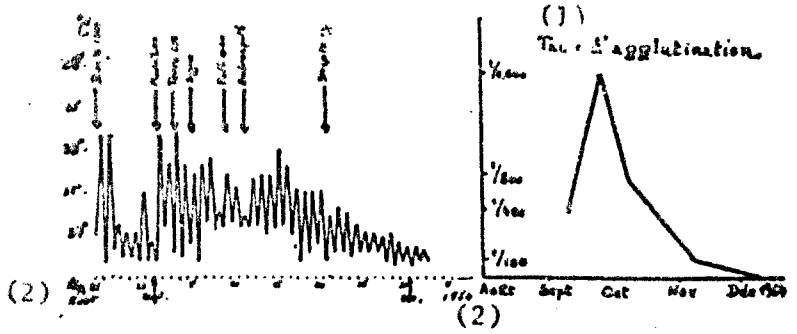

Figure 1. -- Figure 2. [Legend]: 1 -- agglutination titer; 2 -- August.

In short, this left us just about where we started out and we did not even manage to come up with a valid hypothesis as regards the etiological diagnosis.

But a happy combination of circumstances nevertheless enabled us to solve the problem. We were rather struck by the odd agglutination titer for paratyphus B O (1/160). This is why we asked for a check on this reaction

... this is also why we came at the same time, informed the section under Professeur Bruynoghe as to the condition of our patient.

With great perspicacity, which is certainly highly praiseworthy here, he simultaneously performed agglutinoreactions with respect to paratyphus B O and with respect to five strains of the bacillus of Malassez and Vignal. In particular, there are common antigens between these two groups (Toucas, Girard and Le Minor, 1956; Knapp, 1960).

The type II of the bacillus of Malassez and Vignal that time gave us a positive seroagglutination at a rate of 1/400.

As soon as we learned of this result, that is to say, on 21 September, we instituted a streptomycin cure (1 g per day) and, starting on 25 September, in other words, 4 days later, our patient no longer had any fever and remained afebrile. The icterus decreased progressively, his appetite and general condition improved, and the patient was able to go home on 3 October although streptomycin treatment was continued (1 g every other day).

During the following weeks, the patient had a new attack of icterus; little by little, his complaints returned, along with the headaches, the rather vague stomach pains and the intestinal cramps. We also noted a weight loss of 3 kg.

The liver still protruded beyond the costal edge by about half a finger and remained sensitive to pressure. We were able to spot a number of periumbilical painful points and additional painful points in the two iliac fossa.

Here are the biological results (Table I).

TABLE I

	Dates	1954					1953	
		8.9	13.9	22.9	9.11	9.12	13.1	8.2
	Hb (%; /g %)	104		—	14,2	—	15	13,5
(1)	Globules rouges	5 010 000	4 250.000	—	4 800.000	—	4.630.000	4.780.000
(2)	Globules blancs	22 000	21 600	—	4,700	—	6.400	7.800
	Sédimentation	50 mm	45 mm	—	15 mm	—	115 mm	Normal
(3)	Glycémie (mg %)	109	—	—	80	—	102	—
(4)	Urémie (mg %)	49	55	—	—	—	—	—
	Thymol-test	10,6	11,2	13,3	40	11,3	9,6	5,8
	Weltmann	0,8	0,7	0,8	0,8	0,8	0,8	0,7
	Kunkel	18,3	19,4	22,5	50	24,2	24	18,1
	Cholestérol (mg %)	150	127	127	238	176	236	241
(5)	Cholestérol estérifié	—	—	—	99	52	181	117
(6)	Bilirubinémie (mg %)	2,8	1,6	1,8	1,8	—	—	0,8
	BSP	—	—	—	—	—	—	2 %
(7)	Phosph. alc. (BL)	7,2	4	6	7,5	2,4	1,8	2,0
	Electrophorèse:							
	albumine	—	43,12	—	50,76	—	—	63,69
	α^1-globulines	—	7,13	—	2,52	—	—	3,94
	α^2-globulines	—	8,49	—	4,68	—	—	6,83
	β-globulines	—	9,79	—	9,33	—	—	9,83
	γ-globulines	—	31,46	—	31,77	—	—	17,13
	GOT	140	62	172	190	13	12	13
	GPT	190	113	340	260	16	19	13
(8)	Formule:							
	Neutrophiles	85	79	—	59	—	80	72
	Eosinophiles	—	1	—	10	—	4	3
	Basophiles	—	—	—	3	—	—	—
	Lymphocytes	15	20	—	28	—	24	25
	Monocytes	—	1	—	1	—	2	—
(9)	Eosinophiles (par mm³)	—	—	—	—	650	—	111

Legend: 1 — red blood corpuscles; 2 — white blood corpuscles; 3 — glycemia [blood sugar]; 4 — uremia; 5 — esterified cholesterol; 6 — bilirubinemia; 7 — electrophoresis; 8 — formula; 9 — per.

We must note the following here: the hypergammaglobulinemia, which was on the increase at that moment, the flocculation tests which were disturbed to the maximum extent, and the increased eosinophilia.

The results of electrophoresis on agar-gel and of the lactodehydrogenases revealed an attack upon the liver with necrosis of the chronic hepatitis type; we were rather worried about this development of the disease, recalling the high death rate from the septicemic forms.

Next we made a laparoscopy. The liver, rather pale in the left half, revealed very irregular spots with an even lighter tone. The edge was definitely discolored for a depth of about 1-2 cm. The surface was not smooth; instead it was slightly irregular, dotted with many small unevenesses. These uneven points undoubtedly corresponded to the subjacent zones of necrosis. This was undoubtedly the postnecrotic aspect of a microbial hepatitis with multiple foci. The biliary vesicle looked normal; the spleen was not visible; we did not discover any mesenteric ganglia; the colic vascularisation was turgescent.

In view of these results, we decided to combine the streptomycin,

which the patient was still getting, with chloramphenicol (1 g per day for about a dozen days), thus hoping to achieve a synergic action.

To our great and happy surprise, we saw our patient begin on 9 December in a truly excellent state: he no longer revealed the slightest trace of icterus; his subjective complaints had disappeared completely and the biological tests turned out quite normal, among others, the transaminases and the flocculation tests. The eosinophilia was increased even further and this appeared to be a rather likely indication of the recovery phase, following an acute infection.

Further checkups on 13 January and 3 March 1965 confirmed complete recovery (Table I). In the meantime, our patient regained his normal weight.

During the disease, we were able to trace the evolution of the agglutination titer with respect to pseudotuberculous pasteurella, type II. We noted that clinical recovery was paralleled by the disappearance of the agglutinins in the serum: 11 September 1964: 1/400; 21 September 1964: 1/1600; 5 October 1964: 1/800; 9 November 1964: 1/800; 9 December 1964: 0 (figure 2).

TABLE II

		Past. Ps. II	Pseudotbcs II O
1. M. V.P.J.	(21. 9.1964). .	(a) 1/1000	1/160
2. Mme V.P.J. - W.	(28. 9.1964). .	M4qualif	M4qualif
3. M. V.D.K. Alf.	(28. 9.1964). .	1/400	M4qualif
4. Mme V.D.K. - G.	(28. 9.1964). .	M4qualif	M4qualif
5. M. V.P. Em.	(28.10.1964). .	1/400	—
6. Mme V.P.E. - V. Dek	(28. 9.1964). .	1/800	—
	(27.10.1964). .	1/1600	—
7. V.D.K. Gust	(1.10.1964). .	1/800	1/160
8. V.D.K. Jan	(1.10.1964). .	1/400	M4qualif
9. V.D.K. Jef	(1.10.1964). .	M4qualif	M4qualif
10. V.D.K. Leo	(1.10.1964). .	1/400	M4qualif
11. V.D.K. Willy	(1.10.1964). .	M4qualif	M4qualif
12. V.D. Gust	(27.10.1964). .	1/200	—
13. M. J. Aug.	(28.11.1964). .	1/200	—
14. Mme J.A. - V.D.K.	(28.11.1964). .	1/400	—

Legend: a — negative; M. — Mr.; Mme. — Mrs.

This infection turned up in the form of a group food poisoning case; this is why we made a serological examination of the other persons who ate the food involved: out of the 17 people, altogether, we were able to reach 14. The results of this investigation are shown in Table II, above.

We thus obtained 9 valid positive results, all of them for strain II — and this about 1-3 months after the infection!

A minimum rate of 1/200 may be considered positive. On the other hand,

we remember the usual serological evolution: although the antibody titer decreased progressively, it does increase to a maximum, just before it begins to decrease. In all of these cases, the negative result [negativation] occurs within a variable period of time, somewhere between 1 and 4 months, in proportion to the level of the rate reached earlier.

We were able to make our epidemiological investigation only 2 months after the infectant meal had been consumed; we therefore could no longer analyze the food that had been eaten on that occasion. We know that contamination occurs primarily through rodents and cats; these animals very often are the carriers of healthy germs; we therefore made a pathological anatomy examination of the mice and rats caught on that farm. We were unable to discover any pseudotubercular lesion. We did not encounter any dogs or cats on the farm and the cattle, during that time, did not reveal any signs of sickness.

This observation of group food poisoning, in our opinion, constitutes food for thought.

Pseudotuberculous pasteurellosis is considered to be a rather rare sickness in our part of the world; it may look to be just that, because we never even think of diagnosing it. On the other hand, we believe that this disease is much more widespread than we might assume on the basis of the number of cases reported. This infection is very widespread among rodents (guinea pigs, rabbits, hares) and in certain domestic animals (rats, mice, cats, pigeons, etc.); these animals are capable of contaminating man directly or by soiling his foods; it is logical to assume that human infection should be more frequent than we realize today.

Contamination almost always occurs via the digestive tract. Until 1961, we did not have any direct proof of this; all we had was the finding that almost all of the lesions were located along the digestive tract; in other words, we only had an assumption to go on. In 1961, Daniels in Rotterdam furnished the proof when, for the first time, he managed to obtain a positive coproculture in man. Since then, several investigators (Kampelmacher, Bruynoghe) obtained the same results.

We believe that our observation is the first to describe group toxi-infection of food origin, caused by the bacillus of Malassez and Vignal.

We are convinced that, in our observation here, the meal was contaminated in the cellar of the farmhouse during the night, since none of the people who ate the food only during the wedding dinner became sick. It is probable that mice or rats or perhaps a cat soiled the food during the night. Although our pathological anatomy examination of several rodents caught on the spot was negative, we must note that this examination was not made until 3 months after the infection.

Although this is also the first time that we were able to determine the exact moment of the infection, we nevertheless cannot estimate the

incubation time because, in our patients, the symptoms occurred in the same fashion as in food poisoning due to staphylococcus or salmonella.

Looking over the published articles dealing with this pseudotuberculous pasteurella infection, we note that the various authors make a very clear distinction between the two forms of this sickness. On the one hand, the benign and localized form, mesenteric adenitis, only attacks children and adolescents in the vast majority of cases; on the other hand, the malignant form, the septicotyphoidic form, attacks only adults. Mollaret, however, described several cases of mesenteric adenitis with subicterus. In 1962, Masshoff had emphasized the absence of a dividing line between these two extreme aspects. The recent observations by Mollaret, Daniels, Knapp, and Bruynoghe confirm this viewpoint.

We believe, as do these men, that this infection, which, like the salmonelloses, preferably attacks the lymphoid tissues of the digestive tract, may -- like all of the other infections -- occur in different degrees of seriousness; this degree of seriousness would depend here on the intensity of the contamination and the degree of individual resistance. We would like to set up the assumption that the most common form of human infection involving the bacillus of Malassez and Vegnal is acute, subacute, or chronic gastroenteritis, both in children and in adults. In younger people, however, the lymphatic barrier of the intestine is more easily hurdled and the infection would thus spread into the regional ganglia, thus giving rise to mesenteric adenitis. It is a rather common-place finding that children react very easily to any infection by means of a hypertrophy of the ganglia. It is only after this second barrier has been cleared that the germs can attack the liver and the spleen via the portal and lymphatic routes, forming multiple microabscesses. These are the lesions which cause the symptomatology of the septicemic form.

In this second form, the disease usually starts quite abruptly by a sudden rise in the temperature which may go as high as 39-40° C, accompanied by headaches, myalgias and pains in the arms and legs. Digestive signs are also always present: their nature and intensity varies greatly and they can range from nausea all the way to acute gastroenteritis. Hepatomegaly is almost always found here, with subicterus or with open icterus; sometimes we find splenomegaly. The patient complains of abdominal pains, either in the right-hand hypochondrium and the epigastrium, or in the right-hand iliac fossa. The situation rapidly becomes worse: headaches and adynamia become more and more intensive and precede obnubilation and the terminal coma.

An attack on the lymphoid tissue is sometimes clinically manifest, with epistaxis, amygdaline and ganglionary attacks, hemoptysis, and intestinal hemorrhage. Finally, pink spots have been reported on the skin.

We must note that the onset of the disease is not always abrupt and that it sometimes spreads over one (Mollaret, 1964) or several weeks (our observation). We were able to save our patient because of this slower evolution of the disease.

The best medication here is streptomycin, possibly combined with chloramphenicol. Of course, the experience derived from just one observation is certainly not enough to come up with any rules to be followed in treatment. We administered streptomycin at the rate of 1 g per day until the disappearance of the acute symptoms; then we reduced the rate to 1 g every 2-3 days for many weeks to follow. Complete recovery was achieved only after 2 weeks of treatment; combined the chloramphenicol at the rate of 1 g per day for a period of 10 days, with the success we just reported.

Conclusion

This disease, which is due to the bacillus of Malassez and Vignal, does not appear to be as rare as we thought and may appear in various forms; we therefore believe that, in the case of mesenteric adenitis, gastro-enteritis, infectious hepatitis, and even food poisoning, we should -- certainly in a rural environment -- envisage the possibility of infection with pasteurella pseudotuberculosis.

Since we do have effective medication in this case, it is our duty to keep this disease in mind so as to be able to make an early diagnosis, when the time comes. In this case, it will be enough to perform sero-agglutinations with the strains of the five types of pasteurella pseudo-tuberculosis or the culture of pathological products (ganglia). Culture using urine and coproculture may also be useful; we must however remember that pasteurella pseudotuberculosis does reveal many morphological and biochemical characteristics which it shares in common with other germs of the intestinal flora; this means that its identification is a rather delicate matter and it would always be a good idea for the clinician to inform the biologist as to the possible presence of this agent in the product to be analyzed.

Summary

The authors report a case of infection with pasteurella pseudotuberculosis of the septicemic form. They follow through with a clinical description of this disease which is probably more frequent than it would generally be assumed to occur. The diagnosis was made on the basis of seroagglutination tests (for five types of germs). The treatment is effective.