TRICHINOSIS

A REPORT OF THREE CASES SIMULATING MENINGITIS, WITH THE FINDINGS OF TRICHINA LARVAE IN SPINAL FLUID *

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Since Van Cott and Lintz[1] first reported the findings of trichinae in the spinal fluid, there have been reports by Bloch,[2] Elliott,[3] Lintz,[4] Cummins and Carson,[5] and Salzer[6] confirming the observation. These reports do not emphasize the occurrence of meningeal symptoms. Bloch particularly emphasizes the presence of trichinae in the spinal fluid without any symptoms referable to the brain and cord. He says, however, that "the presence of a positive Nonne and Noguchi would indicate meningeal irritation." Elliott mentions a positive Kernig sign, but asserts it is a false Kernig and one due to pain. Bloch and Hassin[7] report a case of trichinosis in a young man, who developed a left-sided hemiparesis, and showed exaggerated knee jerks, a bilateral Babinski reflex, and left-sided ankle clonics. No trichinae were found in the spinal fluid. The following cases are reported because of the definite meningeal symptoms, the changes in the spinal fluid, and the difficulties encountered in early diagnosis.

At the Cook County Hospital, all patients enter the receiving ward, where an examining physician makes a diagnosis. The patient is then sent to the proper ward. In the three cases herein reported, the patients entered the contagious disease hospital, Jan. 4, 1918, with an examining-room diagnosis of epidemic meningitis. The three are members of the same family. No history was obtainable, except from the oldest girl, who is about 12 years of age.

REPORT OF CASES

CASE 1.—S. P., girl, aged 6 years, was sick six days with headache and vomiting. There was no diarrhea and no abdominal distress. The patient, an Italian child, was brought to the ward in an irrational state. The striking feature of the case was marked irritability, in spite of which, the child responded when told to show her teeth, put out her tongue, etc. There was a marked edema of both upper eyelids. The temperature on admission was 100.1 F., the pulse was 112 and the respiration, 24. There was a definite rigidity of the neck, and when the child was lifted by the head, she cried. Photophobia was present. There were a few crusts on the nose but no herpes on the lips. The heart and lungs were normal. There was no tenderness, but an uncertain degree of general rigidity about the abdomen. The liver was negative and the spleen was not palpable. There was tenderness over the extremities. The Kernig sign was strongly positive. The knee jerks were absent and there was no Brudzinski's sign. The spinal fluid was under increased pressure, was clear and showed 58 cells per cubic millimeter; the Nonne reaction was positive and Ross-Jones' test, negative. Haines solution was reduced. The presence of lymphocytes was observed, but there were no organisms. On the basis of these findings, a diagnosis was made as follows: The clinical manifestations of the patient pointed to a definite meningitis. The character of the spinal fluid, together with the absence of knee jerks, pointed to a poliomyelitis, although there was no evidence of paralysis.

The next day, the child was extremely sick. Her temperature was 103, and her pulse, 96. The Brudzinski and the Kernig signs were positive. There was an edema of the legs and the eyes, as well as marked tenderness over the extremities, particularly over the right elbow when held in a position of flexion. The blood count revealed a leukocytosis of 8,000, and an eosinophilia of 10 per cent. Spinal puncture was repeated and revealed fifty cells which were lymphocytes. The fluid was under increased pressure. Trichinae were found, two or three in a field. The Nonne reaction was positive and Ross-Jones' test, negative. Haines solution was reduced. A section of muscle removed from the biceps on the same day showed unencapsulated trichinae. Blood was removed, Jan. 10, 1918, from a vein in the elbow, and examination was delayed until Jan. 14, 1918. It was examined according to the technic of Herrick and Janeway, and many trichina larvae were found. The blood count, January 11, revealed a leukocytosis of 11,000 and an eosinophilia of 8 per cent. As the patient was observed, the edema of the eyelids and the legs grew less, and muscular tenderness was definitely localized; but stiffness of the neck persisted, as well as the Kernig and the Brudzinski signs. The patient was transferred to the Children's Hospital.

CASE 2.—D. P., boy, aged 8 years, who had been sick four days, was admitted to the hospital, Jan. 4, 1918. He was a brother of the child described in the foregoing. He was unable to rise and looked sick. His face was swollen, particularly about the eyelids. His older sister said he had been sick for four days with headache and vomiting. The temperature on admission was 101.8; pulse, 110 and the respiration, 28. The head was large and square. There was a marked edema of the upper eyelids, particularly of the left, which almost closed the eye. There was a herpetic sore on the upper lip. The throat was congested. The heart and the lungs were normal. The abdomen was not tender, but there was a degree of general rigidity present. Neither the liver nor the spleen was palpable. In both axillae, there were numerous small pinpoint hyperemic spots, which tended to fade on pressure. Both the upper and the lower extremities were tender to touch. There was an infected vaccination mark over the left upper extremity. The Kernig sign was strongly positive and the knee jerks exaggerated. The Babinski reflex was doubtful. A spinal puncture was made, and the spinal fluid was under increased pressure, being clear and showing fifty cells per cubic millimeter. The presence of lymphocytes was observed. The Nonne reaction was positive and Ross-Jones' test, negative. Haines solution was reduced. A diagnosis, as in the former case, was made as follows: The physical findings were very suggestive of a meningeal inflammation or irritation, but the etiologic factor was uncertain. Vigorous catharsis was then ordered. Two days later, the patient had definite soreness of the muscles and edema of the legs and the eyes. The blood count revealed a leukocytosis of 30,000 and eosinophilia of 50 per cent. Repeated blood counts revealed a leukocytosis of 15,000 and an eosinophilia of 15 per cent. Another differential revealed an eosinophilia of 24 per cent. The boy improved rapidly. Another special puncture was made two days after admission, but was bloody (traumatic). The blood was examined for trichinae, but none were found. No examination of the muscle was made.

CASE 3.—T. P., girl, aged 12, was the oldest of the three children brought to the ward with a diagnosis of meningitis. She said she had been sick for about two days, complaining only of headache and stiffness of the neck. There was no other history. She did not appear very sick. The temperature was 100.8, and the pulse, 88. The head was negative and eyes were watery as if she had been crying. Both eyelids were swollen and edematous. There was no photophobia.

* From the Contagious Hospital of Cook County Hospital.

1. Van Cott, J. M., and Lintz, William: Trichinosis, THE JOURNAL A. M. A., Feb. 28, 1914, p. 680.
2. Bloch, Leon: Trichinosis; Report of a Case with the Trichina Larvae in the Spinal Fluid, THE JOURNAL A. M. A., Dec. 18, 1915, p. 2140.
3. Elliott, A. R.: Trichinosis; Report of a Case with Trichina Larvae in the Spinal Fluid, THE JOURNAL A. M. A., Feb. 12, 1916, p. 504.
4. Lintz, William: Trichinosis and the Cerebrospinal Fluid, THE JOURNAL A. M. A., June 10, 1916, p. 1856.
5. Cummins, W. T., and Carson, G. R.: A Case of Trichinosis with Embryo in the Spinal Fluid, THE JOURNAL A. M. A., June 10, 1916, p. 1856.
6. Salzer, B. F.: A Study of an Epidemic of Fourteen Cases of Trichinosis with Cures by Serum Therapy, THE JOURNAL A. M. A., Aug. 19, 1916, p. 579.
7. Bloch, Leon, and Hassin, G. B.: Med. Rec., New York, 1917, **91**, 537.

Herpes were present on upper lip. There was a small amount of rigidity of the muscle of the neck, which was apparently not voluntary. The heart and the lungs were apparently normal. The abdomen revealed a slight tenderness in the region of the spleen, but the spleen was not palpable. There was a slight rigidity of the abdomen. There was no pain or tenderness over the extremities, except in the left elbow joint, but it was difficult to localize pain definitely. No evidence of any paralysis was discovered.

The Kernig sign was positive, both knee jerks were absent, and the Brudzinski sign was negative. Forty c.c. of the spinal fluid were removed. It was under increased pressure, was clear, and showed 240 cells per cubic millimeter, and lymphocytes. The Ross-Jones test was negative and the Nonne reaction positive.

The findings present were suggestive of a meningitis. The character of the spinal fluid, on the contrary, suggested poliomyelitis, which diagnosis was further supported by the absence of knee jerks and pain in the region of the elbow.

Jan. 5, 1918, there was no change. The Kernig sign was positive and there was a suggestion of Brudzinski's sign. The throat was congested. The skin of the abdomen revealed a few red pinpoint areas, not petechial, and unlike rose spots, which fade on pressure. There was pain in the region of the elbow anteriorly and not over the joint. The rigidity of the neck was only moderate.

January 6, there was headache with pain in the legs, arms and back. The patient had difficulty in sitting up, and in elevating the right arm. There was no evidence of paralysis. Knee jerks were now present but were hard to elicit. The Kernig sign persisted. The blood count revealed a leukocytosis of 10,800, and an eosinophilia of 8 per cent.

January 7, the patient was very sick, with a temperature of 103 and a pulse of 110. A spinal puncture was made. The spinal fluid was under increased pressure, and the first portion was bloody. When it was examined, actively motile ous trichinae were found.

January 11, the spinal puncture was repeated. The fluid was clear, was under increased pressure, and showed eighty cells per cubic millimeter, as well as the presence of lymphocytes. Trichina larvae were present. The Nonne reaction was positive and the Ross-Jones test negative. The Haines solution was reduced. The nitric acid test for albumin was negative. The biceps muscle was harpooned, and actively motile trichinae were found. The blood examination was made according to Herrick and Janeway technic, and numerour trichinae were found.

No history of the eating of ham, pork or pork sausage was elicited from the children or parents. Subsequently the mother was admitted to the medical ward of the hospital, and gave a good diarrheal history, but no trichinae were found in the muscles.

COMMENT

If we analyze the foregoing it will be observed that we are dealing with three cases showing distinct meningeal symptoms. Also in two of these, the spinal fluid containing the trichina larvae showed marked cellular increase. Van Cott and Lintz,[1] Bloch[2] and others have suggested the possibility of meningeal irritation due to the presence of trichinae in the spinal fluid. None of the previous reports mention any increased cell count. Van Cott and Lintz[1] observed a moderate increase in pressure, as well as a gray sediment on standing. The centrifuged specimen showed a number of lymphocytes and failed to reduce Fehling's solution.

Elliott[3] counted 3 cells per cubic millimeter. Cummins and Carson report a count of 3 cells. Lintz[4] reports an occasional lymphocyte and failure to reduce Benedict's solution in three cases.

The spinal fluid in our cases, as already noted, was clear and under increased pressure. The cell count was as high as 240 and as low as 40 per cubic millimeter. The Nome reaction was positive, the Ross-Jones' test was negative, and Haines solution was reduced. The nitric acid test for albumin was negative. We consider this as definite evidence of meningeal irritation. Our record shows a similar evidence in Case No. 2, in which no trichinae were found in the spinal fluid. It is unlikely that the toxemia associated would cause these changes, and there is a possibility that the trichinae were overlooked in the examination of the spinal fluid. That the meningeal symptoms are very likely due to meningeal irritation is in accord with definite changes in the spinal fluid, so that two of the cases might be called meningitis due to trichina. While it is true that a Kernig sign may be due to muscular swelling and edema, nevertheless the Kernig sign in these cases was present before the edema developed. The edema noted was not similar to the ordinary type, which pits on pressure, but was rather hard, glistening and boardlike, particularly over the extremities. Granting a false Kernig sign, on what basis other than meningeal irritation are we to explain the stiff neck, the suggestive Brudzinski sign, the exaggerated knee jerk (in one case), and the headache and vomiting, unless the cause could possibly be the toxemia? But toxemia cannot account for the cellular change in the spinal fluid.

I wish to call attention to the necessity of differentiating these early cases with meningeal symptoms from poliomyelitis. Van Cott and Lintz state that "in children marked weakness of the limbs is present," and report one case in a child of 8 years, in whom locomotion was difficult because of the great prostration. In Case 2, the patient was unable to arise on the examining-room table and stand, unless supported. In the other two cases, the patellar reflexes were absent. In addition, tenderness was present over the extremities, and patients complained of pain on pressure. In children, it is at times difficult to determine whether one is dealing with a perineuritis or a myositis, as the pain response is very readily obtained. When, in addition to these factors, a physician examines the spinal fluid, and finds it clear, under increased pressure, and observes a cell count ranging from 240 to 40, he may justly suspect poliomyelitis in the absence of any evidence of paralysis. The diagnosis of trichinosis, however, is established by the occurrences of edema, the presence of an eosinophilia in the blood picture, and the isolation of the trichinae from the spinal fluid or muscle.

The high eosinophilia of 50 per cent., in Case 2, and the comparatively low eosinophilia in the other two children, who were extremely ill, is in accord with the observations of Opie,[8] to the effect that the more severe the infection the lower the eosinophilia, and vice versa. In this connection I should also like to make the following observations:

In Case 3 the patient, who was the oldest of the three, developed an urticaria. By many physicians urticaria is considered an anaphylactic reaction. It is known that in the postanaphylactic stage there is an increase in eosinophilia (Herrick[9]). Accordingly, a differential count was made when the urticaria first appeared, and was found to be 12 per cent. Twenty-four hours later it was 10 per cent.

SUMMARY

1. Trichinae in the spinal fluid in two cases produced definite clinical symptoms of meningitis.

8. Opie, E. L.: Am. Jour. Med. Sc., 1904, **127**, 217, 477.
9. Herrick, W. W.: Experimental Eosinophilia with an Extract of an Animal Parasite, Arch. Int. Med., February, 1913, p. 165.

2. The spinal fluid in trichinosis, in addition to the trichinae, showed an increase in lymphocytes, from 240 to 40 per cubic millimeter, reduced the Haines solution, and gave a positive Ross-Jones test.

3. Trichinosis with meningeal irritation must be differentiated from poliomyelitis.

THE DREYER METHOD OF AGGLUTINATION

AS USED AT THE ARMY MEDICAL SCHOOL*

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That agglutination tests, made after typhoid and paratyphoid vaccination or after the diseases themselves, may have uniformity and comparable values, the following technic, a slight modification of that of Dreyer,[1] is offered.

The method consists simply of macroscopic agglutination tests on varying dilutions of serum, using a killed culture of *B. typhosus* or *B. paratyphosus* A or B, the agglutinability of which has been determined by titration against a given standard, established by the Department of Pathology, University of Oxford.

The necessary apparatus is readily available, and consists of a Wright's capsule, for securing blood; about thirty small test tubes, chemically clean, but not necessarily sterile; one 1 c.c. pipet, graduated in tenths, such as used in Wassermann work; one 2 c.c. pipet for making the dilutions; a few ounces of physiologic sodium chlorid solution, not necessarily sterile; and a quantity of the standard culture. By comparison with this standard culture, a new supply may be made for extended work.

The technic for the test is quite simple. Sufficient blood is taken in the capsule to yield 0.3 c.c. of serum. This amount is withdrawn in a pipet and transferred to the first tube. This tube has previously received 2.7 c.c. of saline solution, while the following nine tubes have each received 1.5 c.c. of saline solution. Of this first 1:10 dilution of serum, 1.5 c.c. are carried into the second tube, mixed thoroughly, and 1.5 c.c. of this 1:20 dilution is carried forward. This procedure is carried out through the series of ten tubes, the last 1.5 c.c. being discarded. Beginning in the weaker dilution, the diluted serums are each divided into three tubes, each tube containing 0.5 c.c. of the serum dilution. The tube rack then contains three series of ten tubes containing serum dilutions ranging from 1:10 to 1:5,120.

To each tube in the first series, 0.75 c.c. of the standard culture of *B. typhosus* is added; to each tube of the second series, 0.75 c.c. of the standard culture of *B. paratyphosus* A is added; and to each tube of the third series, a like amount of the culture of *B. paratyphosus* B is added. The tubes are then thoroughly shaken.

The tubes are then placed in a water bath at from 50 to 55 C. for two hours; are removed and cooled for fifteen minutes, and are then read. The highest dilution showing agglutination, without sedimentation visible to the naked eye, gives the reading. The dilution of the serum in this tube, divided by the factor of agglutinability of the culture used, gives a final reading expressed in the number of agglutinin units per cubic centimeter of the serum. (It must be kept in mind that the addition of the culture has increased the dilution of the serum one and a half times, the first tube representing a dilution of 1:25, the last a dilution of 1:12,800.) These readings are comparable with each other, whenever the same technic has been used, and a standard agglutinable culture has been used.

If it becomes necessary to make up a new supply of the standard agglutinable culture of *B. typhosus*, the procedure is as follows: *B. typhosus* is subcultured daily in broth, for about ten days, to increase its agglutinability and reduce its auto-agglutinability. Finally it is planted in broth in partly filled flasks and incubated twenty-four hours. At the end of that time, 0.1 per cent. formaldehyd solution (full strength) is added, it is placed in an ice box for four or five days, and it is shaken repeatedly. The then sterile culture is ready to be standardized for (1) opacity and (2) agglutinability.

To standardize for opacity, two series of fifteen tubes each (tubes of equal size and of clear glass) are set up, and varying dilutions of standard culture in one series, and the culture under standardization in the other, are made in accordance with the accompanying schedule.

DILUTIONS

Culture—														
0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.2	1.4	1.6	1.8	2.0
Physiologic sodium chlorid solution—														
1.9	1.8	1.7	1.6	1.5	1.4	1.3	1.2	1.1	1.0	0.8	0.6	0.4	0.2	0.0

A tube from one series, chosen at random, is matched for opacity with the tubes in the other series. The dilution of each culture in these tubes is noted. This procedure is repeated six times and the average taken. The necessary dilution of the new culture is thus determined, the dilution to be made with physiologic sodium chlorid solution, to which has been added 0.1 per cent. formaldehyd solution. It is then to be bottled and kept in the ice box.

To standardize for agglutinability, an immune serum is procured. A rabbit immune serum of known agglutinin unit content is to be preferred, though human serum, taken soon after inoculation, serves the purpose. The agglutinating serum is set up in two parallel series, in varying dilutions, the variations not to be excessive. To one series the standard culture is added, to the other the culture under standardization. These tubes are then shaken, incubated at 55 C. for two hours and read for the highest dilutions showing agglutination visible to the naked eye. That dilution in the known culture is to that dilution in the new culture as the factor of the known culture is to x (the factor of the new culture).

This method is, of course, similarly applicable to the *B. paratyphosus* A and B. It is also applicable to the three strains of *B. dysenteriae* and *B. coli*, though in the latter cases, at the Army Medical School, it was necessary to establish our own standard.

The foregoing method is an ideal one for the Gruber-Widal method for the diagnosis of typhoid or paratyphoid fever in the uninoculated, and is the best method for following the resistance of the patient as expressed in agglutinin units. For the quantitative determination of antibodies produced after Army triple typhoid vaccine, it offers the only simple and practicable method that will yield results that are comparable not only within themselves, but also with the results of other workers in the same field.

For the diagnosis of typhoid or paratyphoid fever in patients previously inoculated with the Army triple typhoid vaccine, it offers a valuable adjunct to the cultivation of the organism from the blood or the stool, for it has been found that by this method, though a positive Widal exists, owing to a previous inoculation, quantitative fluctuations of the agglutinin content are indicative of active infection.

Cultures of the three types of pneumococci and of four strains of meningococci are being used at the Army Medical School in an effort to procure comparable results in determining the antibodies produced after protective inoculations. It has been found necessary to heat these cultures, in addition to the formaldehyd solution, particularly in the case of the meningococcus, to prevent autolysis.

* From the Department of Pathology, Army Medical School.

1. Dreyer, G., and Torrens, J. A.: Lancet, London, 1915, **2**, 1369.