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A CASE OF ACUTE DIFFUSE MONILIASIS PRESUMABLY CAUSED BY CANDIDA PULCHERRIMA

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With popularization of antibiotics therapy, a considerable number of reports on moniliasis attributable to the antibiotics have appeared in the recent literature. However, only a few cases of acute diffuse moniliasis have been reported in the Japanese literature. Recently we have encountered a case of acute diffuse moniliasis presumably *Candida pulcherrima* and wish to make a somewhat detailed report.

CLINICAL FINDINGS

Patient, a 35 year old man with no significant family or past history, had been perfectly well till December 31, 1952 when started having chill and fever (38°C), general malaise, and backache. He was given by an attending physician 600,000 units of procain penicillin in oil during the first two days and 3gm of aureomycin in the following two days with no improvement. It was on the fifth day of illness January 4, 1953, that we made the first examination on the patient.

Physical Findings: The patient is fairly well nourished, sensorium clear but the countenance somewhat apathetic and the face slightly flushed. The skin moist, showing no exanthema, edema or jaundice. Lymph nodes not palpable. The pulse quality normal, numberring 80 per minute. The body temperature 38.3°C. The breathing regular and chest-abdominal type. Pupils normal. Cyanosis negative. The tongue thickly coated grayish white. Soor not detectable. The tonsils free from inflammation and the chest normal. Careful palpation of the abdomen reveals no masses or ascites. A tender, somewhat firm liver is palpable two fingerbreadths below

the right costal margin. The spleen and kidneys can not be felt. The knee-jerk is normal but the ankle-jerk somewhat weakened. Sensomotoric disturbances negative.

Clinical Course: The patient was kept at his home during the entire course. In spite of aureomycin 2 gm daily for four days, the fever kept remittent between 37° and 39°C. On the 6th day the patient complained of intense headache and sometimes fell into delirious state. From the next morning the Kernig's sign and rigidity of the neck were demonstrated. A lumbar puncture was normal except for a slightly elevated pressure. These symptoms of meningismus continued for the next 6 days (Fig. 1).

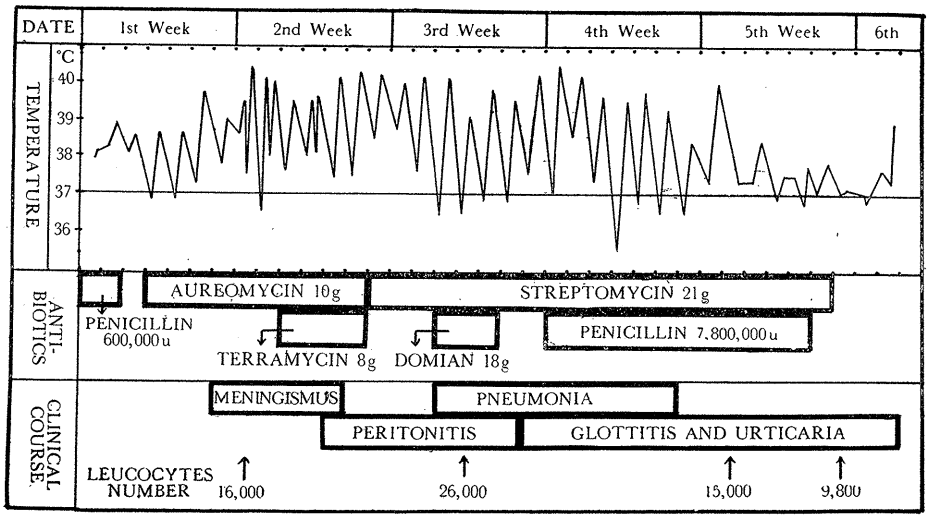

Fig. 1 Clinical Course and Antibiotics

During the 12th and 17th day there was seen such symptoms of purulent peritonitis as muscular defense noted chiefly in the lower abdomen, and leucocytosis. Since, however, the aureomycin and terramycin treatment showed no effect upon the remittent fever (40°C), persistent sweating and chill during these days, we began to speculate that this case might be a sepsis due to some unknown organism which is resistant to the usual antibiotics.

Between the 14th and 27th day the patient was given an injection of 0.5 gm of streptomycin twice daily.

From the 17th day he complained of cough, phlegm and palpitation. Dullness and crepitation were noticed in the left-lower-back of the chest at first, and then gradually on the other side. X-ray findings on the 24th day showed a bronchial pneumonia and congestion in both lungs and a

slight cardiac enlargement in both directions.

From the 17th day 6 gm of Domian (6-sulfanylamide-2, 4-dimethyl-pyrimidine) was given daily and there seemed some degrees of temperature fall, but it had to be given up owing to a serious anorexia. From the 22nd day 600,000 units of penicillin-G was injected beside streptomycin. From the 20th day urticaria appeared on the general body surface and these had grown hemorrhagic two or three days later. Also glottitis appeared at the same time. The liver was reduced to 1.5 fingerbreadths, and the spleen was not as yet palpable.

On the 30th day we encountered a mycosis from the routine blood culture, but did not take it seriously, at first, since at that time the patient's conditions were somewhat improved and, moreover, the mycosis did not have the figures of *Candida albicans*.. However, on the 32nd day, when the same mycosis was demonstrated again on the blood culture, we had to make the diagnosis of moniliasis.

Although the treatments with antibiotics were discontinued then, the patient died on the 37th day owing to the gradually increasing debility.

Laboratory Data: Leucocytosis was noticed throughout the course of illness and in the end stage a degenerative change of leucocytes was noticed. The Widal's and Weil-Felix's reactions were negative. Albuminuria was slightly positive and urobilinogen was positive during the entire course of illness. The blood spectrum by Shibata [1] was as shown in Table I;

TABLE I

Laboratory Examination

	Normal range	8th day	22nd day	35th day
Hemoglobin	14 - 18 g/dl			14.0
Hematocrit	40 - 50 %			43.4
Serum protein	6.5 - 8.0 g/dl	6.3	5.5	4.8
Albumin	3.8 - 4.8 g/dl	3.0	2.3	1.4
Globulin	2.5 - 3.5 g/dl	3.3	3.2	3.4
A/G	1.2 - 1.8	0.9	0.7	0.4
Gros' reaction	1.0 - 1.2 ml	0.85	0.71	0.51
Serum icteric index	4 - 6		4	9
1-min. bilibrin	0 - 0.2mg/dl			0.1
Total bilirubin	0.2 - 0.5mg/dl			0.7
Serum cholesterol	160 - 300mg/dl		135	180
Blood sugar	70 - 100mg/dl		97	140
Serum cholinesterase	0.8 - 1.1 ⊿pH	0.3	0.2	0.2
Serum alkaline phosphatase	1 - 4 U.			7.9
Serum inorganic P.	2 - 5 mg/dl			3.2
Zinc turbidity test	3 - 16 U.		7.8	14.2
Popper's turbidity test	3 - 6 U.		2.9	3.6
Thymol turbidity test	0 - 5 U.		1.4	1.0
Phenol turbidity test	8 - 15 U.		1.5	6.3

i. e. a marked decrease of serum cholinesterase activity was noticed from the beginning of the disease. Day by day the serum protein, serum albumin and A/G ratio was decreased and Gros' reaction and phenol-turbidity test had turned positive. The liver biopsy specimen on the 35th day revealed an intra-cellular jaundice, a slight degree of cell degeneration and a slight degree of increase of connective tissue.

Treatment: Supplementary treatments were given as follows; Vit.B_1 and glucose in the 2nd week; Vit.B_1, Vit.B_2, Vit.B_6, Vit.B_{12}, methionine and glucose for liver disturbance after the 3rd week; blood and plasma transfusion for a treatment of hypoproteinemia after the 4th week. Cardiac stimulants were used as required.

Diagnosis: Acute diffuse moniliasis (sepsis, endocarditis, bronchopneumonia, liver-functional disturbance)

Autopsy Findings

An autopsy was performed but permission to examine the brain could not be obtained.

Gross Examination: Each lung revealed a figure of catarrhal pneumonia with scattering of yellowish-white, half-miliary foci and a picture of pulmonary sclerosis. The liver was spotted with yellowish-white, half-miliary foci, and was jaundiced. The heart cavity was dilatated and the muscle atrophic. The spleen was slightly enlarged. The peribronchial lymph nodes were swollen. The kidneys revealed a picture of 'large white kidney'.

In addition, the following pictures were revealed; pericarditis obliterans, pleuritis adhaesiva bilateralis, perisplenitis adhaesiva, a slight degree of peritonitis fibrosa, erosion of oral and gingival mucosa, primary tuberculous focus in the left upper pulmonary region, and a state of malnutrition.

Microscopic Examination: The lung revealed an interalveolar congestion with thickening of alveolar wall in some regions. There were large mononuclear or polymorphnuclear cells in the alveoli, many of which showing granulation and vacuolization. A small number of lymphocytes, polymorphnuclear leucocytes and fibrin were demonstrated. From the foregoing pictures the lung may be said to present a figure of pneumonia desquamativa. These changes were unequal in some regions. The small nodules composed of epitheloid cells, the cells resembling Langerhans's giant cells, and fibroblasts were scattered all over the lung tissue. These nodules were generally inclined to have a strong fibrosis, but in some regions showed a central coagulation necrosis. The bronchioles were filled with the same exudative cells as mentioned above. Groups of Gram-positive yeast-like fungi were noted in the exudate of bronchioles and alveoli (Fig.2 and 3).

The heart muscle was atrophic, presenting brown pigmentation and granular degeneration.

The liver sinusoids were dilated, the liver cells markedly dissociated and part of their protoplasm was turbid and contained bilirubin pigments. Small necrotic foci with infiltration of leucocytes and monocytes were sporadically found in the hepatic parenchyma. A slight degree of proliferation of connective tissue and its invasion into hepatic parenchyma were demonstrable (Fig. 4).

The splenic follicles were nearly extinguished. The walls of the central artery were coarse and showed a fibrous swelling. The splenic medulla revealed a congestion of blood and proliferation of connective tissue.

The lymph nodes revealed a decrease of lymphocytes with marked congestion.

The kidneys showed a swelling of Bowman's capsules, a small number of glomeruli showed hyaline degeneration; atrophy of tubular epithelium and proliferation of interstitial connective tissue were also observed. In short, the kidneys revealed a picture of subacute glomerulo-tubular nephritis. However, no necrotic foci were demonstrated.

Bacteriological Examination

At autopsy the aspirated fluid specimens from heart blood, lung, liver, spleen and kidneys were cultured on the Sabouraud agar plate. By this procedure the same mycosis was demonstrated from heart blood, lung and kidneys (Fig. 5). This mycosis was the same as that obtained from the blood during the illness. This mycosis caused no mortality either in rabbit or rat. This mycosis was presumed to be *Candida pulcherrima* (Lodder, 1952) after the following tests, viz., Sabouraud agar, Sabouraud bouillon, slide culture, plaster culture, fermentation test for sugar and utilization test for sugar.

Discussion

In foreign countries quite a number of reports concerning the diffuse moniliasis have been presented, but in our country only a few cases[2)3)4)5)6)] are recorded in the literature. Furthermore, we have seen no clinical report on *Candida pulcherrima* which is not fatal to rabbit and rat. Although this mycosis showed no harmful effect on animals, yet it seems reasonable to assume that this mycosis must be the causative agent for death of the patient, since it was detected in his blood while he was alive, and no other pathogenic organisms was demonstrated, despite the fact that the clinical symptoms and pathological findings were clearly those of sepsis. Woods,

et al[7] noted that antibiotics directly accerelate this developement of candida. By what process the candida harmless to animals could have caused the disease fatal to this patient is a matter which offers problems for further study from this standpoint of relationship between antibiotics and the mycosis.

The facts that the mycosis was noted most abundantly in the lung tissue and that specific histological changes for moniliasis were present in the lung suggests a rather strong affinity of the mycosis to the lung.

The mycosis cultured from the aspirating fluid from the kidneys seemed to be supplied from the blood or urine in the kidneys, because no necrotic foci were detected in the kidney tissue. Although other organs showed variable degrees of changes, yet no candida was found in them. It seems that the candida in the blood was suplied from the lung.

Conclusion

We presented a case of acute diffuse moniliasis presumed to be *Candida pulcherrima*. The pathologic changes were found chiefly in the lung, pericardium, liver and kidneys. But the mycosis had no fatal effect on the experimental animals.

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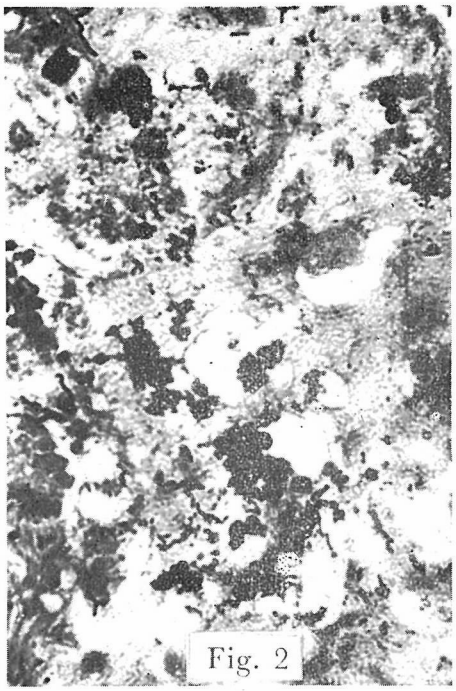

Fig. 2

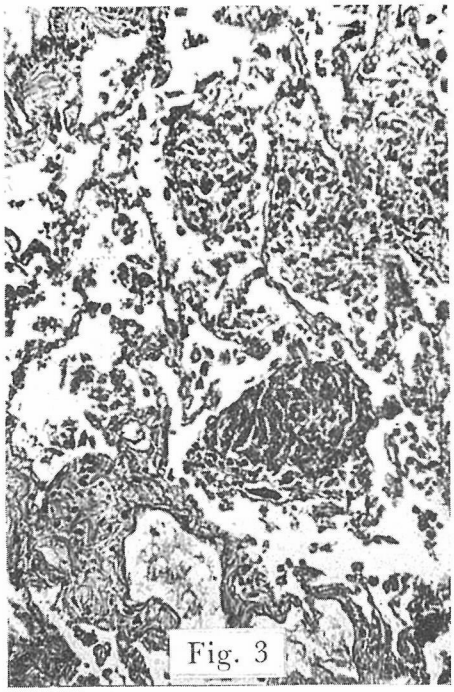

Fig. 3

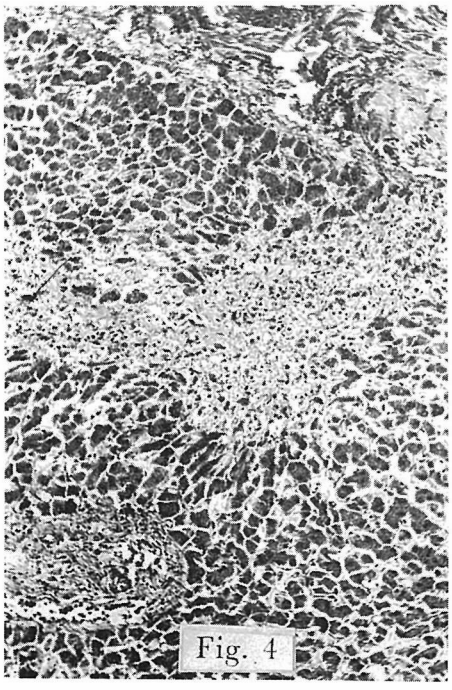

Fig. 4

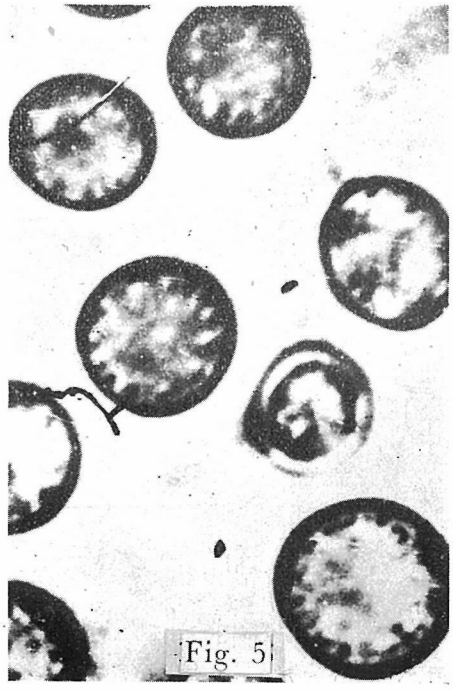

Fig. 5