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Multiple Organ Failure Followed by Intrauterine Klebsiella Pneumoniae Infection Associated with Diabetes Mellitus

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A 49-year-old semi-conscious woman was admitted due to fever and dehydration. Disseminated intravascular coagulation (DIC), renal dysfunction and diabetic ketoacidosis were detected. Whole body computed tomography showed multiple nodular lesions in bilateral lungs and kidneys indicating septic emboli, and intrauterine lesions. We diagnosed multiple organ failure followed by intrauterine infection due to untreated diabetes mellitus. Vaginal discharge and blood culture revealed Klebsiella pneumoniae. We used multi-antibiotics for sepsis, respirator at low tidal volume ventilation, 200mg of sivelestat sodium hydrate and 300mg of hydrocortisone for respiratory failure, gabexate mesilate and anti-thrombin III for DIC, transfusion for bleeding from uterus and regular insulin aiming for a blood glucose range of from 80 to 140mg/dl. When we extracted the myoma uteri, the patient's fever subsided and the C-reactive protein became negative. Treating diabetes mellitus is important for the prevention of severe infection. (Kitakanto Med J 2009；59：151～155)

Key Words： intrauterine infection, diabetes mellitus, multiple organ failure

Introduction

The incidence of infection is higher than normal in diabetic patients and complications that result in death are more frequent.[1,2] However, multiple organ failure induced by intrauterine infection associated with poorly controlled diabetes mellitus is rare.[3,4] Impaired leukocyte functions such as chemotaxis and bactericidal activity in diabetic patients have been shown.[5] Impaired monocyte chemotaxis has also been reported.[6] Abnormalities in the microvascular circulation of diabetic patients generally result in decreased tissue perfusion,[7] and such abnormalities may facilitate the acquisition of infection and impair response to therapy. Here, we report a case of multiple organ failure followed by intrauterine Klebsiella pneumoniae infection associated with diabetes mellitus.

Case report

A 49-year-old semi-conscious woman came to our hospital due to fever and dehydration. She had suffered from general fatigue for the previous 4 weeks and from fever, thirst, polydipsia and polyuria for the previous 7 days. She had been unable to get out of bed for the previous two days. Her weight was 60kg at 20. Her maximal weight was 63kg at 22. After that the weight had gradually decreased to 55kg at 25. She was normally delivered at 26 and 29. Diabetes mellitus had not been indicated during this period. From 30, her weight ranged from 55 to 56kg. Hypermenorrhea occurred at 42, and then diabetes mellitus and myoma uteri were indicated. However, she was not treated for the disease at this time. She recognized bilateral foot numbness at 48 and her weight fell from 55 to 48kg in a year. Other disease had not been indicated. She neither smoked nor drank alcohol. Her father also had diabetes mellitus. Her physical examination showed the following: height 150.5cm, weight 48kg (body mass index: 21.2kg/m^2), blood pressure 110/50mmHg, pulse rate 113/min, respiratory rate 24/min, temperature 38.5°C, lack of consciousness

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(30 by Japan Coma Scale). Funduscopic examination showed proliferative diabetic retinopathy. There were no abnormalities in the neck or chest. Lower abdominal tumor was palpable. There was no tenderness in the abdomen. There was no skin eruption. Diminished deep tendon reflexes and bilateral foot paresthesia indicated diabetic neuropathy. Laboratory data were as follows: chest X-ray film showed bilateral multiple granular lesions in the bilateral lung field (Fig. 1). Electrocardiogram was within normal range. Urinalysis showed glycosuria (+), proteinuria (100mg/dl), acetone 2+ and blood 3+ with casts (red blood cell count 4400/μl, white blood cell count 230/μl). The white blood cell count was 32300/μl (basophil 1%, eosinophil 1%, segmented leukocyte 66%, lymphocyte 23%, monocyte 8%); the red blood cell count was $328\times10^4/\mu$l and hemoglobin; 8.8 g/dl. Platelet count; $6.1\times10^4/\mu$l, prothrombin time (INR), 1.41 and fibrin degradation product (FDP) 59.1μg/dl, indicating disseminated intravascular coagulation (DIC). Liver function was normal. C-reactive protein (CRP) was 27.5 mg/dl, blood urea nitrogen; 81.7 mg/l, creatinine; 2.4 mg/dl, sodium; 114 mEq/l, potassium; 5.5 mEq/l, chloride; 75 mEq/l, total protein 5.5 g/dl, albumin 2.0 g/dl, total cholesterol; 107 mg/dl, high density lipoprotein-cholesterol; 5 mg/l and triglyceride; 258 mg/dl. Fasting blood glucose was 503 mg/dl and HbA1c; 13.7%. The glutamic acid decarboxylase (GAD) antibodies were negative. The urinary C-peptide was 40μg/day, An urinary protein excretion rate of 1.05 g/gCr indicated diabetic nephropathy. Blood gas analyses showed pH 7.214, PCO_2 19.1 Torr, PO_2 88.9 Torr and HCO_3 7.5mEq/l (Table 1), indicating metabolic acidosis due to diabetic ketoacidosis (without serum acetone measurement) and systemic inflammatory response syndrome. Whole body computed tomography showed multiple nodular lesions in bilateral lungs (Fig. 2a) and kidneys (Fig. 2b), indicating septic emboli and a swollen uterus with internal low density area and air (Fig. 3). Urine culture was negative. Sputum culture showed normal flora. Vaginal discharge culture and blood culture revealed Klebsiella pneumoniae. We diagnosed multiple organ failure as a result of sepsis followed by intrauterine Klebsiella pneumonia infection due to untreated diabetes mellitus. We immediately began to administer 1000 mg of PZFX and 1800 mg of CLDM for empiric therapy to which the Klebsiella pneumonia were sensitive as well as gabexate mesilate and regular insulin. However, six hours after admission, the con-

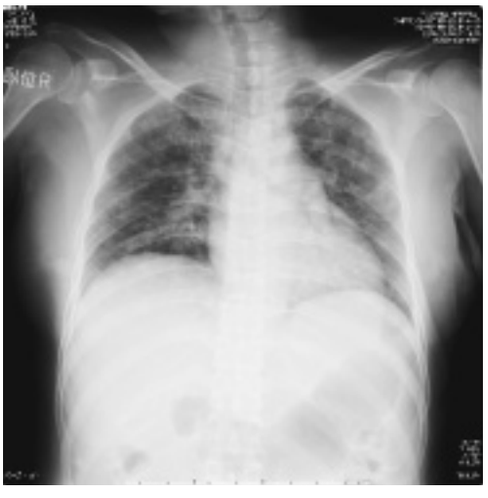

Fig. 1 Chest X-ray film shows bilateral multiple granular lesions in bilateral lung field.

Table 1 1st day

Urinalysis		Chemistry		CRP	27.5 mg/dl
protein	100mg/dl	AST	10mU/ml	FBG	503 mg/dl
glucose	1.0mg/dl	ALT	10mU/ml	HbA1c	13.7%
blood	3+	LDH	306mU/ml	GAD-Ab	0.3u/ml
aceton	2+	ALP	325mU/ml	urine CPR	40μg/day
pH	5.5	γ-GTP	25mU/ml	Coagulation	
RBC	4400/μl	total protein	5.5mg/dl	fibrinogen	281 mg/dl
WBC	230/μl	albumin	2.0mg/dl	Prothrombin time (INR)	1.41
Hematology		T-Bil	0.5 mg/dl	FDP	59.1μg/dl
RBC	$328\times10^4/\mu$l	BUN	81.7 mg/dl	Serology	
Hb	8.8mg/dl	Cr	2.4 mg/dl	STS	(—)
Ht	26.6%	Na	114mEq/l	HBsAg	(—)
MCV	81.1	K	5.5mEq/l	anti-HCV Ab	(—)
platelet	$6.1\times10^4/\mu$l	Cl	75mEq/l	Blood gas	
WBC	32300/μl	amylase	20su/dl	pH	7.214
Baso	1%	T-CH	107 mg/dl	PCO^2	19.1Torr
Eosino	1%	HDL-CH	5 mg/dl	PO^2	88.9Torr
Seg	66%	TRG	258 mg/dl	HCO_3	7.5mEq/l
Lymph	23%				
Mono	8%				

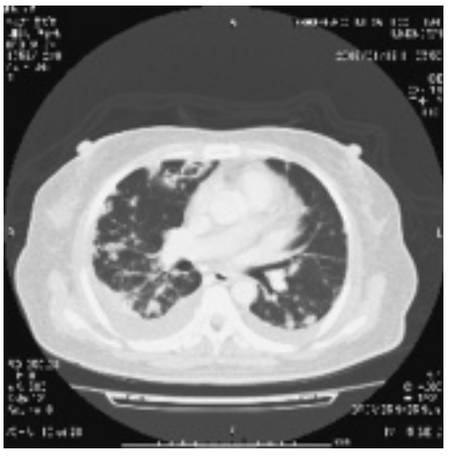

Fig. 2a Chest computed tomography shows multiple nodular lesions in bilateral lungs.

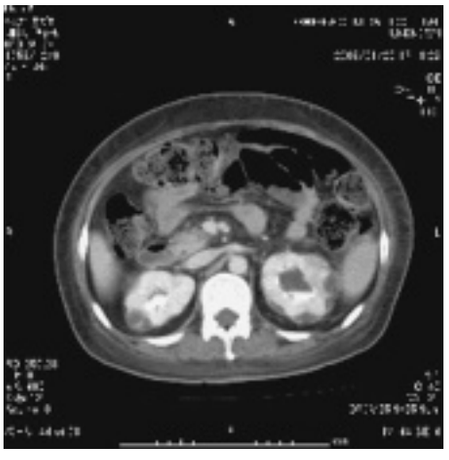

Fig. 2b Abdominal computed tomography shows multiple nodular lesions in bilateral kidneys.

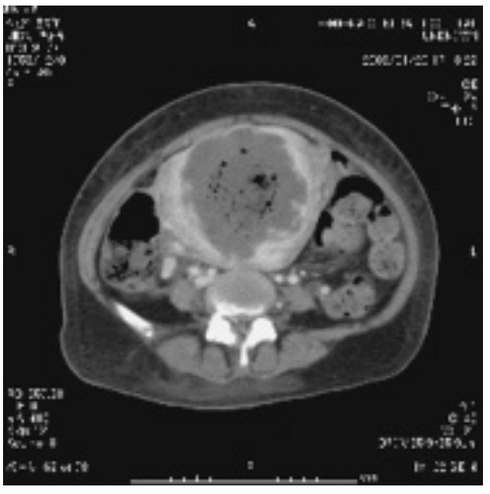

Fig. 3 Pelvic computed tomography shows swollen uterus with internal low density area and air.

sciousness level deteriorated from 30 to 100 by the Japan coma scale. Blood pressure fell and respiratory failure also deteriorated (pH 7.336, PCO_2 32.1 Torr, PO_2 54.6 Torr and HCO_3 16.8mEq/l after the inhalation of 6l/min oxygen). Then the electrocardiogram showed sinus tachycardia while axis deviation or STT change was not shown. The ultra cardiogram did not show abnormal valve and wall motion, or right ventricular dilatation. The estimated right ventricular pressure was 29.4mmHg, indicating that pulmonary septic emboli did not induce pulmonary artery pressure elevation. The patient was moved to the intensive care unit where in addition to multi-antibiotics for sepsis, a central vein pressure catheter was inserted and she was put on a respirator at low tidal volume ventilation and given 250mg of sivelestat sodium hydrate and 300 mg of hydrocortisone (for a three day period) for acute respiratory failure. In addition to gabexate mesilate, we administered anti-thrombin III for DIC and she was given a transfusion for DIC induced uterine bleeding. Administration of regular insulin aimed for a blood glucose range of 80 to 140mg/dl for intravenous hyperalimentation. When blood glucose levels fell below 60mg/dl, insulin dosage was decreased. At levels above 180mg/dl, it was increased. The patient's fever gradually decreased and her respiratory condition improved. At the 8th day the patient did not need the respirator and she became alert. We stopped intravenous hyperalimentation and started diet therapy (1440kcal) and subcutaneous insulin infusion therapy (Humalog mix 50). However, the patient's fever continued. The sputum culture showed normal flora, central venous pressure catheter culture, vaginal discharge culture, and blood culture was negative at the 9th day. However, the fever continued. So we considered MRSA infection or Pseudomonas aeruginosa infection and changed from PZFX and CLDM to 4g of PIPC and 400mg of TEIC. The CRP decreased, serum creatinine, FDP, white cell and platelet count became normal (Fig. 4). However, the patient's fever continued to be slightly elevated and the CRP ranged from 8 to 9mg/dl. Consequently, from the 17th day we changed from PIPC and TEIC to 400 mg of LVFX and 400mg of CAM daily for atypical pathogens such as the Chlamydia species. At the 20th day the whole body computed tomography showed decreased nodular lesions in bilateral lungs and kidneys fewer than on the 1st day film. At the 25th day we extracted the myoma uteri and started 0.9g of BIPM for ESBL and then 4g of ST. The myoma specimen showed coagulated necrotic change surrounding leukocyte infiltration (Fig. 5). Subsequently the patient's fever normalized and the CRP became negative. After discharge the patient continued regular diet and insulin therapy (Humalog mix 50 total dose of 20 units/day). The HbA1c ranged from 5.9 to 6.3%. The weight ranged from 50 to 51kg. The urine pro-

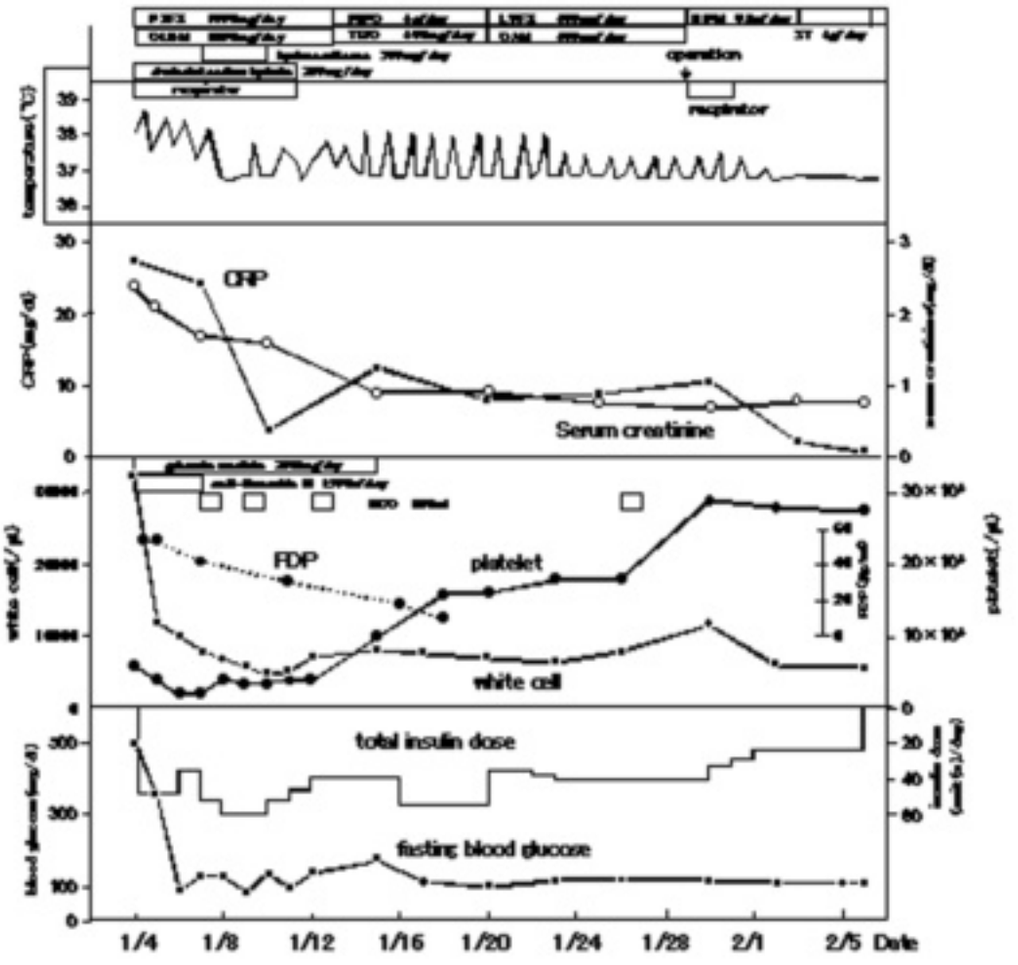

Fig. 4 Clinical course

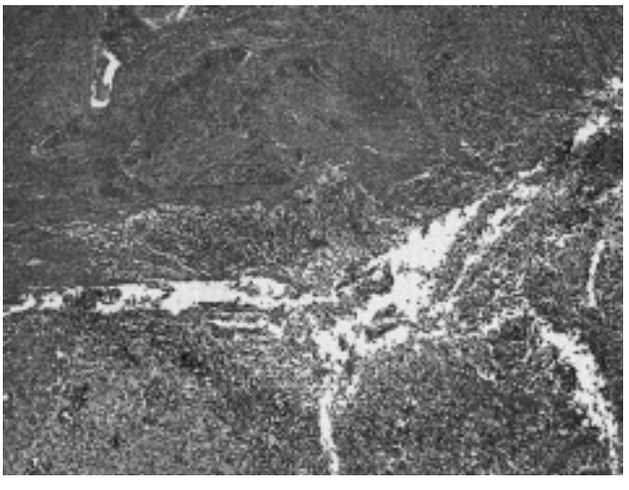

Fig. 5 The specimen of myoma uteri shows coagulated necrotic change surrounding leukocyte infiltration (×200, by hematoxylin and eosin stain).

tein ranged from 150 to 200 mg/gCr and the serum creatinine ranged from 0.8 to 0.9 mg/dl.

Discussion

The patient had clinical manifestations featuring intrauterine Klebsiella pneumoniae infection coupled with induced multiple organ failure and diabetic ketoacidosis with microangiopathy. Intrauterine infection resulting from pelvic abscess associated with poorly controlled diabetes mellitus has been shown.[4] However, these patients had pulmonary and septic complications which were induced by the infection, and were associated with carcinoma of ovary or cervix uter.[4] Our case is rare since it is not associated with malignancy. Pelvic inflammatory disease generally moves from the vagina or endocervix to uterine cavity. Acute pelvic inflammatory disease mainly results from Neisseria gonorrhea or Chlamydia trachomatis. Other bacterial infection, such as occurred in our case, can result from changed vaginal flora following Neisseria gonorrhea or Chlamydia trachomatis infection.[3] Our case was caused by Klebsiella pneumoniae infection. Septic metastatic lesions with diabetes along with Klebsiella pneumoniae infection have been shown.[8] On admission, the patient suffered from diabetic ketoacidosis, which can often cause a clinical syndrome resembling systemic inflammatory response syndrome.[9] Therefore, diabetic ketoacidosis may

have resulted in the intrauterine Klebsiella pneumoniae infection which induced sepsis, resulting in multiple organ failure such as bilateral pulmonary and renal septic emboli, and DIC. Intensive treatment included low tidal volume ventilation which has been shown to be useful for acute respiratory failure.[10] Moreover, we performed intensive blood glucose control. The patient's fasting blood glucose was 503 mg/dl. Diabetic patients suffering from pneumoniae with blood glucose levels of more than 200 mg/dl have a poor prognosis.[11] Surviving sepsis campaign guidelines recommend that the blood glucose levels should be less than 150 mg/dl.[12] Strict blood glucose levels from 80 to 110 mg/dl by intensive insulin therapy significantly reduce morbidity more effectively than conventional insulin therapy for blood glucose levels from 180 to 200 mg/dl, but carry the high risk of hypoglycemia.[13] The blood glucose levels varied in our patient. Therefore, insulin treatment for blood glucose aimed at 80 to 140 mg/dl by changing the insulin dose to less than 60 mg/dl or more than 180 mg/dl. A value less than 140 mg/dl was the result of the guideline for management of postmeal glucose.[14] After that, respiratory condition and inflammatory makers improved. However, slightly elevated fever continued and the CRP levels remained 8 to 9 mg/dl. Aside from antimicrobial therapy, removal of the source of infection is important for treatment of septic emboli.[15] After extracting the myoma uteri, the patient's fever subsided and the CRP became negative. Treating diabetes mellitus is important for the prevention of severe infection.

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