

Treatment of Severe Post-kidney-transplant Lung Infection by Integrative Chinese and Western Medicine

YAO Quan (姚全), ZHANG Shu-wen (张淑文), WANG Hong (王红),
REN Ai-min (任爱民), LI Ang (李昂), and WANG Bao-en (王宝恩)

ABSTRACT **Objective:** To explore treatments of severe post-kidney-transplant lung infection by integrative Chinese and Western medicine (ICWM), in order to elevate the curing rate as well as to lower the death rate. **Methods:** Based on conventional ways of Western medical treatments of 18 cases of severe post-kidney-transplant lung infection, such as putting the patients in single individual ward, antibiotics to prevent infection, respiratory machines, blood filtration, nutritional support, steroids, and maintaining electrolytes balance, we applied integrated Chinese medicinal treatments, like altering conventional prescription “pneumonia III”, and conducted clinical observation of effectiveness, and indexes including white blood cell (WBC), neutrophilic granulocyte, blood urea nitrogen (BUN), blood creatinine (Cr), etc. **Results:** Of the 18 cases studied, 7 were already cured, 8 proved the treatment effective, 3 died. All clinical indexes had statistically significant changes compared with those of before treatment ($P < 0.01$). **Conclusion:** ICWM can increase curing rate and lower death rate.

KEY WORDS post-kidney-transplant, severe lung infection, integrative Chinese and Western medicine

Lung infection is one of the most common post-kidney-transplant complications. About 70% of the post-kidney-transplant patients develop infections within one year of operation⁽¹⁾, of which the rate of lung infection within 1–3 months were the highest, and apparently affected survival rate. Severe lung infection with its severe symptoms, complex status and rapid clinical course, is one of the main causes for the death rate among kidney transplant receivers. The mortality is even as high as 23.8%–52.0%^(1,2–4).

During 2003–2004, the authors used integrative Chinese and Western medicine (ICWM) to treat patients with post-kidney-transplant lung infection and promising results were obtained.

METHODS

Inclusion Criteria

In diagnosing severe lung infection we referred to the diagnostic criteria set by Ren JZ, et al⁽⁵⁾. With acute lung injury (ALI)/acute respiratory distress syndrome (ARDS) we referred to the diagnostic criteria set by Respiratory Society of Chinese Medical Association, 2000.

Clinical Data

During 2003–2004, Beijing Friendship Hospital treated 18 patients with post-kidney-transplant infections, 12 males and 6 females. Age range: 31–69 years, mean age 50.6 ± 11.7 years; 10 of the 18 were younger than 50 years, constituting 55.6% of this group. Disease course 13–74 days, mean 30.1 ± 14.6 days. In 4 cases the lung infection occurred within 2 months of kidney transplant, 6 after

3 months of transplant, 4 after 4 months of transplant, and 4 after 2 to 6 years of transplant.

According to the diagnostic criteria, all the 18 cases were of severe lung infection, among whom 7 were of ARDS, 11 of acute lung injury, and 1 combined with shock.

Immunosuppression treatment: Cyclosporine A (CsA), Mycophenolate (MMF) and Prednisone (Pred) were used in 9 cases, CsA, Rapamycin (RPM), MMF and Pred in 1 case, CsA, Azathioprine (Aza) and Pred in 1 case, Tacrolimus (FK506), MMF and Pred in 2 cases, CsA and Pred in 2 cases, MMF and Pred in 1 case, FK506 and Pred in 1 case and CsA, RPM and Pred in 1 case. Level of CsA was monitored to maintain it at 100–300 ng/ml.

There were 16 in all the 18 severe lung infection cases in whom pathogens were detected (Table 1). Among them 3 were of single infection and 13 of mixed infections. Pathogens were not detected in the rest two cases.

Clinical features: All the patients suffered from fever, the highest temperature exceeding 38.5°C . In 12 of them there developed aversion to cold before fever came on, obvious difficulty in breathing, breath rate when staying quiet $\geq 25/\text{min}$, coughing,

Beijing Friendship Hospital, Affiliated to Capital University of Medical Sciences, Beijing (100050)

Correspondence to: YAO Quan, Beijing Hospital of Integrative Traditional and Western Medicine, Tel: 010–88223570

sputum in small amount, and apparent cyanosis. Physical examination: declined vesicular breathing was audible, and exhale phase lenthened, and in a few of them were detected dry and moist rales. X-ray film showed diffusive interstitial pathological changes, scattered patchy shadow or frosted glass changes. There appeared also various extents of hypoxemia and hypoproteinemia.

Table 1. Laboratory Findings in Pathogen of 16 Patients with Severe Lung Infection

Pathogen type	n	Pathogen type	n
Bacteria		Viruses	
Enteric bacilli	5	Cytomegalo virus	4
Bacillus pyocyaneus	4	Adenovirus	4
Staphylococcus aureus	1	EB virus	4
Bacillus prodigiouus	1	Herpes simplex virus type II	2
Type A hemolytic streptococcus	2	Fungus	
Staphylococci	3	Candida albicans	3
D group Enteric bacilli	2	Other candida	2
Klebsiella pneumoniae	4	Others	
Intermediate enteric bacilli	1	Chlamydia	1
Escherichia coli	1	Mycoplasma	1
Microcosms	1	Pneumocystis carinii	3

Treatment Methods

Because of lowered resistance, the patients should be separated to individual wards; strict oral hygiene should be maintained and ultraviolet used to disinfect the wards regularly to avoid iatrogenic cross infection.

Selection of antibiotics: Immediately after admission, antibiotics should be given on the basis of diagnostic experience. Meanwhile, efforts should be made to find out the causes of disease, and the applied medicine adjusted according to the findings and sensitivities of the drugs. When high fever lasts for 7 to 10 days after repeated administration of multiple antibiotics, or fever reoccurred after getting normal, it should be taken into consideration whether or not its subsequent fungal, viral or pneumocystis carinii infection, and anti-fungal, anti-viral or chemitrim used to treat it. Because severe post-kidney-transplant lung infection patients have lowered resistance to infections, it is possible that they may suffer from infections of several causes. Thus most severe post-kidney-transplant lung infection patients were treated with “triple” or even “tetragenous” medications.

Wholistic support treatment: Patients with com-

bined hypoxemia or ALI were supplied with oxygen by nasal tube, those with combined ARDS were supplied with oxygen by high-frequency spurt through nasal tunnel, with oxygen pressure as 1.2 kg/m², and spurt frequency as 150–300/min. And intratracheal intubation or tracheotomy should be applied when necessary. Blood gas analysis should be monitored, and all indexes of oxygen therapy adjucted to maintain blood saturation of oxygen at above 95%, so as to gradually alleviate hypoxemia. Also during the 2nd week of ARDS course, glucocorticoid methylprednisolone should be used at the dosage of 1–2 mg/kg daily, with the treatment period lasting for one to four weeks. For multiple organ dysfunction syndrome (MODS)/multiple system organ failure (MSOF) patients, continuous hemofiltration was administered to eliminate inflammatory medium agent in patients blood plasma, and blood urea nitrogen (BUN), blood creatinine (Cr), K⁺ level lowered⁽⁶⁾. Sufficient nutritional support was provided. Liquid, electrolyte and acid-base balance must be monitored, and any imbalance corrected. Liver function and plasma proteins had to be monitored, albumin supplied timely, and hypoproteinemia alleviated.

TCM diagnosis and treatment on the basis of overall analysis of the illness and the patients condition: The 18 cases of severe post-kidney-transplant infection patients all had developed persistent high fever, some of them had also aversion to cold or shivering, with or without perspiration, coughing, small amount or no sputum, shortness of breath, lack of strength. So most of them belonged to “heat syndrome” according to tongue picture and pulse condition. They most likely belonged to the category of infectious febrile disease. When firstly admitted to the hospital, 9 cases had evil invaded lung, with Wei and qi both ill; 9 cases had evil heat congested in the lung, with the inner defensive system suffering from heat syndrome; 15 were of Spleen deficiency; 7 suffered from dampness besides other symptoms; and 15 developed weak inner defensive system in yin and qi along with the worsening of their illness. According to TCM diagnosis and treatment on the basis of an overall analysis of the illness and the patients conditions, we applied the altered traditional prescription of “Pneumonia III” (dandelion 30 g, herba patriniae 30 g, giant knotweed 30 g, barbed stullcap 15 g). We added honey suckle 20 g, forsythia fruit 20 g, schizonepeta spike 10 g for patients that had exterior syndrome; added gypsum 30 g, anemarrhena 10 g, Radix scutellariae 10 g, Cape jasmine fruit 10 g for patients who had excessive heat in their inner defensive system; add-

ed ageratum 10 g, eupatorium 10 g, Liuyi powder 15 g, cardamomum 10 g, coix seed 15 g for patients who had dampness; added crude Milkvetch root 30 g, tuckahoe 15 g, atracylodes macrocephala 10 g for patients who had Spleen deficiency and weak inner defense system; added pseudostellaria root 30 g, dried rehmannia root 10 g, glehnia root 10 g, lilyturf root 10 g, dendrobium stem 10 g, etc. for patients who had yin deficiency; added rhubarb 6–10 g for patients who had hard faeces and bowel gas congestion; added almond 10 g, mongolian snakegourd 20 g, thumberg fritillary bulb 10 g for patients who had coughs and sputum; and added dodder 10 g, eucommia 10 g, wolfberry fruit 10 g, epimedium 10 g for those who had Kidney deficiency. Regardless of whether blood stasis syndrome was shown or not, always added were herbs that promote blood circulation to dispel blood stasis, such as red sage root 15 g, angelica 10 g, red peony root 10 g, spatholobus stem 10 g. Every patient was given herbal medication since admission till they were cured. Each dose was concentrated into 400 ml liquid, one dose a day, divided into two portions and taken twice.

Observation Items

Indexes of white blood cells (WBC), neutrophilic granulocyte, BUN, Cr and clinical manifestations were observed before and after treatment.

Standard of Clinical Efficacy

Clinically cured: Disappearance of clinical symptoms and physical signs, absorption of lesions on X-ray, laboratory findings normal or resuming the status of pre-infection; Effective: normal body temperature, other improvement in clinical symptoms and physical signs, lesions largely absorbed on X-ray, laboratory test not completely normal or resuming the status of pre-infection; Ineffective: infection not controlled, status of illness deteriorated.

Statistic Analysis

The *t* test was used for comparison between before and after treatment.

RESULTS

Of all the 18 patients in the treated group, 7 were cured. And 8 were effectively treated. Among the effectively treated cases, 5 showed near absorption of focus on X-ray film, 1 still had abnormal pulse, 4 had abnormal WBC and differential count, 5 had abnormal BUN level, 1 had abnormal blood Cr level, 1 had abnormal blood glucose level, and 1 had abnormal blood oxygen saturation rate with the

total effective rate as 83.8%. Three patients died, with mortality rate reaching 16.7%. All three death cases were male, and died from uncontrollable lung infection combined with ARDS, with one also having spontaneous pneumothorax. Two of them died within two months of transplant and one within three months. Comparison of major indexes before and after treatment, the key areas to address are listed in Table 2.

Table 2. Comparison of Major Indexes before and after Treatment of Severe Post-kidney-transplant Lung Infection by ICWM ($n = 18, \bar{x} \pm s$)

Item	Before Treatment	After Treatment
Body temperature	39.38 ± 0.99	37.08 ± 1.42*
Pulse	116.33 ± 14.95	94.28 ± 25.92*
WBC ($\times 10^9/L$)	14.42 ± 5.05	9.64 ± 5.05*
Neutrophil (%)	87.41 ± 5.50	76.42 ± 10.75*
BUN (mg/L)	271.3 ± 203.4	221.5 ± 140.0*
Cr (mg/L)	18.8 ± 16.6	16.8 ± 15.4*
Blood sugar (mg/L)	1737.8 ± 700.4	1146.7 ± 725.9*
Oxygen saturation index	214.53 ± 63.72	332.78 ± 115.89*

Notes: * $P < 0.01$, compared with before treatment

DISCUSSION

Judging from the observation of the 18 cases of post-kidney-transplant, patients usually had a long history of blood dialysis prior to the surgical operation and relatively weak immune system. Large amount of immune suppressors taken after the transplant damaged their vitality, Spleen and Kidney even more, deteriorating their weak body resistance. Especially when “exterior evil” invaded, they were apt to get ill, inviting all sorts of bacteria (including existing opportunistic disease-causing microbes within the hosts’ bodies) and viruses invading them, which often caused infections on all parts of the body to develop into systemic inflammatory response syndrome, or even severe pyemia⁽⁷⁾. This was one of the main causes of complications and death of post-kidney-transplant patients. Lung infection, which most frequently occurred fell into the category of “acute febrile disease” in Chinese medicine system. The first phase of the illness shows lung symptoms of fever, slight aversion to cold, cough and mild thirstiness. In post-kidney-transplant patients, due to the use of immune suppressors, initial lung infection symptoms are not so obvious, as physical signs are concealed. Once fever develops, it is already in the sever phase, and cases with sin-

gle exterior signs are rarely observed, just like our studied group which shows there was no case with single signs. Because their Spleen and Stomach were damaged which could not carry, transport and convert retention of water, and so in them may appear listlessness and sticky tongue coating, little or no appetite, epigastric fullness, slimy and greasy feeling in the mouth, etc. Treatment of such signs should concentrate on clearing away heat and toxic materials, as well as invigorating the Spleen to eliminate dampness. Laboratory test showed that “Pneumonia Ⅲ” prescription clears away heat and toxic materials by increasing blood neutrophilic granulocyte phagocytic index and blood plasma total complementary level, and enhances the body's ability of fighting infection by strengthening the body resistance and eliminating pathogenic factors⁽⁸⁾. And that is why we chose “Pneumonia Ⅲ” as our base-line principle for our modified recipes.

TCM theory believes that, blood stasis is a clinical entity caused by stagnations of blood vessels, abnormal functional activities of qi, blood stasis, etc. As in acute febrile disease category, the blood slows down in all phases of Wei, qi, Ying and blood, although it is more seen in the sub phases of Ying and blood. Macroscopically, according to TCM diagnosis and treatment on the basis of an overall analysis of the illness and the patient's condition, if the patients show such blood stasis symptoms as petechia, ecchymosi, gargling without the desire to swallow when feeling thirsty, cyanotic lips, dark tongue, etc., showing blood stasis syndromes, herbs that promote blood circulation to dispel blood stasis should be used. When the organic tissues are infected, symptoms of inflammation would be tissue hyperaemia, swollen, and later would turn to effusion, degeneration, necroses, atrophial, hyperplasia and other pathological changes. These are blood stasis symptoms on the microscopic level. Clinical and laboratorial test results showed that patients whose main infection is blood endotoxin syndrome MODS/MSOF had various levels of disturbance in peripheral microcirculation. Especially when clinical signs show low blood platelet, subnormal laboratorial test reading (prothrombin time, activated partial thromboplastin time, TT lengthened, FIB decreased), the patients can be considered microscopically as having blood stasis symptoms of severe infection. The pathologic physiological changes are diffusive intravascular coagulation. This is a more sensitive and reliable indication than blood stasis macroscopic symptoms⁽⁹⁾. For this reason,

the curative effect could be increased by using herbs that promote blood circulation to dispel blood stasis at the early stage when infected patients were not showing any macroscopic blood stasis. We did use herbs like red sage root before patients showed blood stasis symptom.

Post-kidney-transplant patients with lung infection, besides suffering from sthenia of evil, also have obviously weakened body resistance, especially deficiency of the vital energy, deficiency of Spleen and Kidney yang which also slows down their recovery. In treating them with Chinese medicine, we used herbs that nourish qi and consolidate the Kidney essence such as Astragalus root, *Atractylodes macrocephala*, fruit of *Barbary wolfberry*, Dodder, etc. to help strengthen the body resistance.

In treatment of severe post-kidney-transplant lung infection by ICWM, Western medication is used as the regular treatment, and Chinese medicine “Pneumonia Ⅲ”, as the basic prescription is also modified and used to strengthen the body resistance, improve lung microcirculation, so as to accelerate patients recovery, as well as lower the death rate.

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