Diagnosis and treatment Protocol of COVID-19
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Epidemiological characteristics

(1) The source of infection.
- The COVID-19 patients;
- Asymptomatic infected people can also be a source of infection.

(2) Route of transmission
- Respiratory droplets and close contact are the main routes of transmission.
- There is the possibility of aerosol transmission in a relatively closed environment for a long-time exposure to high concentrations of aerosol.
- As the novel coronavirus can be isolated in feces and urine, attention should be paid to feces or urine contaminated environment that leads to aerosol or contact transmission.

(3) Susceptible population.
- All the population are generally susceptible.
Pathological changes

Pathological findings from limited autopsies and biopsies gave the evidence that COVID-19 mainly causes lung damage.

1. Lungs
   – The varying degrees of lungs solid changes.
   – Alveolar damage involves fibro myxoid exudation and hyaline membrane formation.
   – The exudates are composed of monocytes and macrophages.
   – Alveolar interstitium is marked with vascular congestion and edema, infiltration of monocytes and lymphocytes, and vascular hyaline thrombi.
   – The lungs are laden with hemorrhagic and necrotic foci, hemorrhagic infarction.
   – The bronchi are filled with mucus and mucus plugs.
   – On electron microscopy, cytoplasmic virions are observed in the bronchial epithelium and type II alveolar epithelium.
Pathological changes

2. Spleen, Hilar lymph nodes and bone marrow

– The spleen is evidently shrunk with Lymphocytopenia and focal hemorrhage and necrosis, and macrophage proliferation and phagocytosis.

– Lymph nodes are found with sparse lymphocytes and occasional necrosis.

– CD4+ and CD8+ T cells are present in reduced quantity in the spleen and lymph nodes.

– Pancytopenia is identified in bone marrow.
Clinical manifestations

• The incubation period: the incubation period is 1-14 days, mostly 3-7 days.

• Clinical Features:
  – Fever, dry cough, fatigue as the main performance.
  – In severe cases, dyspnea or hypoxemia usually occur one week after the onset of the disease.

• The severe or critical case may have low fever, or even no fever.

• The elderly patients and those with chronic underlying diseases have poor prognosis.
Laboratory test

• In most patients, white blood cells was normal or decreased, with the lymphocyte count decreased.
• C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were elevated.
• Some patients show an increase in liver enzymes, lactate dehydrogenase (LDH), muscle enzymes and myoglobin.
• In severe cases, D-dimer increased progressively.
• Elevated troponin is seen in some critically ill patients.
• Severe and critical patients often have elevated inflammatory factors.
Virological and serological findings

• Virological detection:
  – Viral RNA can be detected in nasopharyngeal swabs, sputum, lower respiratory tract secretions, blood, feces and other specimens using RT-PCR or NGS.
  – Recommend to collect lower respiratory tract samples (sputum or air tract extraction) to increase the sensitivity.

• Serological test:
  – Viral specific IgM antibody becomes detectable around 3-5 days after onset;
  – Viral specific IgG antibody reaches a titration of at least 4-fold increase during convalescence compared with the acute phase.
Chest imaging

• In the early stage, there were multiple spotted shadows and interstitial changes, which were obvious in the extraneous lung.
• Further, multiple ground-glass shadows and infiltration shadows were found in both lungs.
• Lung consolidation was found in severe cases.
Male, 44 years old, fever, fatigue, treatment progress
- **infiltration shadows** appear in the lungs, often initially close to the pleura, and gradually develop toward the center
Progressive CT findings

8 dyas after onset
subpleural
distribution ground-
glass shadows

20 dyas after onset
The infiltration lesion
develops to the
center and presents a
consolidation
1. suspected cases:

- Epidemiological history
  ① History of travel to or residence in communities where cases reported within 14 days prior to the onset of the disease;
  ② In contact with viral RNA positive people within 14 days prior to disease onset;
  ③ In contact with patients who have fever or respiratory symptoms from communities confirmed cases reported within 14 days before disease onset;
  ④ Clustered cases (2 or more cases with fever and/or respiratory symptoms in a small area such as families, offices, school room etc. within 2 weeks).
Diagnostic criteria

1. suspected cases.
   • Clinical features
     ① fever and/or respiratory symptoms;
     ② imaging characteristics;
     ③ The white blood cells was normal or decreased, with lymphocyte decreased.

Diagnostic criteria for suspected cases:
   – Any one of the epidemiological history with any two of the clinical features.
   – All three clinical features.
Diagnostic criteria

2. Confirmed cases:

• Suspected cases with one of the following virological or serological evidences:
  – Real-time fluorescent RT-PCR indicates positive for novel coronavirus RNA;
  – Viral gene sequence is highly homologous to known novel coronaviruses;
  – Viral specific IgM and IgG are detectable in serum;
  – Viral specific IgG is detectable from negative to positive, or
  – Viral specific IgG antibody reaches a titration of at least 4-fold higher in the recovery stage than in the acute stage.
Clinical Types

(1) Mild:
The clinical symptoms were mild, and there was no sign of pneumonia on imaging.

(2) Moderate:
Showing fever and respiratory symptoms with radiological findings of pneumonia.

(3) Severe. In accordance with any of the following:
1. Shortness of breath (RR $\geq$ 30 breaths/min);
2. In resting state, oxygen saturation $\leq$ 93%;
3. Arterial partial pressure of oxygen ($\text{PaO}_2$)/ fraction of inspired oxygen ($\text{FiO}_2$) $\leq$ 300mmHg (1 mmHg=0.133kPa).
4. Cases with chest imaging showed obvious lesion progression more than 50% within 24-48 hours.

(4) Critical: One of the following:
1. Respiratory failure, requiring mechanical ventilation;
2. Shock;
3. With other organ failure that requires ICU care.
The proportion of clinical types in different regions

- Asymptomatic
- Mild
- Moderate
- Severe
- Critical illness

China CDC/NHC 20200303
The proportion of severe diseases increases with age
The proportion of deaths in different age groups
Early warning indicators of severe and critical cases

- The peripheral blood lymphocytes decrease progressively;
- Progressively elevation of inflammatory factors, such as IL-6 and C-reactive proteins;
- Lactate sustained or progressive elevation;
- Lung lesions develop rapidly in a short period of time.
General management

• Rest and symptomatic support therapy; sufficient caloric; water and electrolyte;

• Closely monitoring vital signs and oxygen saturation.

• Monitoring lab test: blood routine result, urine routine result, c-reactive protein (CRP), biochemical indicators (liver enzyme, myocardial enzyme, renal function etc.), coagulation function, arterial blood gas analysis, chest imaging and cytokines detection if necessary.

• Early oxygen therapy and airway drainage.
General management

• **Antiviral therapy:** Some drugs that are already on market can be tried to treat COVID-19 and the efficacy of the drugs need to be evaluated in clinical application.
  – Alpha-interferon: 5 MU, atomization inhalation twice daily;
  – Kaletra (Lopinavir/ritonavir)
  – Chloroquine phosphate
  – Arbidol:

• **Antibiotic drug treatment:** Rational use of antimicrobial agents.
Treatment of severe and critical cases

- Treatment principle: On the basis of symptomatic treatment, the prevention of complications, treatment of underlying diseases, prevention of secondary infections, and timely organ function support should be reinforced.

1. Respiratory support:
2. Circulatory support:
3. Renal failure and renal replacement therapy:
4. Convalescent plasma treatment:
5. Blood purification treatment:
6. Immunotherapy:
7. Other therapeutic measures
Respiratory support: Oxygen therapy

- Nasal cannulas or masks for oxygen inhalation:
- High-flow nasal-catheter oxygenation or noninvasive mechanical ventilation:
  - When respiratory distress and/or hypoxemia cannot be alleviated by oxygen therapy.
- Invasive mechanical ventilation:
  - If conditions do not improve or even get worse within 1-2 hours.
  - Use closed sputum suction according to the airway secretion, if necessary, administer appropriate treatment based on bronchoscopy findings.
- Rescue therapy:
  - Pulmonary reconstruction is recommended for patients with severe ARDS.
  - With sufficient human resources, prone position ventilation should be performed for more than 12 hours per day.
  - If prone position ventilation did not work, extracorporeal membrane oxygenation (ECMO) should be considered as soon as possible.
Convalescent plasma treatment:

• **Indications**
  – Patients with rapid disease progression, severe and critical illness.
  – The course of illness should not exceed three weeks;
  – The nucleic acid test was positive or other evidence of presence of viruses;

• **Infusion dose**
  – The usual infusion dose is 200-500 ml (4-5 ml/kg), two times
Blood purification treatment:

- It can be used for the treatment of severe and critical cases in the early and middle stages of cytokine storm.

- Including plasma exchange, absorption, perfusion and blood/plasma filtration;

- To remove inflammatory factors and block "cytokine storm"."
Other therapeutic measures:

• Glucosteroid:
  – For patients with progressive deterioration of oxygenation indicators, rapid progress in imaging and excessive activation of the body's inflammatory response
  – In a short period of time (3 to 5 days).
  – It is recommended using methylprednisolone 1-2 mg/kg/day.
  – Note that a larger dose of glucocorticoid will delay the removal of coronavirus due to immunosuppressive effects.

• Intestinal microecological regulators:
  – To maintain intestinal microecological balance and prevent secondary bacterial infections.
Traditional Chinese Medicine treatment

1. Clinical manifestations during medical observation
   - huoxiang zhengqi capsule (pill, water, oral liquid)
   - jinhua qinggan granules, lianhua qingwen capsules (granules), shufeng jiedu capsules (granules)

2. Clinical treatment phase (confirmed cases)
Conclusion

• COVID-19 is an emerging infectious disease, that many aspects still need to be elucidated, including the pathogenesis, pathology.

• Early diagnosis and early treatment is critical.

• Effective oxygen treatment are very important.

• We will update the protocol with increased understanding of the clinical manifestations and pathology of the disease, and the accumulation of experience in diagnosis and treatment.
Thanks for your attention!
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