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Review

Non-COVID-19 viral pneumonia in adults in Turkey

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ABSTRACT

The role of respiratory viruses in pneumonia has not been fully understood yet. Viral infections are more easily diagnosed in recent years by nucleic acid tests, which can detect all respiratory viruses simultaneously and are available in many centers. This study aimed to review viral pneumonias in the light of the literature and to evaluate publications in Turkey.

Keywords: Community-acquired pneumonia, hospital-acquired pneumonia, Turkey, viral pneumonia.

Although more common in immunosuppressed patients, viral pneumonia is increasingly recognized as a type of pneumonia seen in immunocompetent patients. Viral pneumonia in adults can present itself as community-acquired pneumonia (CAP), ranging from mild illness to severe illness requiring hospitalization and mechanical ventilation. It may also present itself as hospital-acquired pneumonia (HAP) or ventilator-associated pneumonia. Sometimes it can cause co-infections with bacterial agents.[1]

Viral pneumonia is an important cause of morbidity and mortality in the United States of America (USA) and the world. The organisms that cause pneumonia vary greatly between studies depending on the population studied, the diagnostic method used to detect pathogens, and the seasonal distribution of viruses.[1-3] Lower respiratory tract infections are the fourth most common cause of all deaths according to the data of the World Health Organization (WHO).[4] It has been reported that hospitalization and mortality rates increase in advanced age (>60 years) and the presence of comorbidities.[1-3]

More than 20 virus species have been reported to cause pneumonia.[1] Influenza A (H1N1) and B viruses, avian influenza A (H5N1), H2N2, H3N2, H5, H7 and H9 influenza viruses, H7N9 (bird flu), paramyxoviruses [respiratory syncytial virus (RSV), parainfluenza virus (PIV) serotypes 1, 2 and 3 and human metapneumovirus (HMPV)], human adenoviruses (1, 2, 3, 4, 5, 7, 14, 21 and 35), human rhinoviruses, coronaviruses (HCoV strains; HCoV-229E, HCoV-OC43, HCoV-NL63, and HCoV-HKU1), severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV) and human herpes-viruses [Varicella pneumonia, cytomegalovirus (CMV), herpes simplex virus (HSV)] are known to cause viral pneumonia.[1,5]

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Hantavirus, polyomavirus, erythrovirus (parvovirus) B19, and measles virus have been also shown among the common causes of respiratory tract infections since the beginning of polymerase chain reaction (PCR) studies.[6]

Viruses, particularly influenza viruses, rhinoviruses and coronaviruses, are considered to be the cause in one-third of CAP cases of adults.[7] The majority of causative agents in viral pneumonia are ribonucleic acid (RNA) viruses. The most common causes of viral pneumonia in adults are influenza, parainfluenza virus, and RSV, while the most common cause was CMV in an immunosuppressed patient group.[7]

The role of respiratory viruses in HAP has not been fully understood yet. In recent years, viral infections are more easily diagnosed in these patients with the use of nucleic acid tests available in many centers, which can detect all respiratory viruses simultaneously.[8] Two studies have reported that respiratory viruses are the cause in 22-24% of the patients diagnosed with HAP.[9,10] The need for intensive care and mechanical ventilation, the length of hospital stay and mortality increase when respiratory viruses are the cause.[8]

Molecular diagnostic techniques have greatly increased our understanding of the role of viruses in pneumonia, and the findings suggest that the incidence of viral pneumonia is less than reported.[11]

DIAGNOSIS

Clinical manifestations, laboratory findings, biomarkers and radiographic patterns are not specific to particular viral etiologies.[1] The clinical manifestations of pneumonias with different viral etiologies can be very similar. However, viruses are the more common cause of pneumonia in pediatric and geriatric populations.[12] Viral pneumonia is diagnosed with laboratory tests in addition to medical history and clinical and radiological findings.[5] In the total blood count, leukocytes are usually not increased, and procalcitonin levels are usually unaffected. Fever and upper respiratory tract symptoms are more common than bacterial infections.[12]

While in previous years, the diagnosis of viral pneumonia was based on cell culture and antigen detection, since the introduction of PCR assay, a molecular diagnostic technique shown to be reliable in lower respiratory tract infections, the identification of these pathogens has increased and new microorganisms such as human bocavirus have been discovered.[1,12] The most obvious advantages of the PCR assay over cell culture are that it does not require viable organisms since it is a method based on the replication of RNA or deoxyribonucleic acid (DNA) of a very small sample of microorganisms and thus is not affected by the use of antibiotics, that it is more sensitive in evaluating multiple microorganisms and that it gives fast results. Respiratory system viruses such as rhinovirus, coronavirus, human metapneumovirus, which cannot be evaluated by conventional methods, can be evaluated by PCR.[13] Occasionally, cytological evaluation (intranuclear inclusions in DNA viruses; intracytoplasmic inclusions in RNA viruses), viral culture, and rapid antigen tests are performed in addition to PCR.[5]

The radiological findings in viral pneumonias are non-specific. There may be bilateral involvement on chest X-ray. Many findings such as bilateral diffuse interstitial infiltration, bronchial wall thickening, consolidation, and pleural effusion may be detected. Computed tomography of the thorax may help in the diagnosis.[5]

TREATMENT AND PREVENTION

There is an approved treatment for influenza pneumonia. However, the treatment of respiratory viruses other than influenza is limited. In particular, the level of evidence for drugs to be used in the treatment of immunosuppressed patients is considerably low.[1] The influenza vaccine is the only specific preventive measure available.[11]

Neuraminidase inhibitors have been shown to reduce transmission of viral pneumonia and improve the clinical progression of viral pneumonia patients in intensive care; however, their use is not recommended in common infections. Ribavirin has been used in children with respiratory syncytial virus infection and immunosuppressed individuals. No other antiviral drug is effective. It has been argued that the influenza vaccine and the prevention of respiratory syncytial virus with monoclonal antibodies may reduce the incidence of pneumonia.[12]

The increase in the number of elderly and immunosuppressed patients may complicate the management of this disease. Infection control measures must be emphasized, particularly to prevent the spread of this disease.[1]

Regional variances in causes of pneumonia should be investigated to obtain more data, particularly in developing countries.

EVALUATION OF VIRAL PNEUMONIA CASES REPORTED IN TURKEY

There were no broad-based studies in the literature on the distribution of viral pneumonia agents in Turkey.

A prospective study in Manisa by Özer-Türk et al.[14] found a viral agent in 20 (21.7%) of 92 evaluated CAP cases. Influenza A virus (7.6%), rhinovirus (6.5%), RSV A (3.2%), adenovirus (2.2%), coronavirus 229 E (1.1%) and coronavirus OC 43 (1.1%) were among the most common causes of viral pneumonia. Viral pneumonia was more common in males (70.0%), in the age range of 51.3±19.9 years and winter (33.3%).[14]

A retrospective study in Ankara reported CMV in 30.76%, influenza in 27.47%, rhinovirus in 9.89%, coronavirus in 9.89%, RSV in 6.59%, PIV in 7.69%, HMPV in 4.39% (n=4), adenovirus in 2.19% (n=2) and bocavirus in one of the 91 patients as the cause of disease.[7] Seven of these patients were immunosuppressed patients, and CMV was the most common cause of viral pneumonia in the immunosuppressed patient group.

Doğan et al.[15] found that the incidence of H3N2 pneumonia among all pneumonia patients hospitalized in the chest diseases clinic is 10.1%. The mean age was 57.4 years and female patients constituted the majority (85.7%) of H3N2 pneumonia cases. The most common symptoms were cough (88.7%), sputum (80.6%) and shortness of breath (77.4%), and the most common comorbidities were chronic cardiovascular diseases (71.4%), chronic lung diseases (42.8%), chronic kidney diseases (14.2%).[15]

In a prospective study conducted in Izmir between 2001 and 2002, viruses were found to be the most common infectious agent (57.1%) in CAP.[16] Influenza A (39.2%), PIV 1 (23.2%), influenza B virus (21.4%), adenovirus (19.6%), PIV 2 (14.3%), PIV 3 (10.7%), enterovirus (7.1%), coxsackievirus and RSV (5.4%), Epstein-barr virus (EBV) and HSV (1.8%) were the reported agents.

In a study conducted in Adana between 2015 and 2016, 284 patients were evaluated, and H1N1 (78%), H3N2 (17%), and influenza B virus (5%) were detected.[17] RSV (3.6%), HMPV and coronavirus (2.1%), rhinovirus (1.7%), adenovirus and coronavirus + RSV (0.8%), H1N1 + rhinovirus, adenovirus + RSV and PIV (0.3%) were the other detected agents.

In Turkey, the National Sentinel Surveillance Network was established by the Republic of Turkey Ministry of Health, General Directorate of Public Health, Department of Infectious Diseases in 2005, and influenza surveillance has been carried out ever since. However, the latest information obtained was from 24 February - 1 March 2020, and it was thought that updates could not be processed due to the coronavirus disease 2019 (COVID-19) pandemic[18] and increased workload. The latest data show that the dominant viruses in Turkey vary according to geographical regions during the flu season.[19] Virus distribution according to the regions was as follows: Influenza B virus in the Mediterranean region; influenza A (H1N1) virus in the Marmara region; Influenza B and Influenza A (H1N1) viruses in Eastern Anatolia, Aegean, Southeastern Anatolia, Central Anatolia and Black Sea regions.

Influenza A and B are responsible for half of viral CAP in adults, and the herpes family [HSV, varicella-zoster virus (VZV), CMV] is often the cause of pneumonia in immunosuppressed patients; furthermore, these agents may remain as a lifelong latent infection after the primary infection.[13]

While RSV is the causative agent especially seen in childhood, it has been reported as an agent that causes disease exacerbation in patients with chronic obstructive pulmonary disease, in studies conducted in Turkey.[20-22] Emniyet Sert,[21] reported in his thesis that 13.4% of the patients also have an RSV + adenovirus co-infection. Possible causative agents in viral respiratory tract infections seen in patients with chronic obstructive pulmonary disease and asthma were reported to be PIV-3 and RSV by Çiçek et al.[23] and HMPV by Ilvan et al.[24]

There was no comprehensive study on varicella pneumonia in the local literature. The literature available consisted of case reports.[25-38] Cytomegalovirus pneumonia has been reported in immunosuppressed patients, and the literature on this subject is also limited.[39-44]

In conclusion, data on immunosuppressed and immunocompetent individuals in Turkey regarding clinical results and causative microorganisms in viral pneumonia are insufficient, and further studies are needed on this issue.

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