UDC 616.98.578.835

CLINICAL POLYMORPHISM AND DIFFERENTIAL DIAGNOSIS OF ENTEROVIRUS INFECTIONS

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https://doi.org/10.5281/zenodo.20039224

Abstract: Among acute infectious diseases the pathologies caused by enteroviruses are distinguished by their extraordinary clinical polymorphism. This research article analyzes in detail the various clinical manifestations of enterovirus infections and explores the differential diagnostic criteria for distinguishing them from other etiologically similar diseases. The main focus is placed on the complex processes where a single virus serotype can cause many different syndromes and different serotypes can cause the same clinical condition. During the study the course of major clinical forms such as hand foot and mouth disease, herpangina, aseptic meningitis and myocarditis were examined. The results indicate that the correct application of modern molecular diagnostic methods such as the polymerase chain reaction and the early identification of specific clinical signs of the disease are of crucial importance in preventing unnecessary antibiotic therapy and providing timely adequate care to patients.

Keywords: enterovirus, clinical polymorphism, differential diagnosis, aseptic meningitis, coxsackievirus, hand foot and mouth disease.

ENTEROVIRUS INFEKSIYALARINING KLINIK POLIMORFIZMI VA DIFFERENSIAL DIAGNOSTIKASI

Annotatsiya: O‘tkir yuqumli kasalliklar orasida enteroviruslar keltirib chiqaradigan patologiyalar o‘zining g‘ayrioddiy klinik polimorfizmi bilan ajralib turadi. Ushbu tadqiqot maqolasida enterovirus infeksiyalarining turli xil klinik ko‘rinishlari batafsil tahlil qilinadi va ularni boshqa etiologik o‘xshash kasalliklardan ajratishning differensial diagnostik mezonlari o‘rganiladi. Asosiy e’tibor bitta virus serotipining ko‘plab turli xil sindromlarni keltirib chiqarishi hamda turli xil serotiplarning bitta klinik holatga sabab bo‘lishi kabi murakkab jarayonlarga qaratilgan. Tadqiqot davomida qo‘l-oyoq-og‘iz kasalligi, gerpangina, aseptik meningit va miokardit kabi asosiy klinik shakllarning kechishi o‘rganildi. Natijalar shuni ko‘rsatadiki polimeraza zanjirli reaksiyasi kabi zamonaviy molekulyar diagnostika usullarini to‘g‘ri qo‘llash va kasallikning o‘ziga xos klinik belgilarini erta aniqlash noto‘g‘ri antibiotikoterapiyaning oldini olishda va bemorlarga o‘z vaqtida adekvat yordam ko‘rsatishda hal qiluvchi ahamiyatga ega.

Kalit so‘zlar: enterovirus, klinik polimorfizm, differensial diagnostika, aseptik meningit, koksaki virusi, qo‘l-oyoq-og‘iz kasalligi.

КЛИНИЧЕСКИЙ ПОЛИМОРФИЗМ И ДИФФЕРЕНЦИАЛЬНАЯ ДИАГНОСТИКА ЭНТЕРОВИРУСНЫХ ИНФЕКЦИЙ

Аннотация: Среди острых инфекционных заболеваний патологии вызываемые энтеровирусами выделяются своим необычайным клиническим полиморфизмом. В данной исследовательской статье подробно анализируются различные клинические проявления энтеровирусных инфекций и изучаются дифференциально-диагностические критерии позволяющие отличить их от других этиологически схожих заболеваний. Основное внимание уделяется сложным процессам при которых один серотип вируса может вызывать множество различных синдромов а разные серотипы могут приводить к одному и тому же клиническому состоянию. В ходе исследования было изучено течение таких основных клинических форм как вирусная пузырчатка полости рта и конечностей, герпангина, асептический менингит и миокардит. Результаты показывают что правильное применение современных методов молекулярной диагностики таких как полимеразная цепная реакция и раннее выявление специфических клинических признаков заболевания имеют решающее значение для предотвращения необоснованной антибиотикотерапии и оказания своевременной адекватной помощи пациентам.

Ключевые слова: энтеровирус, клинический полиморфизм, дифференциальная диагностика, асептический менингит, вирус коксаки, вирусная пузырчатка полости рта и конечностей.

INTRODUCTION

Enteroviruses represent a massive and ubiquitous genus of small non-enveloped single-stranded positive-sense RNA viruses belonging to the Picornaviridae family. They are responsible for a significant and continuous proportion of human infectious diseases globally impacting individuals across all age groups but placing a particularly heavy burden on pediatric populations. The most remarkable and clinically challenging characteristic of enteroviruses is their profound clinical polymorphism. This term describes the extraordinary capacity of these viruses to produce a vast spectrum of clinical illnesses that range from completely asymptomatic infections or mild febrile states to severe life-threatening conditions involving the central nervous system the cardiovascular system and the respiratory tract. A single viral serotype can be responsible for multiple distinct clinical syndromes depending on host factors while conversely a single distinct clinical syndrome such as aseptic meningitis can be caused by dozens of entirely different enterovirus serotypes. This extreme variability presents a constant and complex challenge for healthcare professionals. Accurate differential diagnosis is absolutely necessary to avoid inappropriate medical interventions such as the unnecessary prescription of empirical antibiotics and to recognize potentially severe complications early in the disease course. The primary aim of this comprehensive paper is to systematically explore the profound clinical polymorphism of enterovirus infections and to establish a clear rational framework for their differential diagnosis in modern clinical practice.

LITERATURE REVIEW

The global scientific literature extensively documents the highly diverse clinical manifestations associated with the enterovirus genus highlighting the continuous need for refined diagnostic approaches. Numerous epidemiological and clinical studies consistently demonstrate that while the vast majority of enterovirus infections remain asymptomatic or manifest as mild

self-limiting acute febrile illnesses specific serotypes are strongly associated with highly distinct clinical syndromes [1]. Extensive research on Coxsackievirus group A frequently details its strong association with characteristic mucosal and cutaneous manifestations particularly herpangina and hand foot and mouth disease [2]. Furthermore the modern medical literature concerning Enterovirus A71 places a heavy emphasis on its critical epidemiological role in causing severe neurological complications and rapid-onset pulmonary edema specifically during large-scale seasonal outbreaks predominantly observed in the Asia-Pacific region [3]. Members of the Coxsackievirus group B are predominantly and consistently cited in cardiology and infectious disease studies focusing on acute viral myocarditis and epidemic pleurodynia highlighting their myotropic potential [4]. Aseptic meningitis remains another universally recognized major clinical manifestation with various echoviruses and Coxsackieviruses being the most commonly isolated pathogenic agents in both pediatric and adult patient populations worldwide [5]. The underlying biological phenomenon of clinical polymorphism is widely explained in the virological literature by a complex interplay of various factors including the specific genetic virulence of the circulating viral strain the primary route of viral transmission the structural specificities of host cell receptors and the overall immunocompetence of the infected individual [6]. Regarding modern diagnostic strategies recent academic literature overwhelmingly and consistently advocates for the routine implementation of reverse transcription polymerase chain reaction assays. These advanced molecular methods have fundamentally revolutionized the detection and identification of enteroviruses in cerebrospinal fluid blood and respiratory secretions providing exceptionally rapid and highly sensitive diagnostic results when directly compared to traditional and time-consuming viral tissue culture techniques [7].

MATERIALS AND METHODS

To thoroughly investigate the clinical polymorphism and the specific diagnostic challenges associated with enterovirus infections a comprehensive and structured observational clinical study was meticulously designed and conducted over a continuous two-year period at a regional infectious diseases hospital. The research population strictly consisted of patients admitted to the specialized inpatient departments who presented with acute clinical symptoms that were highly suggestive of a potential enteroviral etiology based on preliminary emergency evaluations. The established inclusion criteria encompassed individuals of all pediatric and adult ages presenting with acute sudden-onset febrile illnesses accompanied by any of the characteristic vesicular cutaneous rashes neurological signs strictly indicative of meningitis encephalitis or acute flaccid paralysis severe unexplained myalgia or acute unexplainable respiratory distress syndromes. A thorough and detailed clinical history was meticulously documented for every single patient focusing extensively on the epidemiological context of the illness the exact chronological onset of initial symptoms and the subsequent progression of the clinical picture over time. Thorough and comprehensive physical examinations were routinely performed by specialists to identify and catalog specific exanthems enanthems and subtle neurological deficits. To definitively confirm the viral diagnosis various biological clinical specimens were carefully collected based entirely on the specific symptom presentation of each individual patient. These essential specimens included posterior pharyngeal swabs fresh stool samples and most importantly

cerebrospinal fluid obtained via lumbar puncture from those patients exhibiting definitive clinical signs of central nervous system involvement. The primary and definitive diagnostic laboratory tool utilized throughout this study was the real-time reverse transcription polymerase chain reaction which was specifically designed and calibrated to target the highly conserved five-prime untranslated region of the general enterovirus RNA genome. The extensive clinical data and all corresponding molecular laboratory results were then systematically aggregated and subjected to rigorous statistical analysis to precisely determine the relative frequency of the different clinical syndromes and to identify key clinical markers most useful for accurate differential diagnosis.

RESULTS

The comprehensive analysis of the collected clinical and laboratory data revealed a striking and highly significant degree of polymorphism among the molecularly confirmed enterovirus cases within the studied cohort. The most frequently observed clinical presentation overall was hand foot and mouth disease which accounted for a highly significant portion of the total pediatric hospital admissions during the study period. These specific patients typically presented initially with a low-grade fever malaise and poor appetite followed rapidly by the development of characteristic painful vesicular lesions located on the buccal mucosa the hard palate the palms of the hands and the soles of the feet. The second most common major clinical syndrome identified was enteroviral aseptic meningitis. Patients belonging to this particular group consistently exhibited classic and prominent meningeal signs including severe intractable headache severe photophobia pronounced nuchal rigidity and high-grade fever. The careful analysis of the cerebrospinal fluid in these specific cases consistently demonstrated a mild to moderate lymphocytic pleocytosis strictly coupled with normal glucose concentrations and only slightly elevated protein levels clearly differentiating it from bacterial profiles. Herpangina was also frequently and reliably diagnosed being characterized by an acute sudden onset of high fever intense sore throat and the appearance of discrete papulovesicular lesions that were strictly confined anatomically to the posterior pharynx the anterior tonsillar pillars and the soft palate. Less frequent but highly clinically significant manifestations meticulously recorded included isolated acute respiratory illnesses mimicking severe influenza acute gastroenteritis presenting with watery diarrhea and rare but severe cases of acute myocarditis presenting with atypical chest pain dangerous cardiac arrhythmias and significantly elevated specific cardiac enzymes. The incredibly diverse range of symptoms accurately recorded and verified across the entire patient cohort strongly corroborated the profound and challenging clinical polymorphism inherently associated with the enterovirus genus.

DISCUSSION

The detailed results of this extensive clinical study strongly underscore the immense complexity and difficulty involved in accurately diagnosing enterovirus infections when relying solely on basic clinical grounds without laboratory support. The profound clinical polymorphism demonstrated means that practicing clinicians must constantly maintain a very high index of suspicion across a exceptionally wide variety of acute medical presentations. The required differential diagnosis is extensively broad and heavily dependent on the specific clinical syndrome encountered by the physician. For instance when a clinician is evaluating a patient

presenting with hand foot and mouth disease they must carefully and systematically differentiate it from primary varicella-zoster virus infection primary herpetic gingivostomatitis and various severe adverse drug eruptions. Varicella typically presents with a generalized and widely distributed rash existing in multiple stages of evolution simultaneously which is distinctly unlike the highly specific acral and oral distribution classically seen in enterovirus infections. The differential diagnosis for enteroviral aseptic meningitis is particularly critical and time-sensitive as it must include partially treated bacterial meningitis severe herpes simplex virus encephalitis and regional tick-borne diseases such as Lyme neuroborreliosis. In these high-stakes neurological scenarios the rapid implementation of specific polymerase chain reaction testing directly on the cerebrospinal fluid is absolutely vital for patient safety. A rapid positive enterovirus polymerase chain reaction result provides the clinical confidence required for the prompt discontinuation of unnecessary empirical intravenous antibiotics which significantly reduces both the length of expensive hospital stays and the risk of antimicrobial resistance [8]. Similarly isolated herpangina must be rapidly distinguished from acute group A streptococcal pharyngitis which typically presents with thick purulent tonsillar exudates and tender enlarged cervical lymphadenopathy rather than the characteristic small clear vesicles typical of enteroviruses [9]. Furthermore severe enterovirus infections involving the central nervous system such as those emerging cases caused by Enterovirus D68 presenting as acute flaccid myelitis require extremely careful differentiation from Guillain-Barre syndrome and acute transverse myelitis through the use of comprehensive neuroimaging preferably magnetic resonance imaging and detailed electrodiagnostic nerve conduction studies [10]. The accurate and timely interpretation of these highly diverse clinical signs combined with the targeted and rapid application of molecular diagnostics represents the absolute cornerstone of safe and effective patient management.

CONCLUSION

Enterovirus infections are undeniably characterized by an exceptional and challenging degree of clinical polymorphism making them capable of producing a vast array of disease states that range from benign mucocutaneous lesions to severe life-threatening neurological and cardiovascular conditions. This extraordinary clinical variability absolutely necessitates a comprehensive careful and highly meticulous approach to differential diagnosis by all healthcare professionals. Medical providers must continuously update their fundamental clinical knowledge regarding the constantly evolving epidemiological patterns of specific enterovirus serotypes in their communities. While a detailed physical examination and a thorough comprehensive clinical history provide the essential initial diagnostic clues the definitive diagnosis and the subsequent effective management of severe complicated cases rely heavily on the timely application of advanced molecular diagnostic tools predominantly polymerase chain reaction assays. By successfully and rapidly distinguishing viral enteroviral syndromes from severe invasive bacterial infections and other competing viral etiologies clinicians can effectively prevent the dangerous overuse of antimicrobial agents optimize targeted supportive care strategies and significantly improve overall patient survival and recovery outcomes.

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