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A Review on Tomato Flu

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ABSTRACT –
Tomato Flu is a retroviral infection that can hypothetically be caused by CoxsackievirusA strain. It is associated with Hand, Foot and Mouth syndrome. This viral strain of infection has a reproduction Number R0 ranging between 2-3 respectively. The general pathology is that the virus invades through the oral route and then invades Cardiac Tissue, GIT, muscles and the respiratory system. By invading the myocardial tissue the virus can cause Dilated Cardiomyopathy. Through invading GIT, this virus can cause inflammation of the GIT and may cause diseases like Crohns disease respectively. By invading the lymph nodes, swelling of lymph nodes/inflammation of lymph nodes can be seen. The virus can also spread to the pancreatic tissue and can precipitate Diabetes Mellitus (Juvenile-Type 1) in toddlers. The virus can also invade the Hepatic tissue and can propel into Hepatitis. The virus also had the ability to invade the striated skeletal muscles and can cause Myalgia/Muscle pain. As of now the symptomatic treatment available for the Tomato flu is use of Non Steroidal Anti Inflammatory Drugs such as Paracetomol, Ibuprofen. Other immunosupportive drugs such Vitamins, Ivermectinetc can be given. The treatment is supported with sufficient hydration, good food intake along with quarantine and care.

Keywords- Hand and Foot Syndrome, Coxsackievirus, retrovirus, enterovirus

I. INTRODUCTION-

An unexplained viral organism that causes tomato flu is an infectious disease that was originally discovered in Kerala, India, in May 2022. The term "Tomato flu," sometimes known as "Tomato fever," refers to the illness's initial reddish-colored tiny blister that eventually grows to resemble the shape of a tomato. Children under the age of five are the main victims. Adults serve as compassionate carriers. The enterovirus genus, which also includes the polioviruses, coxsackie viruses, echo viruses, and other pathogens, includes viruses that cause tomato flu, which is referred to as a "Hand, Foot, and Mouth disease" (HFMD). An HFMD is most frequently caused by coxsackie virus A16. Only a moderate form of the illness is caused by coxsackie virus A16 infection in HFMD.

Nearly all patients recover in roughly 7 to 10 days without medical intervention. Through direct touch, infected individuals' saliva, blister fluid, nose and throat secretions, and stool can all spread the infection to others. 9 People's hands, fomites, and contact with infected surfaces are the most common ways in which this virus is spread. Direct contact with the infectious virus, which is found in the saliva, blister fluid, nose and throat secretions, and stool of persons who are infected, is the only way for infection to spread from one person to another. Young children under five are the age group that is most vulnerable. Enterovirus can spread mostly through respiratory droplets, contact with blister fluids, and contact with contaminated faeces.

Up till May 13, 2022, there have been 82 cases of tomato flu reported in Kerala's Kollam district; further instances are anticipated. In Orissa, 26 cases of the disease—presumptively caused by tomato flu—were confirmed as positive for Hand, Foot, and Mouth. As it shares symptoms with chikungunya and dengue infections, such as large, spherical, crimson blisters on various body parts, high-grade fever, dehydration, skin rash and skin irritation, myalgia, and swollen and painful joints, tomato flu might be thought of as the result of such infections. The self-resolving nature of tomato flu means that it typically goes away on its own in 7–10 days.

Since this virus is a rare infectious disease since it has only recently emerged, no specific medications are now available to treat it. Fever and flu symptoms are managed with symptomatic therapy. The medications ibuprofen and acetaminophen, sometimes referred to as paracetamol, can be used to alleviate fever. It is

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advised to drink a lot of liquids because dehydration is a possibility. Rest in bed and good hygiene and sanitation are essential. Affected youngsters must be quarantined for roughly a week, isolated, and under constant watch. [1]

Fig.1-Hand and Foot syndrome Fig.2-Coxsackievirus infection in children.

COXSACKIEVIRUS- A POSSIBLE CAUSATIVE AGENT FOR TOMATO FLU

The Picornaviridae family of non-enveloped enteroviruses includes a few related enteroviruses known as coxsackieviruses. RNA viruses have a single strand and a linear positive sense. It is a member of the enterovirus genus, which also contains the poliovirus and the echovirus. 13 Members of the genus Enterovirus are among the most prevalent and significant human diseases, and they are spread via the fecal-oral route. There are several similarities between poliovirus and coxsackievirus.[14]

Group a [Coxsackievirus]

Hand, foot, and mouth disease (HFM) and herpangina acute hemorrhagic conjunctivitis are typically brought on by group Acoxsackievirus infections of the skin and mucous membranes.

Coxsackievirus A16 (Cox A16) was predicted to have a basic reproduction number (R0) with a median of 2.50 and an interquartile range of 1.96 to 3.67. It typically indicates that it may spread to 2-3 individuals at a time.

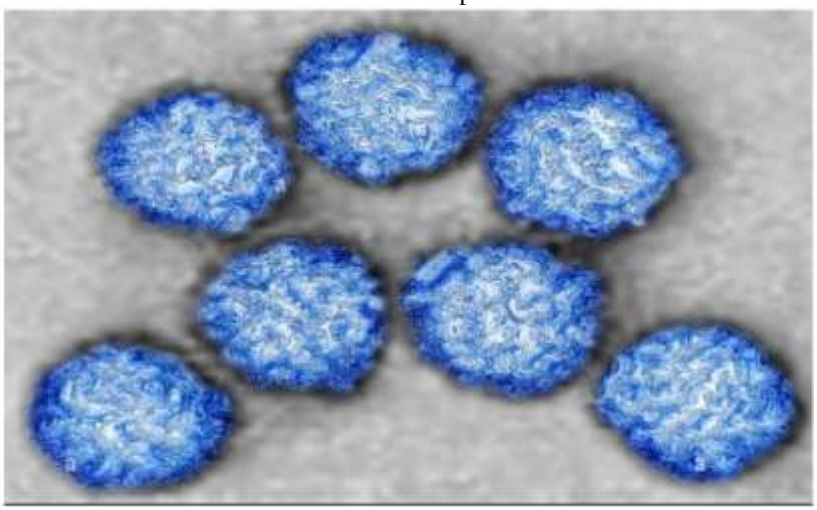

Fig.3- Electron microscopic image of Coxsackievirus.

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GENERAL REPLICATION CYCLE

The family Picroviridae and the genus Enterovirus, respectively, are the home of Coxsackievirus strain A. The genetic makeup of this retrovirus7 is RNA. A reverse transcriptase enzyme, which is in charge of converting RNA into DNA, is typically present in all retroviruses. The virus ingests its genetic material into the host cell after attaching to it and taking up residence there. Reverse transcriptase, an enzyme, then transforms the RNA into DNA. Using the biological mechanism of the host, this DNA penetrates Central Dogma. Transcription and translation occur, resulting in the formation of the polypeptide needed to build the capsid and the viroids.

The general lytic cycle looks like this. [11]

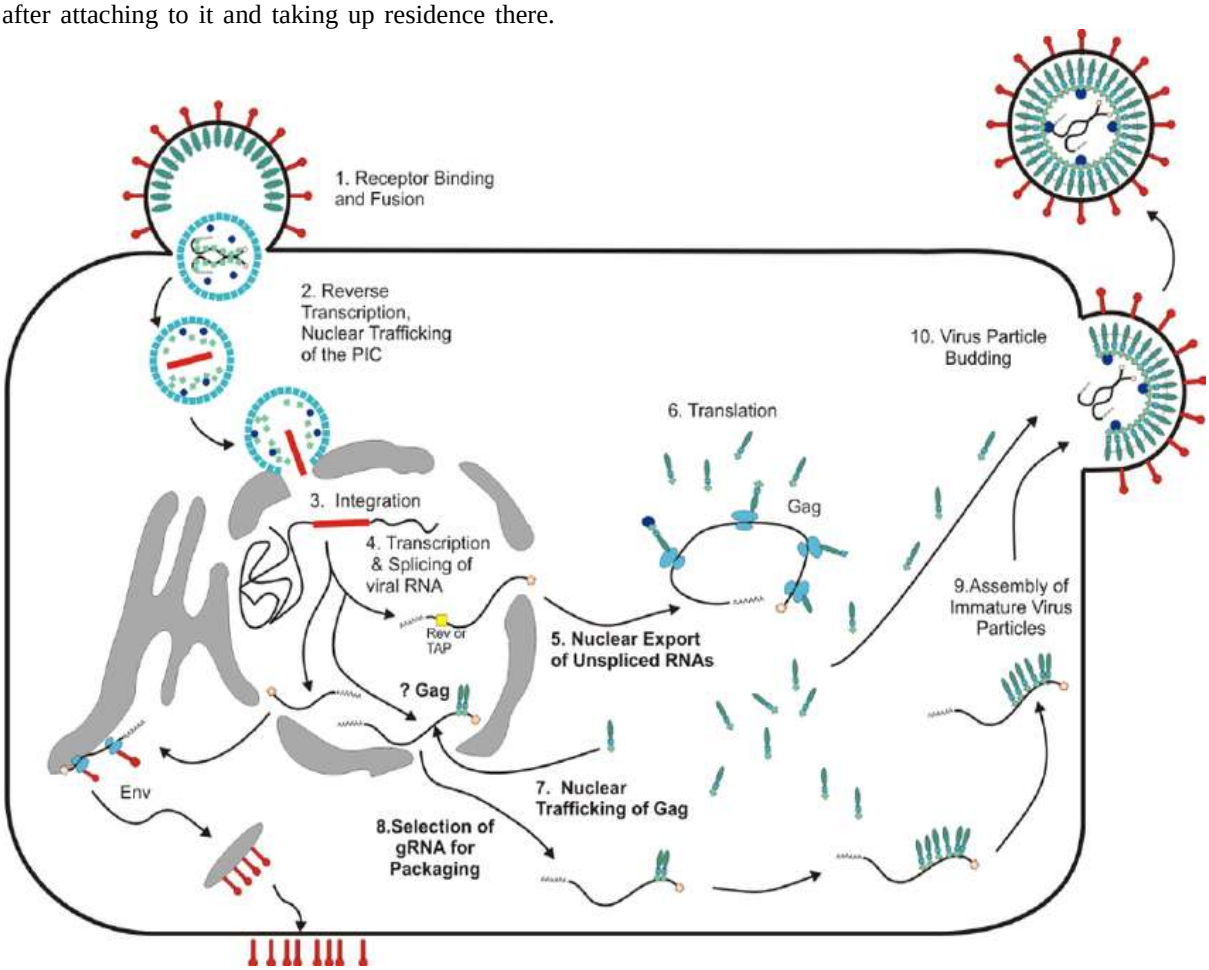

Fig.4- General retroviral replication cycle.

GENOME

The enterovirus A species of the family Picornaviridae, Coxsackievirus A16 (CVA16), is a frequent cause of hand, foot, and mouth disease (HFMD) in children and newborns. A structural polypeptide P1, nonstructural polypeptides P2 and P3, a 3′ UTR, and a 5′ UTR make up an enterovirus's genome. Based on the VP1 gene, CVA16 can be phylogenetically divided into two main genogroups (A and B) and five genotypes (A, B1a to B1c, and B2).

The 7,410 nucleotides (nt), not counting the poly (A) tail, make up the full-length genome of the CVA16 strain. The structural protein P1 has a length of 2,586 nucleotides, whereas the nonstructural proteins P2 and P3 each have lengths of 1,734 and 2,259 nt, respectively. The 3′ UTR was discovered to be 746 nucleotides long (82nt). 27.73%, 23.29%, 23.82%, and 25.16%, respectively, were the contents of A, C, G, and U, with a G+C content of 47.11%[2]

GENETICS

The genomic organisation of the coxsackieviruses with fully sequenced genomes is comparable to that of the other Enterovirus species, particularly Poliovirus. Briefly, the genome has

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roughly 7500 bases and two nontranslating poly (A) sections (NTR-Non translating Ribonucleotide), 5′ and 3′, on either side. The 5′-NTR is connected by the tiny protein VPg. In order for ribosomes to attach even in the absence of a free 5′ capped terminus, enteroviruses' 5′ NTRs contain internal ribosomal entry sequences (IRES). A high-molecular-weight polyprotein called p220 is encoded by the RNA acting as an mRNA and is made up of three segments that each code for one of the three precursor proteins, P1, P2, or P3.The virus-encoded serine proteases (2A and 3C) carry out a series of cleavages that result in the production of 11 polypeptides that collectively make up the capsid, the virus's exterior protective coat. These structural proteins are derived from the P1 section (mol. wt. 97000) of p220, respectively.

PATHOGENESIS

The virus enters through the oral route.[10]

The lymph nodes, small intestine, and throat are where it then multiplies. The virus then makes its way to the target organs through the lymphatic drainage system or circulation. The virus enters the lower intestine through the M cells and travels to the Peyer patches.

Prior immunological condition, immune deficiencies specific to particular strains, the higher pathogenic potential of mutant strains, genetic HLA composition, and/or hormonal interactions with viral multiplication are some of the factors that may increase vulnerability. When gender is taken into account, this virus affects men more often than it does women.

Clinical Signs of the Viral Infection on Different Body Parts

There is substantial evidence that coxsackieviruses cause a wide range of acute illnesses. The prevalence of asymptomatic diseases or the appearance of symptoms not specifically related to an infection (febrile sickness, persistent rash, flu-like syndrome) is another typical clinical aspect of enterovirus infections.Coxsackievirus utilizing cell lines, A strains are challenging to cultivate and isolate. They have received attention specifically for those of their serotypes that proliferate rapidly in cultured cells, including CA7, 9, 16, 21 and 24. Coxsackievirus can produce a variety of clinical symptoms depending on the target organ. [19]

Effect on the Nervous system

Rarely, polio-like paralysis has been linked to CA7, CA9, and CB1-6. 12) Coxsackieviruses and echoviruses both cause aseptic meningitis, but coxsackieviruses are less frequently the culprit.

Skin and mucosa

In youngsters of school age, asthma is prevalent. The tonsils, soft palate, tongue, and throat all have mildly irritated mucosa that is covered with clear crimson vesicles. It presents as a severe Mouth Ulcer or a self-limited stomatitis. From the vesicles, CA1-6, 8, 10, and 22 have been isolated. Vesicles on the palms of the hands and feet, as well as on the limbs and trunk, are symptoms of hand, foot, and mouth disease, which is occasionally accompanied by stomatitis. The primary serotypes involved are CB2 and 5, as well as CA4, 5, 9, 10, and 16. Majority of outbreaks are caused by CA16. Vesicular rashes that resemble herpes have been reported, and CB1 has been isolated from the fluid around the vesicles. Rashes resembling rubella are frequently accompanied by other, more common clinical signs.

Striated muscles

The symptoms of pleurodynia, also known as "epidemic Myalgia" or Bornholm disease, include a sudden discomfort in the chest (mostly caused by the diaphragm being involved) and a general malaise accompanied by a headache, sore throat, and fever. Summertime is the season when it most frequently affects children.[16]Patients who are recovering from CA infections have been documented as having persistent myalgia. A brand-new idea has just emerged known as "post-viral fatigue syndrome" (also known as "Myalgia encephalomyelitis"), which is characterised by extended muscular fatigue (lasting longer than six months) frequently accompanied by additional functional and/or psychological symptoms.

Heart

One of the primary etiologic agents of acute myocarditis, pericarditis, and myopericarditis is coxsackievirus B strains. While the condition frequently results in death in newborns, adolescents and adults typically have a favourable prognosis.[17]

The only treatment for Dilated Cardiomyopathy (DCM), a chronic cardiac condition marked by ventricular congestion that results in heart failure, is heart transplantation. This has something to do with an ongoing CB infection.

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High antibody titers (IgM included) against CB and the identification of its unique CB RNA by hybridization or polymerase chain reaction (PCR) in patient myocardium imply that CB has a role in DCM in humans. The disease's pathophysiology involves autoimmune, viral, and genetic elements.

Alimentary tract and liver

A few instances of hepatitis connected to CB have also been reported, particularly in newborns. One typical prodromal sign of coxsackievirus infections is gastroenteritis.

The combination of a genetic predisposition, the proliferation of a diabetogenic strain of CB in the islets of Langerhans, and antigen mimicry between CB proteins and pancreatic cell components is assumed to be the cause of the disease, which results in cell lysis.

Respiratory tract

Coxsackieviruses are in charge of respiratory tract infections. Pneumonia has been linked to CA9 and CA16. CB2, 3, 4, and 5 are linked to upper and lower respiratory tract infections, while CA21 and 24 are connected to the common cold. The symptoms displayed are comparable to those of myxo-, rhino-, and coronavirus-caused respiratory illnesses. Although they can happen at any time of year, enteroviral infections are most frequently detected in the summer.

Eye

It is known that a CA24 variation is the cause of this acute conjunctivitis. Clinically speaking, it is not as severe as enterovirus 70-caused acute hemorrhagic conjunctivitis. However, there haven't been any reports of ocular paralysis in the regions where the biggest epidemics took place.

Coxsackievirus, pregnancy and the neonatal period

It appears that there is little chance that pregnant women exposed to coxsackieviruses will have an abnormal foetus. The virus is transferred during labour or right away after birth when the sickness manifests in a newborn within the first two or three weeks of life. Infant infections can range in severity from mild to severe. Pancreatitis, hepatitis, pneumonia, encephalitis, meningitis, and myocarditis can also occur. Coxsackievirus outbreaks of severe nosocomial proportions have been documented in newborns.

PATHOLOGY AND HISTOPATHOLOGY

The incubation period ranges from two days (conjunctivitis) to one month or more, with the average being between ten and fourteen days. A examination of histopathological lesions found a variety of lesions in more than 400 patient isolations from a UK hospital. Although there are differences between Coxsackievirus strains A and B in terms of the frequency of lesions, The most commonly afflicted muscles in CA patients with polymyositis are the thoracic, abdominal, and thigh muscles. Though less frequently than CB, encephalitis, poliomyelitis, brown fat necrosis, and myocarditis are all seen. On the other hand, the primary pathologies seen in animals with CB infection include encephalitis, poliomyelitis, brown fat necrosis, endomyopericarditis, and pancreatitis.Numerous mononuclear cells enter inflammatory foci whenever histological lesions are present.

The virus is found in the myocardium of experimentally infected susceptible mice using a cardiotropic strain of CB3 administered intraperitoneally as early as two days after the infection begins. Within a week, the virus invades lymphocytic cells and is linked with calcifications in the centre or area of necrosis. During the second week, inflammation and necrosis reach their height. Following that, these lesions recede and are gradually replaced by fibrosis. The heart can be used to recover infectious virions during the acute stage of myocarditis. Some strains of mice can develop a chronic myocarditis at the end of the first month that is characterised by interstitial fibrosis and a moderate mononuclear cell infection.At this point, it is not possible to culture any infectious viruses, but in situ hybridization has identified the RNA genome in a tiny subset of myocytes around the fibrosis core. The formation of both acute and chronic lesions is heavily influenced by specific cytotoxic T cells and autoantibodies.

IMMUNE RESPOSE

Although the circumstances for this can greatly vary in geography and time, antibodies are thought to be everlasting. When the virus's present level of community transmission diminishes, naturally acquired immunity also declines.

Particularly in the gut, specific mucosal IgA functions as a protective agent. The presence of particular immunoglobulin M has been proven by a number of technological methods.[20]Virus surface epitopes are the only antigens that neutralising antibodies can bind to. Less than half

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of the proteins encoded by the genome are found in the total constitutive proteins of the capsid. Mononuclear cells predominate in the inflammatory foci found in the infected tissue in both human and mouse disorders; particular cytotoxic T cells are likely crucial in the regulation of Coxsackievirus infection. [19]

It is believed that coxsackieviruses elicit a largely type-specific immune response. The investigation of sera from infected individuals, however, frequently reveals antigenic crosses of neutralising, precipitating, and complement-fixing antibodies. For subgroups or serotypes, this raises the potential of shared epitopes. On VP1, a region shared by the majority of theenterovirus genus's members, including CA and CB, is a group-specific epitope that has been found in earlier investigations. Similar to this, in the presence of different enterovirus serotypes, T cells that have been primed with a specific serotype can multiply in vitro.[18]

PREVENTION AND TREATMENT

There are no specific vaccines for prevention that are now available or anticipated in the near future. Among the preventive measures is a comprehensive hygiene code. Particular attention must be devoted to individual hand washing because the virus is primarily spread via contact with contaminated water or food or by using dirty hands.[8]

Coxsackieviruses are resistant to several popular disinfectants, including alcohols, quaternary ammonium compounds, and chlorhexidine, thus those used in child care facilities must be carefully chosen. They are stable between pH values of 3.0 and 10.0.

Cleaning restrooms and other surfaces is advised using chlorine. Chlorinated or iodinated disinfectants ought to be used for hand cleaning. If the instruments have been cleansed before being immersed in the decontaminating bath, and the contact is for more than 30 minutes, disinfectants containing aldehydes (such as formaldehyde or glutaraldehyde) are sufficient.Coxsackieviruses are quickly destroyed by exposure to temperatures above 50°C, although the presence of Ca2+ or Mg2+ salts can shield the virus from heat inactivation. There are no therapeutic antiviral agents available. Globulins have only sometimes been found to be helpful.

Ibuprofen and paracetamol administration is a symptomatic therapy option for the management of tomato flu, which is a theoretically caused by the Coxsackievirus strains. Administration of serum plasma, also known as plasmapheresis, from a healed person to an infected individual, is a form of further treatment. Monoclonal antibody administration can also help with the treatment of this infection.

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