



Review Article

JMR 2020; 6(5): 243-245
September- October
ISSN: 2395-7565
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www.medicinarticle.com
Received: 28-07-2020
Accepted: 16-09-2020

A review on cytomegalovirus causing cancer in human

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Abstract

Cytomegalovirus is a kind of herpes virus, HHV-5. It primarily causes congenital infections and the fetal abnormalities during pregnancies. Sometimes, very serious complications and consequences may occur. As human cytomegalovirus is a ubiquitous virus occurring worldwide in nature their infections are very common in human. It has got lifelong latency in human with their reactivation causing cancer in future. The present paper deals with the study of causes and consequences of disease complex and the development of cancer by primary infection and the reactivation of HCMV in human.

Keywords: Human cytomegalovirus, Congenital infection, Disease complex, Reactivation, Cancer.

INTRODUCTION

Cytomegalovirus, also known as human herpes virus-5 is an enveloped, double stranded linear DNA virus belonging to the family *Herpesviridae*. It is one of the TORCH infections developing different diseases including cancer in human. Human cytomegalovirus (HCMV) is a ubiquitous herpes virus whose frequency of infection ranges from 50 % to 100 % in the general adult population. It causes significant morbidity and mortality in children during pregnancy (Michaelis *et al.* 2009 and Georges and Amit 2014) [1, 2]. If a female contracts the virus for the first time while pregnant or reactivated the same hidden virus she has, her unborn baby is at higher risk of receiving the virus vertically (Leung *et al.* 2003) [3]. The virus produces several anomalies in the developing fetus and the child thus delivered might be suffering from certain diseases including cancer in future. Griffith 2002, Rawlinson and Scott 2003, Michaelies *et al.* 2009) [1, 4, 5]. The present paper discusses the human cytomegalovirus primary infection, reactivation and the development of various diseases and cancer in the light of recent researches done so far in the field of viral origin of cancer. The present paper is prepared on the basis of researches done so far in the field of viral origin of cancer. The authors have gone through several original research papers in order to explore the facts regarding the cytomegalovirus causing different diseases including cancer in human.

CMV belongs to the group 1 (ds DNA), order *Herpesviridales*, family *herpesviridae* and the subfamily *Betaherpesviridinae*. This is a very common asymptomatic infection in human adults (Schottstedt *et al.* 2010) [6]. This is usually developed during pregnancy as congenital infections or in the patients who are immunosuppressed. According to an estimate by CDC approximately one of every 150 newborn child is being already infected from her mother at birth. Similarly, every hour a child is disabled due to congenital CMV infections. These infections may cause fatal abnormalities in newborn children as premature birth with low birth weight (Guillaume *et al.* 2013 and Kristen *et al.* 2014) [7, 8]; yellowing of the skin with rashes as petechie and purpura (John *et al.* 2017) [9]; dysphagia, diarrhea, colitis, splenomegaly, liver and spleen failure (Taniwaki *et al.* 1997, Kaufman *et al.* 1999, Patra *et al.* 1999, Dinesh *et al.* 2013, Talwani *et al.* 2013 and D'cruz *et al.* 2018) [10-15]; hearing loss (Kristen *et al.* 2014) [8]; ratinitis, blurred vision and blindness (David *et al.* 2007) [16]; nervous disorders, microcephaly, mental retardation, cerebral palsy, cerebral calcification, decreasing I.Q. levels causing psychomotor retardation, neuromotor loss, seizures, lack of coordination, weakness and numbness in legs (Anders and Goebel 1999 and Natacha *et al.* 2014) [17, 18].

Further, the relationships between cytomegalovirus infection and the development of Gullain Barry Syndrome and the association of CMVs with veneral diseases have also been established (Jordan *et al.* 1973 and Lunn and Hughes 2011) [19, 20]. In addition, thrombocytopenia is also caused by the cytomegalovirus (Simpson *et al.* 2016) [21]. The CMV infection of the heart is common in patients with fatal myocarditis. It may cause heart failure (Schonian *et al.* 1995, Kyto *et al.* 2005, Magno *et al.* 2016) [22-24]. Similarly, cytomegaloviruses sometimes, developed gastrointestinal infections causing enterocolitis (Patra *et al.* 1999, Kaufman *et al.* 1999) [11, 12], inflammatory bowel disease (Rowan and Cannon 2018) [25], gastric mucosal lesions (Himoto *et al.* 2009) [26], multiple ulcers of the ileum (Taniwaki *et al.* 1997)

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[10], intestinal obstruction (Dinesh *et al.* 2013) [13] and perforations in the human gut (D'cruz *et al.* 2018) [15]. The healthy children and immunocompromised individuals are more prone to have CMV infections. Similarly, most of the peoples are quite unaware of the fact that they are continuously being infected with HCMV from others especially in their teen age. As CMV virus has got lifelong latency in human if reactivated in future, it may also cause mononucleosis in 15 % of them. Unlike mononucleosis caused by the EBV, the CMV associated mononucleosis has a negative monospot test due to negative heterophyll antibodies. The symptoms of mononucleosis included fatigue, malaise, fever, muscle aches, loss of appetite, sore throat, lymphadenopathy and splenomegaly that can last for several months (Klemola *et al.* 1970, Fiala *et al.* 1977, Horwitz *et al.* 1986, Porath *et al.* 1987) [27-30].

Acquired CMV are spreading through liquid transmission via body fluids such as saliva semen, blood, urine, vaginal fluids and breast milk. It is known to infect most organs of the human body including brain, breast, colon, eye, kidney, liver and lungs. But healthy people very rarely become significantly sick from CMV infection. Although, CMV may be found at any part of the adult human body, their most preferable place has been reported to be the salivary glands (Koichi *et al.* 2007) [31]. HCMV remains latent within the body throughout life but it may reactivate at any time causing mucoepidermoid carcinoma of salivary gland (Melnick *et al.* 2011) [33] and other malignancies like prostate cancer in men (Geder *et al.* 1977) [32] and breast cancer in women (Georges and Amit 2014 and Richardson *et al.* 2019) [2, 34]. Similarly, HCMV significantly accelerated the development and progression of glioblastoma, a deadly form of brain cancer (Price *et al.* 2013, Wolfgang and Michael 2014, Christian *et al.* and Rahman *et al.* 2019) [35-38].

Further, anti CMV antibodies produced as IgM and/or IgG could be used as a marker for acute (IgM) or chronic infections (IgG) of the same virus in the body. A definitive diagnosis is done by culturing the virus or by detecting its DNA or specific protein named PP65 produced. In addition, tissue biopsy of the affected organ gives the inclusion bodies picture as look like an "owl's eye" under the microscope (Mattes *et al.* 2000)^[39]. Lastly, there is no vaccine available for CMV infection. However, an antiviral drug named ganciclovir (cytovene) is a first approved drug of choice for the same infection (Baldanti 2003, Glock *et al.* 2003, Lake 2003, Bennekov *et al.* 2004 and Revello and Gerna 2004) [40-44].

Acknowledgements

This piece of research work is dedicated to the memory of one of my friend Late Professor, Dr. Mahendra Pratap Singh who died of oral cancer in his young age. The authors are also deeply appreciating the institutions concerned for providing us necessary facilities during the course of this research work.

Financial Support and Sponsorship

Nil

Conflict of Interest

There are no conflicts of interest. The authors have approved the final version of the manuscript contributing equally.

CONCLUSION

CMV infections are very common creating no any problem to the carrier because it remains dormant in the body lifelong and can cause complications only during pregnancy or when the body becomes either immunocompromised or immunosuppressive especially after organ transplantations (Razonable and Paya 2003)^[45]. Some very serious complications and consequences may occur during pregnancy suffering from CMV infections are premature birth, weight loss, microcephaly,

hearing loss, blindness, mental retardation, cerebral calcification causing psychomotor retardation, low I.Q., cerebral palsy, lack of coordination, muscular weakness and seizures. Further, it has also been observed that very rarely healthy people become significantly sick from CMV infections in their later half of life but unfortunately, if the same virus is reactivated it may cause even cancer in human like salivary gland and prostate cancers, brain tumour and breast cancer in human female. Currently, there is no vaccine available for the treatment of CMV infections. However, an antiviral drug named ganciclovir (cytovene) is a drug of choice these days (Baldanti 2003, Landolfo *et al.* 2003, Rawlinson and Scott 2003, Schottstedt *et al.* 2010) [5, 6, 40, 46].

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