REVIEW OF INFECTIOUS AGENT IN CARCINOGENESI OF BRAIN

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Abstract

This study focuses on anatomically localized tumors in the head and neck areas. Brain cancers and head and neck cancers cause more than 873,000 cases worldwide each year, increasing every year. With late survival rates, brain and head and neck cancers are more likely to be serious conditions. Oncology is a multi-step process and the role of infectious agents in this development has not been fully identified. A major problem with such research is that the role of many infectious agents can be underestimated due to a lack or discrepancy in the experimental data obtained worldwide. As for brain cancer, no infection is directly accepted as cancer, although many viruses and parasites are associated with malignancies. Our analysis of the literature showed that human cytomegalovirus (HCMV) exists in different types of brain tumors, namely Cleoplastoma Multiform (GPM) and Meduloblastoma. In particular, GPM models have reports of up to 100% virus protein. Several epidemiological studies have reported links between brain cancer and toxoplasmosis seropositivity. In head and neck cancers, there is a distinct link between Epstein-Barr virus (EPV) and nasopharyngeal carcinoma (NBC). Considering that each undifferentiated NPC is EPV-positive, the virus titer size can be measured to show high risk people. In addition, there is an obvious link between the human papilloma virus (HPV) and head and neck squamous cell

carcinoma (HNSCC); In particular, 26% of HNSCCs are positive for HPV. HPV type 16 is the most common type diagnosed in HNSCCs (90%) and its prevalence is higher than reported in cervical cancer. Despite numerous studies showing the association of infectious agents with cancer, there is a dearth of articles covering the role of infection in brain and head and neck cancers, with different levels of involvement and direct or indirect causal effects. We review recent studies on the infectious origin of these cancers and present our current understanding of mechanisms for cancer, thereby providing possible new approaches to cancer treatment.

Keywords: cancer, brain cancer, head and neck cancer, cytomegalovirus, poliovirus, toxoplasma, Epstein-Barr virus, human papilloma virus, HIV, streptococcus anginoses.

Introduction

More than 237,000 people are diagnosed annually by brain therapy. Central nervous system. CNS tumours are classified by the World Health Organization based on hytological method, chelbehavior and cytogenetics. A significant proportion is neuroepithelial tumors, including glycel and non-glyphyl tumors. Classification Addition- includes tumors in the meninges (meningioma); Germ cell tumors; Tumors of the vendor area, CNS Lymphatic tissue, and peripheral nerves; And metastatic tumors. Tumor historical features and malignancy from grade 1 to grade IV are standardized for homogeneous and prognostic purposes.

Each year, more than 500,000 new head and neck cancers are diagnosed worldwide. The classification of these tumors is largely based on histological and clinical findings. Most head and neck cancers are squamous cell carcinomas that progress from the thin epithelial lining of the head and neck tissue.

Although many risk factors for brain and head and neck cancer have been identified, smoking and chewing tobacco, alcohol consumption, Poor diet combined with a hypodynamic lifestyle, acid reflux disease, hematopoietic stem cell transplantation, ionizing radiation, exposure to electromagnetic fields and carcinogenic chemicals, and various pathogenic infections pose an undesirable but significant risk. The International Agency for Research on Cancer (IARC) estimates that epidemics account for 16% of cancer deaths worldwide in 2008 and 20% of cancer deaths. Infectious agents are thought to cause a variety of pathological changes, including DNA mutations, cell cycle modulation, regulation of DNA repair mechanisms, chronic inflammation, and immune system dysfunction . Therefore, treatment for such conditions and their cause (i.e., infections) may interfere with car-synogenesis or prevent cancer. This approach is universally recognized for Helicobacter pylori, Hepa-Tides B and C viruses and human papilloma viruses, and prevents cancers such as gastric, liver and cervical cancers.

This review focuses on the latest updates on brain and head and neck cancers, which are linked for analysis due to general localization in the head region. Although these cancers are associated with many pathogens, it is not yet clear

whether infectious agents actually cause cancer or act as co-factors or spectators. Therefore, mechanisms underlying carcinogenesis associated with preexisting conditions and infections will be discussed.

Brain cancer

Brain and CNS in brain cancers. Of the neuroepithelial tumors, the most independent (50–60%) is the cleoplastoma. Cleoplastoma Multi-Form (GPM) is a highly anaplastic and diffuse astrocytoma or dermato . GPM is most often found in the cerebral hemispheres and its peak occurrence occurs between the ages of 45-70. Some tumors, such as mediloplastoma, brain stem glioma, ependymoma, and pineal tumor, are more common in children. Metelloplastoma is most often found in the cerebellum and spreads to other parts of the CNS. Histopathology Indicates that the myeloblastoma is formed from primitive immature cells. Some brain tumors may be benign, such as meningiomas and CNS that arise from the membranes of the brain .

Cleoplastoma and cytomegalovirus

The role of human cytomegalovirus (HCMV) in the pathogenesis of bath tumors is attracting increasing interest. CMV DNA or antigen levels are elevated in many types of cancer, and CMV is directly detected at high frequency in brain cancers. Using highly sensitive detection techniques such as immunohistochemical de-texting and PCR amplification, HCMV nucleic acids and genes> 90-95% of GPM tumors and CMV proteins pp65 or IE1 were detected at approximately 50% GPM Exposure to IE1, pp65 and delayed antigens was detected in 100% of 27 gpm samples, but not within the surrounding brain tissue or other brain pathology samples .However, in a different study, circulating CMV was not detected in the

blood of each of the five GPM patients, which may be due to a subtype difference Furthermore, it should be noted that the incidence of cleoplastoma and cytomegalovirus seropositivity vary between races .

Metelloplastoma and cytomegalovirus

HCMV proteins were also found in human medulla-plastoma cell lines, which accounted for 92% of the immediate early protein and 73% of the late protein. In addition, high levels of CMV DNA and viral protein were identified in primary myeloblastoma, myeloblasto-toma cell lines, and genocrafts .Together, these findings of cell or tissue culture and patient blood analysis suggest the role of CMV in different types of brain cancer. However, as discussed further, more research is needed on the basic mechanisms.

Clear tumors, meduloblastoma, CNS tumors and paleoma viruses

Brain cancer is commonly associated with polio-viruses such as SV40, PKV, and JCV .The association of SV40 with the development of brain tumors was first observed in infected scientists working with viral cultures .Direct induction of SV40 oncogenesis was subsequently demonstrated experimentally in several murine specimens . Although some documents have reported central nervous system tumors associated with PKV consolidated reports have shown no association .Exposure to JCV proteins and nucleic acids has been detected in many cases, such as clot tumors localized to the nervous system, meduloblastoma, and lymph nodes. JCV infection can cause neurotransmitter abnormalities in the central nervous system (CNS), for example in advanced multi-focal leukoencephalopathy, which is dangerous .Common mechanisms for all polioviruses are further discussed.

Brain cancer and endogenous parasites

The Association of Neurocysticercosis with Brain Cancers and Infections has been reported in several reviews and is still under investigation. Some geographical associations have sparked interest in further searching for this topic. Recent works by Thomas et al. showed that the incidence of brain tumors was higher in the geographical areas common to the protozoan para-site Toxoplasma .In another study, increased D in France. Increased brain cancer mortality due to Gondi seroprevalence .

It was observed in experimental animals that Gondi infection caused glaucoma. With regard to human profiles, d. Gondi antibodies were found in the astrocytoma and meningioma samples. Further research should be done on the role of infectious particles directly in such associations and brain tumors, the role of parasitic infection for cancer at the molecular level, or the development of a predisposing environment.

Brain cancer and bacteria

Interestingly, there is not much information about getting brain cancer with a bacterial infection. Myco-plasma infections have been found in a wide variety of cancerous tissues, including glioma ,although such infections are commonly associated with cytokine-mediated damage and inflammatory lesions ,leading to various CNS diseases .Although one study suggests that 20 meduloblastoma tumors identified by the OMP31 primer / prop set may have brucellosis DNA, the association of neuroprotectomy with meduloblastoma remains uncertain .Currently

a small number of people do not support the association and the authors suspect that the DNA came from food rather than from infections. Although some bacterial species are suspected to be present in cancerous tissues, there is currently insufficient data to conclude that bacteria play a role in brain cancer.

Head and neck cancers

Biologically, head and neck cancer refers to a group of cancers located in the aerodynamic tract, including the lip, oral cavity, nasal cavity, paranasal sinuses, larynx and larynx, oropharynx and hypopharynx, as well as the salivary-ivory glands and local lymph nodes. Most cases (approximately 90%) of head and neck cancers are square cell cancers. Head and neck squamous cell carcinoma (HNSCC) derives from the mucosal lining throughout the local area and stimulates tumor growth in the nasal and oral cavities, nasopharynx, larynx, oropharynx, hypopharynx, and paranasal sinuses. Nasopharyngeal carcinoma and EPV

Epstein-Barr virus (EPV) is associated with nasopharyngeal carcinoma (NBC), Burkitt's lymphoma, and Hodgkin's lymphoma and, to a lesser extent, HIV-positive CNS lymphomas and hypopneumatic and laryngeal tumors .NPC is a head and neck cancer that is prevalent in the central region and some countries in Asia, where EPV antibody titers can be measured to show high risk populations. It is a leading cancer of the epithelial cell lining and is responsible for nasopharyngeal neoplasms in adolescents and children. All types of NPC occur

Men are twice as likely as women, and type 2 and 3 cancers are associated with EPV virus titre levels .

Every indistinguishable NPC is EPV-positive, regardless of geographical appearance .The EPV virus is classified as a group 1 cancer by the IARC.

Oral squamous cell carcinoma (OSCC) and bacterial and mycotic infections

There is an obvious link between certain types of bacteria and certain types of cancer. In addition to tobacco and alcohol consumption, S.C. Angina pectoris is a risk factor for esophageal and head and neck cancer, early leukoplakia and squamous cell carcinoma, although the exact mechanisms are not known .A report on PCR and Southern Blood analyzes (100% and 33%, respectively) of S. Angi-noses refer to the positive nature of DNA. S. Angina pectoris is more frequently detected in squamous cell carcinoma than other types of cancer and has been shown to be associated with aerodynamic tract cancer .

Other bacterial pathogens include Privodella melanino-genica, Eubacterium sapurium, c. Gingivalis, Leptotrichia buccalis, and Streptococcus mydis species were found to be more concentrated in OSCC patients than in control groups .It has been proposed that altering tumor cell receptors may alter the adhesion of certain bacterial species .

Execobacterium oxytocin, b. Most of the microorganisms isolated from tumors are sacrolytic and acid-tolerant, such as yeast, acti-nomocytes, phytobacteria, lactobacilli, streptococci, and villonella, which characterize the acidic and hypoxic tumor environment.

Fungal infections, such as chronic hyperplastic candidiasis caused by Candida species, have been linked to invasion of the oral epithelium and progression to dysplastic changes .

Mechanisms for carcinogenesis

Mechanisms in brain cancers

While HCMV has been shown to interact with key signal pathways in cancer development, consensus on the oncomodulatory role of HCMV in cleomas has recently been reached .The mechanism of cryoplastoma growth has recently been clarified by Flickr et al., Showing that many modifications include PI3K / AKT, ret-inoblastoma (Rb) and p53 Interestingly, CMV-infected cells exhibit reduced p53 and Rb activity. CMV cancer is caused not only by the expression of cell proliferation factors, but also by the immune system. CMV interleukin (IL) -10 has been shown to convert mono-sites and microglia in cleoplastoma into immune-promoting vegetative phenotypes . CMV infection is asymptomatic in immunocompromised individuals, but constant antigenic pressure leads to a fold in CD8 + CD57 +, CD4 + CD28- and CD8 + CD28-.

Cells specific to CMV antigen pp65. These cells express encephalin-inhibiting receptors, thus inhibiting the activity of cytotoxic lymphocytes .In addition, analysis of CMV proteins shows that US28 is an active chemical receptor that induces a carcinogenic phenotype by producing expression of COX-2, PGE2 and IL6 .

A characteristic feature of JCV infection is the initial activity of the JCVE, a human neurotrophic virus promoter, that initiates the transcription of large D-antigen .The main molecular mechanisms of paleoma virus oncogenesis are tumor

suppressors by viral D-antigens and inhibition of epigenetic transcriptional regulation by histone acetylation. The D-antigens of all Paphova-viruses bind to Rb, which interferes with cell cycle regulation. They bind to and inactivate CBP / p300 and p53 proteins. Large D-antigen shows mutation towards cellular DNA and prevents DNA repair. The oncogenic properties of small D-antigen are less well known, but it is known to play a mitogenic role and is involved in cell proliferation and uncontrolled cell proliferation .Other viral proteins (e.g., agnoprotein) bind to p53 and enhance the activity of p21 / WAF-1 .

The effect of parasites on host immunity is to increase the risk of brain cancer by inducing chronic inflammation, preventing apoptosis, and genetic mutation from parasite to host .For example, d. Gondi continues in human pseudocysts, macrophages and neurons. In the latent stage the parasite is in the Brady-Zoid state and causes mild inflammation as a result of the host's immune response .However, dying cysts can cause severe inflammation. In the case of Dania solium and Plasmodium ,persistent cysts trigger the mitogenic response of lymphocytes to achieve immunity. In addition, d. Cysticercosis of the psoriasis initially stimulates the immune system to deliver a protein source to the parasite, which then receives the host membrane proteins, thus avoiding immunosuppression. The larvae of Scystosomula resemble novel lymphocytes and avoid the immune response .In summary, any disruption or disruption of the host immune system can predispose an organism to cancer, although much needs to be learned about the links between parasites, the host immune response, and the development of brain cancer.

Mechanisms in head and neck cancers

In EPV-associated cancers, the virus affects lymphocytes by binding to the main envelope glycoprotein GB350 IP cell CD21 receptor and by binding to the second glycoprotein, GB42, MHC class II molecules. The cytoplasm eventually transforms EPV virus particles [Epstein-Barr nuclear antigens (EPNAs), latent membrane proteins (LMP) and Epstein-Barr virus-encoded small RNA (EPR) from B cells into recently infected lymphoblastoid cell lines, , Regulation of genetic instability and stable reproduction occurs. EPV is also said to enter nasopharyngeal cells through IgA-mediated endocytosis. Because the EPV gene is monoclonal in nature, EPV infection occurs prior to clonal proliferation of malignant cells .

Recent studies have shown that non-polydenylated RNA (EPR) is present in all affected cells. This supports the notion that EPV infection is involved in the early stages of NPC cancer. Molecular abnormalities in NPCs are complex and include inactivation of genes that suppress RASSF1A and p16 in chromosomal regions 3p21 and 9p21. These events occur early in the pathogenesis and may precede infection of the abnormal epithelium by the spread of EPV and B-cells derived from adjacent lymphoid tissues. Inactivation of DSCL1, EDNRP and death-associated protein kinase genes via stimulus methylation is frequently observed. Regulation of PI3K / Akt, Wnt / cat- catenin, TGF-8, and mitogen-activated protein kinase (MAPK) signaling pathways in the NPC by regulating the genetic expression specification, NI-k82, Survivin, and PLC-2. Showed. -catenin, and regulation of synapses .Almost all EPV genes are expressed in the active phase of the infection. The earliest genes are BRLF1 and BZLF1, which encode trans-cryptal transactivator proteins that promote cell replication, which trigger the

expression of viral genes. BZLF1 and BRLF1 proteins also inhibit tumor suppression p53 and pRb, respectively .

HPV-related cancer involves the synthesis of HPV DNA in the host cell and the expression of viral oncoproteins E6 and E7. E6 protein stimulates the breakdown of p53 by epicidin-mediated proteolysis, which leads to loss of p53 function. E7 protein binds to pRb, stimulates S-phase entry and leads to proliferation, malignant transformation, and cell-cycle variation. E6 and E7 proteins can activate somatic cell delo-merase expression, inducing proliferation and cellular division. In humans, 85% of malignant neoplasias show elevated telomerase activity, compared with only 27% of benign tumors. Telomerase activity in HPV-infected cells Reduces exposure to pRb and p53 and increases exposure to p21WAF1 and p16INK4a. Furthermore, p21WAF1 is inactivated, probably due to binding to E7 protein. These changes lead to a loss of control of G2 / M mutation and consequent accumulation of mutations, resulting in genetic instability of the affected cell .

The pathogenesis of KS involves a variety of mechanisms dependent on viral and cellular activity, and is associated with inflammation and angiogenesis induced by endothelial growth factors (β-FGF, PDGF, VEGF) and HIV-DOT. As well as cell proliferation and anti-apoptotic activity by vBCL2 .The role of HIV-1 infection in the initiation and progression of AIDS-KS involves two important paracrine mechanisms: enhancement of HIV tod protein production and cytokine production .The HIV-1 dot is an 86-amino acid protein that has the primary function of enhancing the processing of RNA polymerase II and transcription initiation .In contrast, there is no clear evidence for the role of HHV-8 in the development of KS pathogenesis. Based on current data, HHV-8 infection is essential for the

development of KS, but not sufficient, with additional concomitant factors such as hormones, genetic pre-transfer and / or co-infection with other infectious agents. It may be necessary for the development of the disease

Several mechanisms for bacterial cancer have been proposed. Studies indicate that many bacteria can cause chronic infections by producing toxins that interfere with cell cycle and lead to changes in cell growth .Other chronic bacterial infections induce cell proliferation by activating MAPK pathways and cyclin D1 ,and many infections can suppress apoptosis by modifying PLC-2 proteins or by inactivating BRP .Such infections may reflect some of the major events in tumor development, and in fact the pre-existing lesions that develop in such infections may be reversed with antibiotic treatment and elimination.

Bacteria

Various studies have shown that antiviral and antibacterial drug therapies have a positive effect on the prognosis by preventing tumorigenesis. Therefore, oncologists can benefit from developing novel cancer treatment strategies by understanding the mechanisms of infection-related cancer.

Recently developed vaccines to prevent infection with HPV types 16 and 18 include cervical and cortisol, which work against cervical cancer many years after vaccination .Numerous, recent preliminary studies of multivalent vaccine targeting E7 proteins in vaccinated mammals (e.g., mice and rhesus monkeys) against HIV 16, 18, 31, 45, and 52 subtypes. Tumor responses and reduction of TC-1 tumor cells [82,83]. Restorative protein-based vaccine Pentarix reveals a CD8 response against five strains of HPV in humans. These findings suggest that prevention of

infection with HPV subtypes is important in preventing tumor growth in HPV-associated ma-lignant neoplasia. Another study involving the synthetic vaccine against high-risk HPV type 16 demonstrated a potent T-cell response reduction and viral elimination in 9 out of 20 women with complete relapse of all lesions and high-grade vulvar intrapithelial neoplasia.

CMV is detectable in most GPMs and may be a potential target of treatment. Even low levels of CMV gene expression can be used to target immunity .Interestingly, T-cell therapy was most effective in CMV + GPM patients and entered stage I / II clinical trials .Such therapies amplify CMV-specific T-cell populations that recognize pp65 + and IE1 + targets and kill CMV-infected autoimmune GPM cells

Similarly, in EBV-related nasopharyngeal cancer, treatment of the infection produced promising outcomes in relation to cancer prevention. Yoshisaki et al. EPV treatment demonstrated suppression of tumor growth by injecting the antiviral drug cytoflavir into the tumor once every 3 weeks, and EPV-encoded RNA analysis revealed reduction within the tumor cells

Population. In addition, many CNS diseases, including encephalitis, encephalitis, post-transplant lymphoproliferative-dive disease (PDLT), and CNS lymphoma, have been associated with EBV infection, although antiviral therapy has been ineffective or successful .Therefore the results on clinical efficacy are inconsistent. In another study,co-administration of adjuvant interferon-beta after radiochemotherapy for 17 cell cancers and nine undifferentiated cancers showed a 100% survival rate at 96 months .It is known that adjuvant interferon-beta therapy in combination with adjuvant-dose-hyperprocessed radiation enhances the effectiveness of modified radiation therapy.

Despite the numerous cases, the role of inactive agents in mechanisms of cancer requires extra attention from physicians. Statistically, infections appear to be associated with a wider area of brain and head and neck cancers, and it seems that such infections are less likely to cause cancerous pathogens. However, it is not clear whether the infectious environment triggers the patient's cancer by controlling the host's immune system or whether the cancer cells weaken the cellular and immune response so that the infectious agents can easily overcome the protective mechanisms and avoid the host cells. Nevertheless, the efficacy of antiviral, antimicrobial, and therapeutic vaccines against onco-related infections in the treatment of cancer has been reported in several studies. Based on the data reported in this review, we believe that antimicrobial resistance is an important treatment strategy to reduce or prevent brain and head and neck disorders.

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