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Short Communication

HPV Related Disease and Cancers-Increased incidence of HPV-Positive Oropharyngeal Cancers

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Human pappiloma virus (HPV) is a double stranded circular DNA virus belonging to the pappiloma virus family, it is transmitted by skin to skin or mucosa to mucosa contact and enters the body via cutaneous or mucosal trauma. HPV infectionis the most common sexually transmitted disease although it is usually cured by the immune system. Worldwide, the risk of being infected at least once a lifetime among both men and women is 50%. HPV infection causes common anogenital warts, along with non dermatological diseases. Role of HPV has been extensively studied, initially in cervical cancer, but also in other types of cancer [1].

As per WHO statistics, common cancers are one of most prevalent causes of mortality worldwide with 8. 2 million deaths in 2012, with this trend not changing in recent years. Viral infections contribute to 15-20% of all human cancers whereby several viruses play significant roles in the multistage development of malignant cancers. The circulation between a given virus and its associated cancer ranges from 15-100% [2]. Cervical cancer is the second most common cancer among women all over the world with>85% of cases occurring in developing countries [3]. Practically 90% of Cervical cancer cases are caused by HPV infection [4]. HPV are a large group of viruses that consists of more than 180different types, among which 15 have high oncogenic properties [5]. HPV infection can lead to a variety of disease varying from benign lesions to cancer. In 2007the Agency for Research on Cancer (ARC) working group classified 21 HPV types (HPV6, 11, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 70, 73and 82) as the most prevalent for their association with cervical cancer [6].

Thus Aimagambetova and Aizan reviewed the distribution of HPV infection in Kazakhstan where they reviewed 39relevant articles published till 31st july 2017. Inclusion criteria used were; general population data, cytology results available and use of polymerase chain reaction (PCR) and/or hybridcapture2 Digest group –USA for HPV detection. As reported in limited studies the prevalence of HPV infection in Kazakhstan ranged from 43. 8% to 55. 8%. Thus the scenario regarding epidemiology of HPV Related Cancer in Kazakhstan was not very clear. One study reported a reduction in laryngeal cancer observed during the years studied. while cervical cancer incidence increased to about 3000 new cervical cancer cases and about 1000 cervical cancer deaths every year. Thus concluding that the high incidence of cervical cancer with a significant mortality rate in Kazakhstan is an evidence that HPV infection is abundant despite an absence of HPV screening along with low public awareness of the problem. To Have a well-informed, understanding population regarding role of HPV infection in Kazakhstan could increase the public acceptance of screening and intervention programs for decreasing morbidity and mortality due to HPV infection [7].

Head and neck squamous cell carcinoma include cancers of the oral cavity, larynx, hypopharynx and oropharynx [8]. The oropharynx comprises of tonsils and the base of the tongue. Despite a steady reduction in the incidence of head and neck cancers in the last few decades, the incidence of oropharyngeal cancer (OPC) has shown an overall rise which largely attributes to the increase of infections with the HPV [9]. Habbou., *et al*. [10] calculated that

the prevalence of HPV positive OPC in 6Canadian centres increased from 47% in 2000to about 74% in 2012. In the USA, the incidence of HPV positive OPC rose by 225% between 1988 and 2004 [11] and now constitute as high as 90% of all new cases of OPC. The patients are often younger and healthier (median age at diagnosis; 54years) [12] with a high socioeconomic status and minimal to no smoking history, that marks a shift in cause from the traditional older patient having a long history of tobacco and alcohol abuse [9,13]. With the absence of traditional factors, a combination of inherent genetic factors, HIV exposure and behavioral risk factors (that include an increased number of sexual partners, earlier onset of sexual activity and In men a history of anogenital warts) are thought to contribute. Once treated HPV positive OPC is also associated with a more favourable prognosis. But problem is this increasing prevalence is mostly unfamiliar to many treating physicians, which is compounded by complacence on the part of young and healthy patients who don't have a history of smoking regarding seeking medical attention for cancer symptoms, thus diagnosis and treatment usually gets delayed. As per the WHO, HPV is the commonest STI worldwide [14]. Though, most cases go unreported the US Centers for Disease Control and Prevention estimates that up to 75% of the US reproductive age population has been exposed to HPV [15]. At any one time, 6.9% of individuals are harbouring detectable levels of HPV in the oral cavity or oropharynx [2]. Transmission of HPV occurs mainly through sexual contact, and orogenital contact can =>oral or oropharyngeal HPV infections [13]. Though most infections are asymptomatic and get spontaneously cleared within the2 years, at least 15 of more than 100 viral types are characterized by high oncogenicity [16]. The greatest proportion of HPV related cancer cases are HPV 16 positive and are thus amenable to preventive methods like vaccination [7,13].

HPV Vaccination

2 HPV Vaccines are available currently; the quadrivalent HPV vaccine Gardasil (Merck Sharp and Dolime, Kenilworth, NJ, USA) that protects against HPV 6, 11, 16 and 18 and the bivalent Cervarix (GlaxoSmith Kline, Brentford, UK) that protects against HPV type 16 and 18 [17]. Trying to wait for data which evaluates the longterm effects of those vaccines on cervical cancer outcomes data that has been collected show its role in preventing precancerous lesions. Recent Cochrane review of 26 trials that included 73, 428 participants showed high certainty evidence that the vaccines decrease rates of cervical pithelial intraneoplasia (CIN) grade 2 to 2/10, 000, from 164/10, 000, grade 3 to 0/10, 000 from 70/10, 000, and adenocarcinoma *in situ*, to 0/10, 000 from 9/10, 000 in women 15-26 years of age [18]. No increase in side effects have been found with these vaccines. Moreover recent studies showed that vaccination is also effective in preventing cancer recurrence following loop electrosurgical excision procedures with reduction in grades 2 and 3 CIN by upto 86. 5% in one prospective trial [19]. In Canada, the National Advisory Committee on immunization has recommended routine HPV vaccination for all girls, women, boys and men between 9 and 26years of age and permissive vaccination in persons>26yrs of age if earlier were unvaccinated [20]. Yet coverage of boys and men regarding vaccination varies in view of beliefs regarding vaccination is less effective. In the US, new guidelines regarding routine vaccination advice for all children of 11 or 12 years of age or for all girls and women up to 20yrs of age and for boys and men 13-21yrsof age if earlier were unvaccinated. ''Permissive vaccination'' for men between 26yrs and those who have sex with men who are at high risk of anogenital cancers [21]. Efficacy, immunogenicity and safety of HPV transmission has been validated in older patients [22]. Initially thought this vaccination was to prevent cervical cancer, but now there is evidence that HPV vaccine have a definite role in prevention of many other non- cervical cancers. In a cohort study of 202 patients with a previously treated high grade anal intraepithelial neoplasia, the quadrivalent vaccine was associated with a reduced risk of recurrence at 2yrs after study entry (hazard ratio: 0.47; p=0.05) [23]. Moreover by 2020 the number of HPV positive OPC's between 2.9 and 4.5 times the risk of their female counterparts. These numbers highlight the need for further studying the burden of disease and possibly reemphasize male vaccination, given the likely hood that an even >better benefit from the vaccines will be realized [7].

Treatment related concerns with management

Head and cancer remains a relatively rare disease accounting for only 5%of cancers worldwide, the consequences of treatment and patients patients needs after treatment are less widespread. The epidemic of HPV –positive disease needs clinical concerns for understanding not only new risk factors and clinical presentations, but also a set of treatment related concerns for a younger population of patients with a better prognosis.

General treatment considerations

Recently traditional standard of-care treatment for all patients except for those with early stage OPC is combined cisplatin based chemoradiotherapy. This therapy has been shown to be very effective with a long term as of upto 95% in HPV –Positive patients. However that success requires a high cost in overall quality of life

for the patients. A dry mouth, with loss of taste are almost present. Dysphagia is of more importance that very severe –to the extent that 20-30% patients never go back to eating entirely by mouth and need a percutaneous gastrotomy to be lifelong [23]. With the new understanding of HPV –Positive OPC, the Quality of life (QoL) implications of side effects of treatment for affected younger patients with an excellent prognosis has caused a lot of studies which aimed to de intensify treatment while preserving antitumor efficacy. 2 approaches have been used to decrease the morbidity of chemoradiation, that has been the main stay of treatment for >25years. One approach considers decreasing the dose of minimizing the field of irradiation or both. The 2nd approach has introduced surgery again into the treatment of the disease. Before the1990's surgery was used routinely. These largely invasive transcervical approach was given up in favour of chemotherapy. But newer techniques which rely on robotics surgery have become popular. As compared to approaches via neck, new transoral procedures are not that intensive, with recent systematic reviews showing less swallowing problems [24]. patients can return home after surgery within a few days and return home, eat by mouth.

The treatment of HPV positive disease is in flux and ongoing but guarded. interest in safe de-escalation continues. Recently phase IIIR adiation therapy Oncology group 2016 [25] and. De escalate HPV [26] trials have been published recently. Both rejected cetuximab as a treatment equivalent to cisplatin, showing similar rates of toxicities, but inferior survival outcomes with cetuximab. Deescalation trials should be under taken with these findings. A list of trials can be found on http://Clinical trials. gov/. including the phase III Trans-Tasman Radiation Oncology Group 12 that is supposed to finish in 2019.

Thus You., *et al*. summarized how delays of up to 40yrs following infection before the disease presents itself, physicians are now having the responsibility of recognizing the presentation of this slow growing epidemic. These cancers usually present in younger, healthier subjects who might not have the typical risk factors for head and neck cancers and thus can go unnoticed. Mainstay of treatment is combined chemoradiotherapy with good prognosis for survival. Still many patients will have long term experience with the debilitating side effects of therapy. Thus, an interdisciplinary team approach with special attention to psychosocial problems represents the main stay for getting best outcomes and QoL during the survivorship periods [27].

Bibliography

1. Brianti P., *et al*. "Review of HPV-related diseases and cancers". *New Microbiology* 40.2 (2017) 80-85.

2. Mc Laughlin-Dubin and M Munger K. "Viruses associated with human cancer". *Biochimica et Biophysica Acta* 1782.3 (2008): 127-150.

3. SenapathY JG., *et al*. "The present scenarioof cervical cancer and HIV epidemiology in India-An outline". *Asian Pacific Journal of Cancer Prevention* 12.5 (2011): 1107-1115.

4. Schiffman M., *et al.* "Classification of weakly carcinogenic human papilloma virus types-addressing the limits of epidemiology at the borderline". *Infectious Agents and Cancer* 4 (2009): 8.

5. Bernard HU., *et al.* "Classification of pappiloma viruses (PVs) based on 189PV types and proposal of taxonomic amendments". *Journal of Virology* 401.1 (2010): 70-79.

6. International Agency for Research on Cancer Monographs on the Evaluation of Carcinogenic risk to Humans. 90. Human papilloma viruses. WHO Press, Lyon, France (2007): 35-38.

7. Aimagambetova G and Azizan A. "Epidemiology of HPV –Related Cancers in Kazakhstan:a Review". *Asian Pacific Journal of Cancer Prevention* 19.5 (2017) :1175-1180.

8. Du J., *et al.* "Prevalence of oral Human papilloma viruses infection among youth, Sweden". *Emerging Infectious Diseases* 18.9 (2012): 1468-1471.

9. Guo T., *et al.* "The potential impact of prophylactic Human papilloma viruses. Vaccination in oropharyngeal cancer". *Cancer* 122.15 (2016): 2313-2323.

10. Habbous S., *et al*. "Human papilloma viruses in oropharyngeal cancer in Canada:analysis of 5comprehensive cancer centres using multiple imputation". *CMAJ* 189.32 (2017): 1030-1040.

11. Chaturvedi AK., *et al.* "Human papilloma viruses and rising oropharyngeal cancer incidence in the United States". *Journal of Clinical Oncology* 29 (2011): 4294-4301.

12. Elrefacy S., *et al.* "HPV in oropharyngeal cancer: the basics to know in clinical practice". *Acta Otorhinolaryngologica Italica* 34.5 (2014): 299-309.

13. Pyrynia LR., *et al.* "Epidemiology of HPV –associated oropharyngeal cancer". *Oral Oncology* 50.5 (2014): 380-386.

14. World Health Organization (WHO). "Human papilloma viruses a and cervical cancer (Web page) Geneva". Switzerland WHO (2018).

15. Cates JR., *et al.* "Human papilloma viruses: A hidden epidemic in the United States". Washinton DC. Population Reference Bureau (2001).

16. Banu D., *et al*. "Novel immunotherapeutic approaches for head and neck squamous cell carcinoma". *Cancers* 8.10 (2016): E87.

17. D'Souza G and Dempsey A. "The role of HPV in head and neck cancer and review of the HPV Vaccine". *Preventive Medicine* 53.1 (2011): S5-11.

18. Arbyn M., *et al. "*Prophylactic vaccination against Human papilloma viruses to prevent cervical cancer and its precursors". *Cochrane Database Systematic Reviews* 5 (2018): CD309069.

19. Kang WD., *et al.* "Is vaccination with quadrivalent HPV vaccine after loop electrosurgical excision procedure effective in preventing recurrence in patients with high grade cervical intra epithelial neoplasia (CIN2-3)?". *Gynecologic Oncology* 130.2 (2013): 264-268.

20. Rational Advisory Committeeeon Immunization. Updated Recommendations on Human papilloma virus vaccines-9 valent HPV Vaccine and Clarification of Minimum Interval between Doses in the HPV Vaccination Schedule, Ottawa, Public Health Agency of Canada (2016).

21. Meites E., *et al.* "Use of a 2 –dose schedule for Human papilloma virus 1vaccination-updated recommendations of the Advisory Committee on Immunization Practices". *Morbidity and Mortality Weekly Report* 65.49 (2016): 1105-1108.

22. Wheeler CM., *et al*. "On behalf of the VIVIANE Study Group. Efficacy, safety and immunogenicity of the Human papilloma viruses 16/18 ASO-4-adjuvanated vaccine in women older than 25years:7years follow up of the phase 3, double blind randomized controlled VIVANE study". *The Lancet Infectious Diseases* 16 (2016): 154-166.

23. Swedish KA., *et al*. "Prevalence of recurrent high grade anal neoplasia with quadrivalent Human papilloma virus vaccination of men who have sex with men: a nonconcurrent cohort study". *Clinical Infectious Diseases* 54.7 (2012): 891-898.

24. Dison I., *et al.* "Long termpatient reported swallowing functions following chemoradiotherapy fororopharyngeal caecinoma". *Radiotherapy and Oncology* 128.3 (2018): 452-458.

25. Dawe N., *et al.* "Functional swallowing outcomes following treatment for oropharyngeal carcinoma:a systematic review of the evidence comparing transoral surgery versus non-surgical management". *Clinical Otolaryngology* 41 (2016): 371-385.

26. Gillison MLTrom AM., *et al.* "Radiotherapy plus cisplatin or cetuximab in low risk Human papilloma viruspositive oropharyngeal cancer (DE ESCALATE HPV) :an open label randomized controlled phase 3 trial". *Lancet* 393 (2019): 51-60.

27. You EL., *et al*. "Human papilloma Virus-associated oropharyngeal cancer: a review of current evidence and management". *Current Oncology* 26.2 (2019) :119-123.

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