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Human immunodeficiency disease in new diagnoses of head and neck squamous cell cancer: are we testing?

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Main Article

Miss K McNamara takes responsibility for the integrity of the content of the paper

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Abstract

Background. Human immunodeficiency virus infected patients have a three-fold increased risk of head and neck squamous cell carcinoma. The British HIV Association recommends human immunodeficiency virus testing in all new diagnoses of head and neck squamous cell carcinoma.
Objectives. This observational study aimed to examine the current routine practice of human immunodeficiency virus testing in patients with newly diagnosed head and neck squamous cell carcinoma, and to address the importance of this test in promoting the early diagnosis and treatment of human immunodeficiency virus.
Methods. All head and neck cancer multidisciplinary teams in England were questioned on their protocol for human immunodeficiency virus testing in new diagnoses of head and neck squamous cell carcinoma.
Results. Only 1 out of 30 hospitals leading head and neck multidisciplinary teams (3.3 per cent) routinely offered human immunodeficiency virus testing in this high-risk patient group.
Conclusion. This observational study highlights that head and neck specialists are not aware of, and are consequently not complying with, routine human immunodeficiency virus testing as recommended by the British HIV Association guidelines.

Introduction

Head and neck squamous cell carcinoma (SCC) is considered an indicator condition for human immunodeficiency virus (HIV) infection by the British HIV Association. Indicator conditions are those that occur more frequently in HIV-positive individuals.[1,2]

The HIV Indicator Diseases across Europe Study ('HIDES I') investigated the prevalence of HIV in 9471 patients with 1 of 14 indicator diseases.[3] The overall prevalence was 2.5 per cent, with over 70 per cent of these newly diagnosed patients classed as late presenters (cluster of differentiation 4 count of less than 350 cells/μl). Patients with HIV have a three-fold increased risk of head and neck SCC compared to their HIV-negative counterparts, although the reasons behind this remain unclear.[3]

A review of UK specialty guidelines for HIV indicator conditions showed that only half (52 per cent) of UK guidelines acknowledged an association between these conditions and HIV infection, and only 39 per cent of these guidelines recommend HIV testing.[4] These included prominent guidelines from the National Institute for Health and Care Excellence and the Scottish Intercollegiate Guidelines Network. Prompt diagnosis of HIV infection in patients with head and neck cancer will allow timely and appropriate management of their complex medical needs. These patients should be managed by specialised HIV oncology services, where research has confirmed they receive better care.[2]

This observational study aimed firstly to examine the current routine practice of HIV testing in patients with newly diagnosed head and neck cancers in head and neck cancer multidisciplinary teams (MDTs) across England, and, secondly, to address the importance of this testing in promoting the early diagnosis and treatment of HIV.

Materials and methods

Forty-nine head and neck MDTs in England were identified in the National Peer Review Programme's Head and Neck Services Report 2012/2013.[5]

Head and neck teams working within the MDTs were sent an e-mail asking whether the MDT routinely perform HIV tests on patients with a new diagnosis of head and neck cancer. Departments were followed up with a telephone call if there was no response to the initial e-mails. The most frequent responders to the e-mails and calls were the clinical nurse specialists, but MDT co-ordinators and clinical leads were also contacted.

Results

We obtained a 61 per cent response rate (30 out of 49 departments). Only 1 out of 30 (3.3 per cent) of the hospitals leading head and neck MDTs followed a protocol of routinely offering an HIV test in this high-risk patient group.

The overwhelming response from the majority of head and neck departments was a lack of awareness around the existence of British HIV Association guidelines and their recommendations for the investigation of head and neck cancers. There was, however, awareness that HIV testing should be offered in patients who were considered 'high-risk' based on their medical history, although no widely used standard for this was identified.

Discussion

There were an estimated 89 400 people in the UK living with HIV at the end of 2016; this is equivalent to a prevalence of 0.16 per cent.[6] During this year, 42 per cent of newly diagnosed individuals were late presenters and 10 400 people (12 per cent of the total number of HIV patients) were living unaware of their diagnosis.[7,8]

Patients with HIV are at a substantially higher risk of developing cancer than those who are not infected.[4] Infection-driven cancers in HIV-positive individuals are already well recognised in the literature, and include: hepatocellular carcinoma caused by hepatitis B and C infections, and lymphoma related to Epstein–Barr virus.[9,10] Human papilloma virus (HPV) is known to be an important risk factor for developing head and neck SCC. However, head and neck SCC is also the third commonest head and neck cancer in HIV-infected individuals, behind Kaposi's sarcoma and non-Hodgkin's lymphoma. For this reason, head and neck SCC, although not an acquired immunodeficiency syndrome (AIDS)-defining condition, is an indicator condition for HIV.[1]

Testing for HIV infection in patients with indicator conditions is believed to be an effective strategy to help bridge the HIV diagnosis gap that exists in the UK and to help reach the 90-90-90 Joint United Nations Programme on HIV/AIDS target (90 per cent of people living with HIV infection diagnosed, 90 per cent of people diagnosed receiving treatment and 90 per cent of people receiving treatment being virally suppressed).[11]

Late diagnosis of HIV leads to increased morbidity and mortality, poorer response to antiretroviral therapy, and increased healthcare costs. Late presenters have a 6.6–13-fold increased risk of death, particularly in the first year after diagnosis. The initiation of antiretroviral therapy is now recommended in patients with cluster of differentiation 4 counts of more than 500 cells/μl, because of the decreased risk of malignancy, cardiovascular disease and infection in those who receive early treatment.[12,13]

The purpose of highlighting an indicator condition is to raise awareness that this patient cohort is more likely to have HIV infection, and their contact with the medical profession is an opportunity to test and therefore potentially avoid late presentations.[3]

Human papilloma virus, and traditional risk factors such as smoking and alcohol intake, are still the most important risk factors in this HIV-positive cohort with head and neck SCC. However, it is also known that these lifestyle risk factors are more prevalent in HIV-infected individuals compared to their HIV-negative counterparts.[14]

It has been reported that patients with head and neck cancer and concurrent HIV infection have an excess mortality compared to their HIV-negative counterparts.[15] Exposure to oncogenic factors as listed above certainly contributes to the increased mortality rates, but there is some evidence that this in part could also be because head and neck cancers are more aggressive in HIV-positive patients. Singh *et al.* showed one and two-year survival rates of 57 per cent and 32 per cent in HIV-positive patients, and 74 per cent and 59 per cent in non-infected patients, respectively.[16] These findings were most likely related to the cancer being at a more advanced stage on diagnosis; however, it is unclear as to whether this is related to the presence of HIV.

In the largest case series of HIV-infected head and neck cancer patients to date, D'Souza *et al.* determined the characteristics and survival of 94 patients.[14] Seventeen per cent of all head and neck SCCs and 55 per cent of oropharyngeal cancers contained HPV16 DNA. There was no significant difference in overall survival between HIV-infected individuals and those who were HIV-negative (63 *vs* 61 months). It was, however, found that those with cluster of differentiation 4 counts of 200 cells/μl or less at diagnosis had significantly reduced survival than those with counts of over 200 cells/μl (16.1 *vs* 72.8 months, $p < 0.001$).[14] Thus, despite risk factors being similar, the relative importance of HPV-driven cancers and their outcome in late-stage HIV infection does determine patient outcome.

- Human immunodeficiency virus (HIV)-infected patients have a three-fold increased risk of head and neck squamous cell carcinoma (SCC)
- British HIV Association recommends HIV testing in all new head and neck SCC diagnoses
- British HIV Association classes head and neck SCC as an indicator disease for HIV
- Late diagnosis of HIV increases morbidity and mortality rates, and healthcare costs, and negatively effects treatment responses
- The HIV testing is cost effective, easily accessible and reduces morbidity

This observational study indicates that HIV testing amongst newly diagnosed head and neck SCC patients is widely underperformed and poorly understood. Historically, there has often been a stigma around discussing HIV risk factors and addressing HIV testing with patients. However, it seems that the main barrier to HIV testing has been the lack of awareness of head and neck SCC being an indicator condition for HIV.

It is important that healthcare professionals who do not work in the field of HIV are aware of the importance of HIV testing for indicator conditions and have the confidence to consent patients for testing on a routine basis. The HIV testing has to be built into the patient's diagnostic investigation, to ensure there are no missed cases. This is true of other conditions within the scope of the head and neck MDT, such as lymphoma, which often presents to ENT clinics early in the patient journey. Once a patient is diagnosed with HIV infection, there need to be clear and timely referral pathways in place, to ensure that both the HIV and head and neck cancer are treated expediently. Increased testing provides us with the opportunity to decrease the number of people living with HIV who are not aware of their status, and allows us to improve the outcome of individual patients under our care with head and neck SCC.

Limitations

We made every effort to contact all MDTs in England, and considered the responses of the main contact point to be the MDT consensus opinion. However, it is possible that there is variation amongst individual clinicians within an MDT. The main limitation is the lack of information from the non-responding and non-reachable MDTs; however, with the number that did respond, a clear pattern emerged.

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Competing interests. None declared

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