EXPLORING THE NON-VIRAL INFECTIOUS CAUSES OF CANCER

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This article discusses the contribution made by non-viral infections to the global burden of cancer and describes the bacterial, protozoan and fungal organisms that are believed to cause cancer, either directly or indirectly.

In the 19th century, it was widely believed that cancer was an infectious and transmissible disease. Although this is untrue, in the developing world in particular many cases of cancer are in part caused by infection with specific agents.

Viruses replicate by invading a host cell and in many cases they insert viral DNA into the host genome and cause malignant changes. An example is the human papilloma virus that causes cervical cancer. Bacteria and protozoa do not have mechanisms for DNA integration and cannot alter the DNA of a host cell directly.

Many products of bacterial metabolism are potentially mutagenic (cause changes in cellular DNA). It has been suggested that these may increase the risk of certain cancers, particularly colon cancer, but research findings have been inconsistent (Parsonnet, 1995). Ohshima and Bartsch (1994) proposed that the key component in carcinogenesis may be the chronic inflammatory process associated with many infections.

Several tropically acquired parasite infections are associated with specific malignancies. One of the most common is schistosomiasis, which is associated with bladder cancer and liver cancer, and various liver fluke infections that cause cholangiocarcinoma (bile duct cancer).

A small number of bacterial and parasitic diseases cause cancer directly (Risser, 2001):

| Helicobacter pylori (stomach cancer);
| Schistosoma haematobium (bladder cancer);
| Opisthorchis viverrini (liver cancer – cholangiocarcinoma).

The only fungus known to cause cancer in humans is aspergillus, which produces a compound called aflatoxin. This binds to DNA and can cause liver cancer – especially in people with hepatitis B.

BACTERIAL INFECTIONS

The most ubiquitous non-viral cause of cancer is H. pylori, which it is estimated has infected at least half of the world population. It is the only organism that can survive in and colonise the acid environment of the stomach.

A high proportion of gastric ulcers are secondary to infection with H. pylori and it causes both gastric adenocarcinoma (Peek and Blaser, 2002) and lymphoma of the stomach, known as mucos-associated lymphoid tissue (MALT) lymphoma (Du and Isacsson, 2002).

Gastric adenocarcinoma

There are two types of gastric adenocarcinoma, which are morphologically and clinically distinct. The diffuse form is characterised by early onset and equal sex distribution, while the intestinal type occurs in later life and affects males more than females.

H. pylori is implicated in both forms but epidemiological evidence suggests that the diffuse form may be an endemic condition with a relatively constant incidence, whereas the intestinal type is epidemic and its incidence rises and falls.

This may be a reflection of different lifestyles, for example, dietary habits (Ahmed, 2005). There is evidence that H. pylori infection may reduce the risk of cancer of the cardia of the stomach, although it increases incidence of distal cancers, and of oesophageal cancer. A hypothetical model of the impact of H. pylori on cancer incidence clearly shows that protection from H. pylori-induced cancer outweighs any negative impact of eradicating the infection (Nakajima and Hattori, 2004).

Gastric non-Hodgkin lymphoma

Many sections of the gastrointestinal tract contain lymphoid follicles (MALT), which are also found in the respiratory and urogenital tracts. These are mainly made up of B lymphocytes organised into lymphoid follicles.

The healthy stomach has no MALT. Its defences are the low stomach pH and the thick layer of mucus lining the organ. In response to chronic infection with H. pylori the stomach acquires MALT. Initially the acquired MALT is polyclonal (non-malignant) and depends on the continued presence of H. pylori – it disappears following eradication of the H. pylori infection.

At a later stage, probably in response to chronic immune stimulation, the MALT becomes monoclonal, acquires genetic abnormalities and persists in the absence of H. pylori. Following this, malignant changes occur and the MALT transforms into full-blown extra-nodal non-Hodgkin lymphoma (Du and Isacsson, 2002).

LEARNING OBJECTIVES

- List the non-viral infectious causes of cancer identified in this article
- Outline the types of cancers caused by Helicobacter pylori
- Discuss the advantages and disadvantages of an eradication strategy for Helicobacter pylori
- Identify three infections that do not directly cause cancer but create conditions in which cancer is more likely to occur
GUIDED LEARNING

- Outline your place of work and why you were interested in this article
- Describe a patient you have nursed with a non-viral infectious cause of cancer. Consider patients with gastric cancers
- Identify information in this article that could assist you in helping a patient to understand their illness
- Explain how you intend to disseminate what you have learnt among your colleagues

PARASITIC INFECTIONS

Unlike bacteria and viruses, many parasitic species, including those implicated as carcinogens, have lifecycles that require non-human (intermediate) hosts at some stage (Khurana et al, 2005). They are rarely, if ever, transmitted from human to human, and cannot become endemic species in regions where their intermediate hosts are not found – this includes the UK and Northern Europe.

Schistosome species (S. haematobium, S. mansoni and S. japonicum) are parasitic flatworms (blood flukes), which are major factors in the incidence of certain cancers in areas where they are endemic.

S. haematobium, in particular, is associated with bladder cancer. It has been suggested that a progression from parasite-dependent metaplasia (abnormal cell changes) followed by parasite-independent neoplasia may occur, which resembles the process of H. pylori-induced MALT lymphoma (Hodder et al, 2000).

S. mansoni and S. japonicum are associated with hepatocellular carcinoma (Abdel-Rahim, 2001).

LIVER FLUKES – CHOLANGIOCARCINOMA

Liver flukes are flatworms and several species are considered to be risk factors for the development of certain forms of liver cancer. Among these are Opisthorchis viverrini, which is the most common cause of liver cancer in northeast Thailand, where it is estimated that approximately 70% of the population is infected.

Other liver fluke species are also known to cause liver cancer, and these include Opisthorchis felineus and Clonorchis sinensis (also known as Opisthorchis sinensis). Each of these species is associated with an increased risk of cholangiocarcinoma (Abdel-Rahim, 2001).

OTHER ASSOCIATIONS

Causal associations between a number of infections and specific cancers have been postulated, although the evidence for these associations is inconclusive:

- Trichomonas vaginalis (cervical cancer);
- Toxoplasma gondii (central nervous system tumours, leukaemia/lymphoma);
- Taenia solium (pork tapeworm) (CNS tumours, leukaemia/lymphoma).

Although not directly identified as a cause of cancer, several other infections create conditions in which cancer is more likely to occur:

- Malaria (immunosuppression leading to endemic Burkitt’s lymphoma);
- HIV (immunosuppression leading to increased incidence of several cancers);
- Aspergillus sp. (while not direct carcinogens, food contaminated by these contains aflatoxins, which are potent carcinogens that are known to cause liver cancer).

CONCLUSION

The main non-viral infection contributing to cancer aetiology is H. pylori, which causes numerous cases of stomach cancers. Although H. pylori may protect against some forms of cancer, eradication policies would reduce the incidence of cancer overall.

In the developed world, improving community hygiene standards have already done much to reduce infection rates for H. pylori.

It is necessary for nurses to be aware of the significant contribution made by infections to the overall cancer burden, and of the current issues relating to vaccination and other protective measures that can be used to avoid it.

Although some infectious causes of cancer are rare in the developed world, others are common and nurses have a vital role to play in reducing the burden of infection-associated cancer.

REFERENCES


