

HISTORY OF ONCOLOGY

Melancholy as a risk factor for cancer: a historical overview

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Summary

In antiquity, physicians related depression or melancholic humour to cancer's pathogenesis. Galen (130-201 AD), sustained that melancholy could give rise to a tumour and his theory was repeated by the Byzantine and Arab physicians. In the 19th century, malignancy and depression became synonymous and people attributed their cancer to sadness. In 1893, the London surgeon Hebert Snow (1847-1930), performed an epidemiological study in order to clarify that link. The results revealed a probable connection. His

work was followed by several large scale prospective studies some of which identified depression as a risk factor for cancer where others found no association. However, a possible explanation could be given by our current knowledge in immunology: inflammation and nonspecific immune activation play a role in the pathophysiology of depression and cancer growth.

Key words: carcinogenesis, depression, history of oncology, innate immune system, malignancy

Introduction

In the 2nd century AD, Galen (130-201), following the Hippocratic tradition in describing cancer as a growth arising from an excess of the black bile, stated that depression or melancholy, could give rise to a tumour. He further believed that several cancer patients were depressed and subsequently those who were depressed developed cancer [1]. His idea on cancer's melancholic diathesis dominated medical science for years.

In a similar manner the byzantine physician Aetius (391-454) attributed to cancer "the melancholia concentrating in the brain" [2]. Centuries later, Arab physicians such as Avicenna (980-1037) and Avenzoar (1094-1162), in an attempt to explain cancer's pathogenesis, assigned a contributing role to melancholic humour [3]. During the

following centuries a great number of physicians believed that melancholic conditions were the prerequisite for the development of a malignant tumour.

At the beginning of the 17th century, the French surgeon Claude Chapuys de Saint-Amour (?-1620) in his treatise: "Traité des cancers, tant occultes qu'ulcérés" (Treatise on cancer, as occult as ulcerated) stated that cancer appears after "sadness, boredom, anger and wrath" [4]. In his turn, Guillaume de Houpeville mentioned that sadness, compassion, grief and excessive work could exacerbate the appearance of a melancholic humour and the development of a malignancy [5]. In 1740, Gilles Levacher (1693-1760), surgeon in Besancon, France, in his dissertation on breast

cancer, emphasized the carcinogenic effects of a poorly regulated existence: “a sedentary life with sorrows may cause a deep and permanent sadness, resulting to the appearance of breast cancer” [6]. Mental depression became part of cancer’s pathogenesis in such a way that the famous obstetrician Antoine Dubois (1756-1837) supported that “nervous diseases” and cancer represent different degrees of the same affection [7]. Women which are susceptible to develop cancer have a specific psychological profile according to the French physician J.B.A. Burdel [7]. Burdel points out that sorrows and regrets associated with ageing and the loss of beauty is the main cause of breast cancer [8]. Around the same time, Viel-Hautmesnil expresses a similar idea, that ageing and depression may affect the genitalia and breasts, increasing the probability of developing cancer [7]. Cancer and melancholy became synonymous and people attributed their cancer to sadness. According to the memoir writer Mme de Motteville (c. 1621-1689), the breast cancer of the queen consort of France, Anna of Austria (1601-1666) was provoked by continuous torments and sorrows [9,10]. Several were the cancer patients who attributed their disease to misfortunes. One sees in her uterine cancer the effect of the violent grief she felt, during the Revolution, when her father was guillotined; other attributed her breast cancer to the pain she felt from the death of her son, aged 27; a third blame her husband who abandoned her, taking their savings [7]. More amazing is the case of a patient who believed that a blow she received in her abdomen was at the origin of her digestion disturbances. But when doctors asked her to identify the exact location where she had been struck, “she confessed that she did not receive any blow but she was afraid that she could be beaten”. However, the patient died several months later of cancer of the stomach. According to her personal physician, Joseph-Claude-Anthelme Récamier (1774-1852), in the past, she experienced “sad reverses of fortune and great anxiety of mind” [11].

By the middle of 19th century, physicians and patients strongly believed that melancholy causes cancer. According to Beauvoisin: “we have questioned at least two hundred patients and they mentioned that the death of a child or of a parent, the loss of a husband usually preceded the onset of cancer” [7]. Another medical writer stated: “grief and sadness, as my patients confessed, preceded the appearance of cancer” [7]. Collective anxiety can trigger real epidemics of cancer as Édouard Burdel observed that the number of

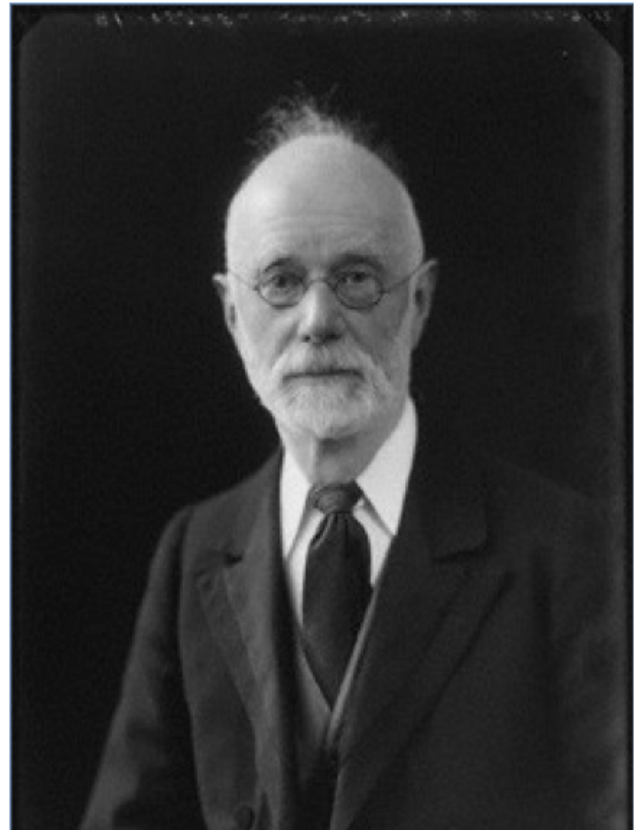


Photo 1. The English surgeon Hebert Snow (1847-1930) who performed an epidemiological study in order to clarify the connection between depression and cancer.

breast cancer cases increased after the Revolution. The majority of the patients were nuns who were enjoying a regular life and were obliged to leave the monasteries and live in poverty [8]. The thesis of Jean-Baptiste Doyen in 1816 entitled: « Dissertation sur le cancer considéré comme une maladie du système nerveux » (Dissertation on cancer, considered a disease of the nervous system), reflects the dominant scientific idea of that period. In his thesis we may read several examples of patients diagnosed with cancer after long periods of sorrows such as the case of Thérèse Lenné who after two misfortune weddings, the loss of her fortune and children was diagnosed with breast cancer at 43 years and died 18 months later [12].

In the last decades of the 19th century, the advent of medical statistics and epidemiology revealed a probable link between cancer and melancholy. In 1893, Hebert Snow (1847-1930), a London surgeon, best known for the first elective lymph node dissection in melanoma, based in his clinical experience, stated that cancer of the uterus and breasts may appear after an “antecedent emotion of depressive character” [13] (Photo 1). For this reason, he performed an epidemiological

study in 250 cancer patients and he revealed: "Of 250 out- and in-patients at the Cancer Hospital, with cancer of the mammae or uterus, 43 gave histories permitting a suspicion of mechanical injury; 15 of these 43 also described themselves as having undergone much recent trouble; 32 others spoke of hard work and privation. In 156 there had been an immediately antecedent trouble, often in very poignant form, as the loss of a near relative. In 19, no causation-history could be proved" [13]. In 1926, the psychologist Elida Evans mentioned in her manuscript: "A psychological study of cancer" that cancer is a symbol of something gone wrong in the patient's life, a warning to him to take another road. On 100 of the patients which had been evaluated through intensive psychotherapy, she reported that all of them had lost or had disrupted, an important emotional relationship, prior to develop cancer [14].

Almost one hundred years later, do we still believe that depression may predispose to cancer? Prospective studies did not conclude with certainty. Several large scale studies identified

depression as a risk factor for cancer where others found no association. The prospective cohort study of Penninx et al. published in 1998 which included 4,825 persons, aged 71 years and older, revealed that when depression is present for at least 6 years, it is associated with a generally increased risk of cancer [15]. In 2010, the first large scale prospective epidemiological survey of psychiatric disorders in general USA population was published by Gross et al. Cancer free patients (N=3,177) who were diagnosed with depression were followed for 24 years [16]. The results were impressive revealing that a history of major depression was associated with a higher risk for cancer and a statistically significant increase in risk for breast cancer among women [16].

What ancient physicians observed in clinical practice may be explained by our current knowledge in immunology: inflammation and innate immune activation play a role in the pathophysiology of depression and cancer growth.

History of medicine has still important lessons to teach us.

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Correction

In vol. 21, no.2, page 522, 2016 issue (Letter to the Editor) the name of Dr. Sarigoz was mistakenly written as Sarigo. We apologise for this error.