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Paleo-oncology in the Dakhleh Oasis, Egypt: Case studies and a paleoepidemiological perspective

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ABSTRACT

This article describes six cases of cancer from the Dakhleh Oasis, Egypt. A mummy had a confirmed 'primary' diagnosis of adenocarcinoma of the rectum. The remaining diagnoses were based on the distribution and types of skeletal lesions in conjunction with age, sex, and/or the molecular phylogeny of the Human Papillomavirus (HPV). HPV is a confirmed cause of cancer of the uterine cervix (UC) and testes (TC) and it evolved in Africa long before *Homo sapiens* emerged. Today these cancers are common in young adult females and males, a fact which was pivotal in respectively including them in the differential diagnosis of UC and TC. The remaining diagnoses were acute lymphocytic leukemia in a 3–5 year old child and an older female with metastatic carcinoma. Due to problems of determining specific diagnoses and their prevalence in 'paleo' populations, we opted for a lifetime cancer risk statistic (LTCR). The LTCR in ancient Dakhleh was ~5/1000 (6/1087). In modern Western societies the LTCR cancer approaches 50% (500/1000). Thus the LTCR in today's western societies is 100 times greater than in ancient Dakhleh. These cases demonstrate that oncogenes and their environmental cofactors were present in antiquity, but were significantly less pervasive than today.

1. Introduction

> "In industrialized societies, cancer is second only to cardiovascular disease as a cause of death. The history of this disorder has the potential to improve our understanding of disease prevention, aetiology, pathogenesis and treatment. A striking rarity of malignancies in ancient physical remains might indicate that cancer was rare in antiquity, and so poses questions about the role of carcinogenic environmental factors in modern societies. Although the rarity of cancer in antiquity remains undisputed, the first published histological diagnosis of cancer in an Egyptian mummy demonstrates that new evidence is forth coming" (David and Zimmerman, 2010: 728).

It is well known that for the past half century malignant neoplastic diseases have generally ranked 2nd as the cause of mortality in western countries, although in several of these today (e.g., Canada), cancers have surpassed cardiovascular disease (CVD) as the no. 1 cause of death. A main reason for this is that western medicine has had considerably more success in treating CVD than cancers (Spector, 2010). Spector (2010) offers many reasons for the limited success of cancer treatments today, particularly noting that the cause/pathogenesis of the majority of cancers is unknown. We now know that cancers are complex genetic diseases that share one property: they metastasize. Moreover, they adapt to our chemotherapy treatments in ways analogous to microbes becoming resistant to antibiotics. The resistance to chemotherapy by cancer genomes was not known when President Nixon initiated his 'war on cancer' via the National Cancer Act in 1971 (Spector, 2010). That the war on cancer at that time should focus on chemotherapy is easily rationalized due to the success western medicine had in preventing and treating microbial diseases, respectively with vaccines and antibiotics. Moreover, molecular genetic analysis was still in its infancy as a major diagnostic technique in disease research. The war on cancer favoring the 'chemical model' was especially justified because the underlying hypothesis that cancer cells are less resistant to cytotoxic drugs than normal cells was demonstrated (e.g., tumor masses shrinking with cytotoxic drugs) and accepted at that time (Mukherjee, 2011).

Since the late 1970s with the development of DNA sequencing and the concomitant explosion of molecular biology in studying the organic world, the intricate and complex genetic foundation of cancers has gradually been deciphered (Cooper, 2000). This research, in conjunction with the complete sequencing of the human nuclear genome in the early part of this century, has led to the identification of at least 350 oncogenes, which constitutes about 1% of the genes in the human

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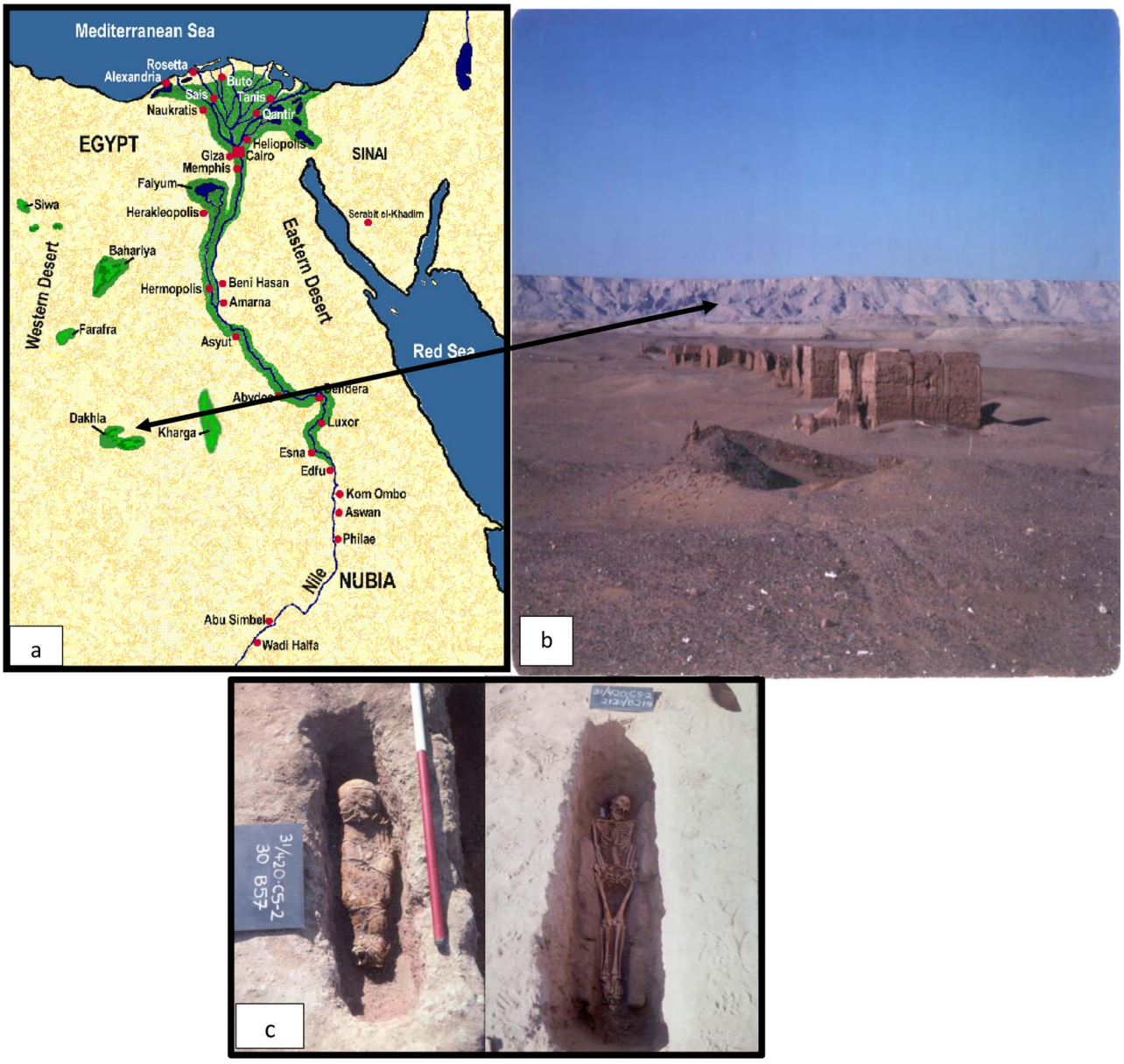

Fig. 1. (a) The location of Dakhleh, one of five oases in Egypt's western desert. The Dakhleh Oasis is approximately 640 kms as the crow flies from Cairo and 270 km from Luxor. (b) An Oasis is actually a depression in the desert the surface of which is closer to the underlying Nubian sandstone aquifer system which, in the past and today, facilitates agricultural pursuits. The top of the apparent mountain range (arrow) is actually the original surface of the western desert. Shown in the foreground are tombs from the Kellis village. The climate of the Dakhleh Oasis has been hyper-arid since before Pharaonic times and has facilitated the preservation of (c) skeletal and sometimes soft tissue remains. The infant and adult burials are from the Roman Period at Kellis demonstrating the ideal preservation which facilitates all aspects of bioarcheological research.

genome (Stearns and Medzhitov, 2016). The role and complexity of genetics in the etiology of cancers was recently highlighted by Mukherjee (2011) in his treatise on the evolution of cancer treatments; "In one breast cancer sample from a forty-year-old-woman, 127 genes were mutated – nearly one in every two hundred genes in the human genome. Even within a single type of tumor, the heterogeneity of mutations is daunting" (Mukherjee, 2011, 452). Understanding this viral-gene heterogeneity in individual cases is the key to treating cancers in the future.

With the war on cancer now broadening its focus and embracing genetic laboratories there is a growing interest in the antiquity of cancer. Our co-evolutionary genetic interaction with cancer causing agents (i.e., viruses and other environmental carcinogens) is the fundamental to ultimately understanding cancer pathogenesis (David and Zimmerman, 2010). While debate is minimal on whether cancer is a new disease (David and Zimmermann, 2010), paleopathologists (e.g., Steinbock, 1976; Aufderheide and Rodriguez-Martin, 1998; Capasso, 2005; Roberts and Manchester, 2005; Rothschild and Martin, 1993; Strouhal, 1994) and scholars of evolutionary medicine (e.g., Ewald, 2010; Neese, 2010, Stearns and Medzhitov, 2016) know that cancer is part of our legacy (Greaves, 2000; Capasso, 2005; Akiptis et al., 2015; Caulin and Maley, 2015; Greaves, 2015; Greaves and Emini 2015). In fact, practitioners of evolutionary medicine hypothesize that humans are more susceptible to cellular malignancy than most other species and point out that once a cancer occurs it undergoes a process of clonal selection (Stearns and Medzhitov, 2016). Initially, it was thought that our body size and life expectancy were the reasons for our susceptibility. However, animals with a 1000 times more cells than humans do not exhibit increased cancer risks, suggesting that natural mechanisms can suppress cancer much more effectively in other large mammals than in humans. The lack of correlation between body size and cancer risk is called Peto's Paradox (Peto, 2015; Caulin and Maley, 2011).