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Cutaneous Sarcoma Epigenetics

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Abstract

Epigenetic changes have an impact on a variety of physiological and pathological conditions in the human body. Recent advances in epigenetic studies of the skin have highlighted the significance of epigenetic modifications in skin diseases. Cutaneous sarcomas are incurable skin cancers with no curative treatment options for advanced forms. The detailed molecular effects of epigenetic modifications on skin sarcomas such as dermatofibrosarcoma protuberans, angiosarcoma, Kaposi's sarcoma, leiomyosarcoma, and liposarcoma are discussed in this review. We also go over the use of epigenetic-targeted therapy for skin sarcomas.

Keywords: Skin sarcoma; Epigenetics; Dermatofibrosarcoma protuberans; Angiosarcoma; Kaposi's sarcoma; Leiomyosarcoma; Liposarcoma

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Introduction

Sarcomas are a type of cancer that begins in the connective tissue. The treatment of a patient with a mass suspected of being sarcoma begins with a biopsy to obtain tissue for pathology evaluation. The primary role of current imaging modalities in general is to identify patients with typically benign disease, in whom further invasive staging can be avoided, and to select patients with a suspected malignancy, in which biopsy should be performed. Because soft tissue sarcomas are often large and heterogeneous, there is growing interest in using imaging modalities to guide biopsies. Imaging modalities, in conjunction with pathology, form the foundation for accurate staging, evaluation of the locoregional extent of the primary lesion, screening for occult metastases, evaluation of response to cancer treatment, and detection of tumour recurrence. This chapter provides an overview of the use of 18F-FDG PET in these settings, including its advantages and disadvantages [1-5].

Sarcoma is uncommon and heterogeneous, with different subtypes having varying prognoses. GIST with KIT mutation responds massively to target treatment as IMATINIB, whereas soft tissue sarcoma and leiomyosarcoma are extremely aggressive with poor response to systemic therapies. Interventional radiology is important in the diagnosis of sarcomas, with image-guided percutaneous core needle biopsy being the most commonly used biopsy technique. The surgeon and I discuss biopsy access routes, and skin access is tattooed. Surgery is the cornerstone of sarcoma treatment; the resection can be extensive. Indeed, the resection goal is R0 because surgical margin quality affects local control and survival. To improve local control rate, radiotherapy can be used as a neoadjuvant or adjuvant treatment. Recently, a radiotherapy enhancer injected percutaneously into soft tissue sarcoma patients has been shown to improve the rate of R0 complete surgical resection. Several studies have found that post-operative radiotherapy improves local control rates. Because complete remission is required for cure in patients with oligometastatic disease, complete surgical resection of all metastatic sites is considered the primary treatment. The decision to use local therapies is complicated, depends on various presentations and histologies, and should always be made in the context of a multidisciplinary discussion. Percutaneous image-guided ablation treatments (radiofrequency ablation, cryotherapy, microwave ablation) now provide a high rate of durable local control for small-sized malignant deposits in many organs, including the lung, liver, and bones. Sarcoma must be treated with a multimodal approach in expert reference centres [6-10]. This type of management has a significant impact on the prognosis.

Discussion

The Skin as a Site of Exposure to Environmental Stimuli

Various environmental stimuli have the most direct effect on the skin, the human body's outermost organ (reviewed in). The skin is the most vulnerable organ to external factors, and ongoing skin reactions to environmental factors exacerbate tissue damage caused by inflammatory reactions. Skin physiology has been found to involve many epigenetic mechanisms that regulate

gene expression without changing genetic information in recent studies. In addition to assisting in environmental adaptation, epigenetics plays a role in skin cancer carcinogenesis (reviewed in). As a result, it has been proposed that cutaneous malignancies may gain a selective advantage within the body through an epigenetic mechanism.

The Structure and Functions of the Skin

The skin is a three-layered structure made up of the epidermis, dermis, and adipose tissue, each with its own set of cells, and its significance has been studied in numerous studies. It maintains homeostasis in the human body by performing barrier, sensory, thermoregulatory, immune, and secretory functions (reviewed in). Keratinocytes produce moisturising factors that increase the stratum corneum's water retention capacity, thereby contributing to skin barrier function. Skin keratinocytes, dendritic cells, and lymphocytes play critical roles in immunity. Toll-like receptors on these cells recognise the specific molecular pattern of invading pathogens and activate innate immunity, promoting the production of various cytokines and antimicrobial peptides. Skin also serves as an important sensory organ. Itching exists only in the skin, and the scratching action that comes with it contributes significantly to the exacerbation of skin diseases. Furthermore, proper thermoregulation of the skin surface, which includes capillary vessel dilation and sweating, is critical for maintaining homeostasis. Hair follicles, sebaceous glands, and sweat glands are mini-appendages that produce sebum and sweat, causing skin diseases. Soft tissue tumours of various types have been observed to develop in the skin.

Angiosarcoma: Angiosarcoma is a type of cancer that affects endothelial cells in the blood or lymphatic vessels. Local recurrence and distant organ metastases have been reported at high rates. The current therapeutic options for high-grade malignancies are inadequate. Angiosarcoma occurs at a rate of 1.5 cases per million people per year. It accounts for about 0.4% of all cutaneous soft tissue sarcomas and about 2.0% of all soft tissue sarcomas.

Kaposi's sarcoma: Human herpesvirus-8 (KSHV) is an opportunistic pathogen that infects vascular endothelial cells in immunocompromised people such as those on immunosuppressive agents (e.g., after organ transplantation) and AIDS patients. KSHV is a double-stranded DNA virus that infects a variety of cells, including endothelial and immune cells, and causes either latent or lytic infections. Kaposi's sarcoma patients develop purpura or dark brown macules or plaques that are prone to bleeding and ulceration. In patients with untreated acquired immunodeficiency syndrome (AIDS), Kaposi's sarcoma can spread to the rest of the body within a few months. Locally limited Kaposi's sarcoma of the skin can be surgically removed.

Leiomyosarcoma: One of the most common types of soft-tissue sarcomas is leiomyosarcoma, a type of malignant smooth muscle tumour. Dermal leiomyosarcoma arises from the smooth muscles surrounding the sweat glands or the pilar follicle erector muscles, whereas subcutaneous leiomyosarcoma arises from the smooth muscles of arteries and veins. The annual incidence of leiomyosarcoma is between 0.7 cases per 100,000 people. It is responsible for 0.6% of all cutaneous soft tissue sarcomas and 11.4% of all soft tissue sarcomas.

Conclusion

We present here the effects of epigenetic modifications on skin soft-tissue malignancies, as well as strategies for targeting such modifications for future therapeutic applications. Soft tissue malignant tumours are affected by epigenetics in a broad sense. Because oncogenesis is determined by the characteristics of the originating cell type, the impact of specific epigenetic modifications in each tumour type must be investigated. Clinical trials are needed to further investigate this option based on the promising antitumor effects of epigenetics-targeted therapy on cutaneous sarcomas in previous studies. Because curative treatment for soft-tissue sarcomas remains elusive, the development of epigenetic-targeted treatment for this tumour type could hold great promise.

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