ABSTRACT

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Brain Metastases and Microenvironment.

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The formidable advances in cancer treatment have led to remarkable improvements in patient's survival, so that the major concern shifted from primary tumors to metastatic disease. Brain metastases represent a life-threatening condition with a poor prognosis due to the lack of reliable biomarkers that preclude their timely identification and to the scarce therapeutic possibilities considering that the blood-brain barrier limits the access of most of the drugs to the brain and surgical resection is discouraged in cases of multiple metastases. Moreover, brain metastases have been scarcely investigated, which precludes a comprehensive understanding of the determinants and players, as well as of the complex cross-talk and signaling pathways involved. This chapter summarizes the impressive numbers about cancer and brain metastases and the estimates of progression in the years to come. It also gathers together the relevant concepts about the metastatic cascade, focusing in the extravasation step across the microvascular endothelium that leads to the formation of brain metastases. Moreover, it comprehensively explores the brain tumor microenvironment, detailing on the pre-metastatic niches and their relevance for tumor cell development in the target organ. Additionally, the cellular and acellular components, as well as their interplay, activation status, and acquired phenotypes, are addressed. Collectively, by bringing together historical concepts and state-of-the-art knowledge, this chapter shall contribute to a better understanding of the brain metastasization process, essential for the development of novel approaches to improve patients' life quality and expectancy.

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