Ontogenetic anatomy and the compartment theory of tumor permeation

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Abstract

Current surgical treatment for local tumor control is based on functional anatomy and on a view of radial progressive tumor spread. However, resecting the malignant tumor with a metrically defined margin of tumor-free tissue is frequently associated with considerable morbidity. Moreover, despite microscopically complete tumor resection local relapses occur in up to 50% often indicating incurability of the disease. Enlarging tumor-free margins is not a robust means to improve local control. To prevent local recurrences adjuvant radiation may be effective but at the cost of a further increase of morbidity and without proof of prolonging overall survival with most tumor entities.

Ontogenetic anatomy and the compartment theory of tumor permeation provide consistent explanations for the weaknesses of current local tumor treatment and falsify their underlying principles. Ontogenetic anatomy refers to the systematics of mapping morphogenetic units in the mature human body. Morphogenetic units are differentiated tissue compartments derived from distinct precursor tissues, the anlagen or primordia. The morphologically invariable morphogenetic units may consist of both functional tissue and tissues with no known or no apparent physiological function. The compartment theory of tumor permeation states that (i) malignant solid tumors are locally confined for a relatively long phase during their natural course to a permissive compartment representing their morphogenetic units, (ii) compartment borders are functionally tumor suppressive, (iii) transgression into adjacent compartments of different embryonic origin necessitates phenotypic changes and is initially accompanied by focal inflammation at the compartment border.

Ontogenetic anatomy and the compartment theory set up new principles for surgical tumor treatment, namely the resection of the tumor-bearing compartment at its intact borders irrespective of the metrical margin width. Non-lymphatic adjacent tissues of

embryologically different compartments can safely be retained despite their close proximity to the tumor front. Compartment resection should result on one hand in maximum local control without adjuvant radiation and on the other hand in minimal treatment-related morbidity. Compartment resection with total mesorectal excision for rectal cancer has proven its advantages over conventional cancer surgery. In our hands, new operations based on this principle for gynecologic oncology such as total mesometrial resection have resulted in outcomes which by far surpass the results of traditional surgery in terms of tumor control and treatment-related morbidity.

The investigation of the mechanisms underlying tumor spread within permissive compartments may also be useful in non-surgical anti-neoplastic therapy. One avenue of research could be the study of the molecular communication between neoplastic cells and their stroma which is mandatory for clinically significant tumor growth determined by the common embryologic precursor tissue. Another intriguing research perspective would address biophysical mechanisms common to developmental and neoplastic compartment formation.