



UPDATE IN RADIOLOGY

Perineural spread in head and neck tumors[☆]



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Received 30 November 2013; accepted 13 April 2014

Available online 8 November 2014

KEYWORDS

MeSh terms;
Neoplasm metastasis;
Cranial nerve
neoplasms/diagnosis;
Cranial nerve
neoplasms/secondary;
Head and neck
neoplasms/diagnosis;
Head and neck
neoplasms/secondary;
Magnetic resonance
imaging;
Computed
tomography;
X-Ray;
Multimodal imaging;
Neoplasm
invasiveness

PALABRAS CLAVE

MeSh Terms;
Metástasis;
Tumores Nervios
Craneales/Diagnóstico;

Abstract Perineural spread is the dissemination of some types of head and neck tumors along nervous structures. Perineural spread has negative repercussions on treatment because it requires more extensive resection and larger fields of irradiation. Moreover, perineural spread is associated with increased local recurrence, and it is considered an independent indicator of poor prognosis in the TNM classification for tumor staging. However, perineural spread often goes undetected on imaging studies. In this update, we review the concept of perineural spread, its pathogenesis, and the main pathways and connections among the facial nerves, which are essential to understand this process. Furthermore, we discuss the appropriate techniques for imaging studies, and we describe and illustrate the typical imaging signs that help identify perineural spread on CT and MRI. Finally, we discuss the differential diagnosis with other entities.

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Diseminación perineural en tumores de cabeza y cuello

Resumen La diseminación perineural corresponde a una forma de extensión de algunos tipos de tumores de cabeza y cuello por las estructuras nerviosas. Su existencia repercute negativamente en el tratamiento porque requiere resecciones quirúrgicas más extensas y campos de irradiación mayores, está asociada con un incremento en las recurrencias

[☆] Please cite this article as: Brea Álvarez B, Tuñón Gómez M. Diseminación perineural en tumores de cabeza y cuello. Radiología. 2014;56:400–412.

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Tumores Nervios
Craneales/Secundarios;
Neoplasias Cabeza
y Cuello/Diagnóstico;
RM;
TC;
Imagen Multimodal

locales y se considera un indicador pronóstico independiente en la clasificación TNM para estadiar el tumor. Sin embargo con frecuencia pasa desapercibida en los estudios de imagen. En esta actualización revisaremos el concepto, la patogenia y las principales vías y conexiones entre los nervios faciales, que son esenciales para comprender este proceso. Además, valoraremos la técnica apropiada para realizar un estudio correcto, presentaremos los signos de imagen típicos para reconocer esta entidad en la TC y RM y abordaremos los diagnósticos diferenciales.
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Introduction

Perineural spread is how some types of tumors spread from head to neck through nerve sheaths. Jean Cruveilhier was the first to talk about this way of tumor spread in 1835,¹ so it is not a new way of neoplasm spread due to changes in behavior thanks to the advances of medical care. However it often goes unnoticed in such a way that it does not usually show up in radiological reports.²

Perineural spread, perineural invasion, perineural macroscopic invasion, perineural affectation, small or big nerve affectation are terms that can be used indiscriminately in literature yet they show very different processes. Perineural invasion (PNI) or small-caliber nerve invasion (SCNI) is the macroscopic affectation of nerve fascicula that can be seen anatomopathologically and found where the main tumor rests. Perineural spread (PNS) or large-caliber nerve invasion (LCNI) is the macroscopic shape that can be seen in image studies or found clinically and is located beyond the main tumor lesion.³⁻⁵

The goal of this article is get to know this kind of tumor spread, its meaning, its spread patterns and its radiological features in order to understand the condition and avoid false negatives in radiological reports.

Basic anatomical concepts

Peripheral nerves are made up of three layers called from the inside out epineurium, perineurium, and endoneurium (Fig. 1). In the epineurium both the most external component of the vasa nervorum and lymphatic channels can be found. Perineurium is the intermediate layer—one concentrically arranged multilayered structure of endothelial cells.⁶ Endoneurium is not a layer *per se* rather the laxus vascular connective tissue surrounding the Schwann cell-axon-complex making up the nerve fiber or small nerve. Various nerve fibers and the adjacent endoneurium gather around by the perineurium creating nerve fascicula. The cluster of several fascicula surrounded by the epineurium is what makes up the peripheral nerve or large nerve. Endoneurium is isolated from the extracellular compartment by the perineurium and from blood flow by the strong links of endothelial cells of endoneurial capillary. This is what is called hematoneural barrier. Its disruption allows the outflow of perineural contrast that in PNS patients is responsible for nerve pathological enhancement in image modalities.

Controversy on perineural affectation

There are several controversies in the actual literature on this type of tumor spread due to several reasons:

- There is not a standard use of different terms. In most cases each publication uses a different term and does not specify on what grounds.
- Not even among anatomopathologists there is a clear consensus on what PNI really means. Some authors define PNI as the malignant cells located in the perineural space with total or almost total affectation of nerve circumference in the tangential anatomopathological cutting.⁷ Others like tumor affectation of one third of nerve circumference or tumor cells in any of the component layers.⁴
- According to the American College of Pathologists PNI needs to be present in the reports filled out by anatomopathologists⁸ (present, absent or undetermined) and is conditioned by sampling methods, staining and immunohistochemical processing of tumor.

Studies show variable and contradictory results depending on the anatomopathological features and anatomical location of primary tumor:

- PNI has been reported in many tumor lineages but is more common in the cystic adenoid carcinoma (CAC) (20–80%)⁹⁻¹¹ and in the squamous carcinoma (SC) (27–82%).^{12,13}
- PNS is rare in SC at the level of the mouth floor, tonsillar fossa, larynx, pharynx and in the presence of PNI in the primary tumor recurrence is also rare according to some authors.^{5,14} However, other authors claim that survival is worse when PNI is found in tongue tumors.^{15,16} It seems that in the CAC there are no differences in the incidence of PNS among those located in the major salivary glands or other regions. Also its repercussion on overall survival, or the very capacity of tumor to invade adjacent structures is not clear.^{11,14,17-20}
- Prognosis of PNI in mucoepidermoid carcinoma is poor even though it is not characteristically associated with this type of tumor.^{11,21,22}

Despite contradictions, it seems evident that PNS has a negative impact in treatment (more extensive surgical

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