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(12) 神経節腫のＭＲimaging:組織との関連

神経節腫の MR imaging ： 組織との関連

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今回我々は，手術にて組織学的に確診が得られ，MRI が施行された後腹膜・後縦隔・頚部の神経節腫に対し MRI 所見・組織像との関連を検討した．検討項目は画像の形態学特徴(サイズ，被膜，周囲への浸潤と whorled appearance の有無)，信号，dynamic enhancement pattern，および粘液基質，膠原線維，と細胞成分の量などを含む．

被膜は，組織像で薄い膠原線維として，画像(造影後の T1 強調像)でリング状の enhancement として認められる． T1,T2 強調像で腫瘍内部に存在する線状・曲線状又は結節状の低信号領域（いわゆる whorled appearance）は，組織上は，束状・島状に集簇する schwann 細胞と膠原線維に相当する． T2 強調像で著明な高信号を呈する腫瘍には，組織上は，腫瘍内部に大量の粘液基質が認められるが，細胞成分と膠原線維が相対的に少ない．一方，T2 強調像で中等度信号～高信号を呈する腫瘍は細胞成分と膠原線維を富み，内部の粘液基質が乏しい．また，Dynamic study にて腫瘍は経時的な漸増の enhancement 効果を示す．

腫瘍信号の変化は組織成分(主に粘液基質・線維成分の量)の変化と一致する．後腹膜・後縦隔・頚部に被膜を有し，漸増の enhancement を呈する腫瘍が認められる時，可能性として神経節腫が挙がるべきと思われる．

Key Words: Neoplasms-ganglioneuromas-magnetic resonance imaging

研究報告

PURPOSE :

Ganglioneuroma is an uncommon benign neurogenic tumor arising from sympathetic ganglia. There have been many studies to clarify the cross-sectional imaging features of ganglioneuroma (1-7). To our knowledge, however, the contrast-enhanced dynamic magnetic resonance (MR) imaging features of this tumor have been reported for only a small series of patients (1). A relation between the MR images and histologic findings of ganglioneuroma has not yet been completely evaluated (8). The present paper attempts to correlate findings from spin-echo (SE) and contrast-enhanced dynamic MR images with histologic findings in 10 cases of ganglioneuroma. Imaging features that help differentiate this tumor from other neurogenic tumors and adrenal tumors are also described.

MATERIALS AND METHODS

The study population consisted of 10 patients (8 female, 2 male) with ganglioneuroma. The mean age at diagnosis was 27 y (range, 3-71 y). Tumors originated in the retroperitoneum (n = 4), the left adrenal gland (n = 1), the posterior mediastinum (n = 4), and the right parapharyngeal space (n = 1). Initial symptoms and signs included abdominal pain (n = 1), nausea and vomiting (n = 1), chest pain (n = 1), and a palpable mass (n = 2). In the remaining five cases, the lesions were incidentally discovered with imaging studies performed for other reasons. All 10 cases were confirmed pathologically by means of complete resection.

MR images were obtained using a superconducting magnet operating at 1.5 T (n = 3), at 1.0 T (n = 1), or at 0.5 T (n = 6). Both T1-weighted (repetition time msec / echo time msec =450-800 / 15-25) SE images and T2-weighted (1500-4500 / 80-120) SE images with a section thickness of 10 mm were obtained; the section gap was 2 mm, the image matrix was 256 x 162 to 180 pixels. Dynamic MR examinations were performed with a T1-weighted gradient echo sequence (190/6) at 1.5 T (n = 1), and with a T1-weighted SE sequence (140-150/15-20) at 1.5 T (n = 3), at 1.0 T (n = 1), and at 0.5 T (n = 6). One slice or two to four contiguous slices were obtained. Gadopentetate dimeglumine (0.2 mL/kg body weight) was manually injected (1 mL/s) through an antecubital vein. Dynamic MR images were obtained immediately after the injection and then every 40 s for 5 min. Ten minutes after administration of gadopentetate dimeglumine, post-contrast T1-weighted SE images were obtained in the same plane as used for the unenhanced images.

The MR images were evaluated in conference by two radiologists (Y.Z., H.N.) with knowledge of the diagnosis of ganglioneuroma, but without knowledge of the histologic findings. The radiologists reached a consensus regarding the following features: (a) tumorous morphologic features including size and

capsule; (b) signal intensity and signal homogeneity; (c) contrast enhancement; (d) so-called whorled appearance; and (e) dynamic enhancement pattern. The capsule was determined to be present when a ring-like enhancement structure was identified to partially or completely surround the tumor on post-contrast T1-weighted images, and the whorled appearance was present when a linear, curvilinear, or nodular structure of low intensity was demonstrated within the tumor on T1- and/or T2-weighted images.

Low signal intensity was defined as equal to or less than that of muscles on both T1-weighted images and T2-weighted images, intermediate intensity as greater than that of muscles but less than that of fat on both T1-weighted images and T2-weighted images, high intensity as equal to or higher than that of fat on T1-weighted images but less than that of water on T2-weighted images, and markedly high intensity as equal to that of water on T2-weighted images (1).

For conventional histologic observations, formalin-fixed paraffin embedded sections were stained with hematoxylin-eosin. The sections were also stained with Azan and Elastica van Gieson methods for determining the collagenous tissues and vascular components, respectively. In all cases, immunohistochemical staining for S-100 protein and neuron specific enolase were performed for confirmation of neurally-derived cells and for highlighting neurites. Both primary antibodies and an LSAB staining kit were obtained from DAKO Japan (Kyoto, Japan) and staining proceeded according to the manufacturer's instructions. These sections were reviewed by a board-certified pathologist (S.K.) without knowledge of the MR findings, and all cases were confirmed as benign ganglioneuromas. Histologic findings were described, focusing on (a) tumor capsule, (b) Schwann cells with sheathed neurites and ganglions, (c) interstitial collagen, and (d) stromal myxoid tissues. The amount of myxoid stroma, fibers, and cellular components were analysed on visual appearances.

We retrospectively reviewed the T1-, T2-weighted images and the dynamic MR images, directly comparing the findings with the microscopic histologic findings. Because some resected specimens were not cut in the exact same plane as those of MR images, correlation of pathologic descriptions by the pathologist with image findings on a site-to-site basis could not be obtained.

RESULTS

Morphologic features

The mean largest diameter of the tumors was 85 mm (range, 32-120mm). Capsules were observed as thin and not striking collagen bundles (Fig. 1D) at histologic examination in all tumors. The boundaries between capsule and tumor components were indistinct in some cases. Surrounding normal tissue, however, was not observed in any specimens. All the tumors were encapsulated and well circumscribed. A ring-like enhancement structure on post-contrast T1-weighted images, which suggested the presence of

a capsule, was depicted in five cases (Fig. 1C). A definite low intensity ring around the tumor on T1- or T2-weighted images, however, was not present in any case.

Signal intensity and contrast enhancement versus amount of myxoid stroma, fibers, and cellular components

In four tumors, histologic examination revealed a large amount of myxoid stroma, a relatively small number of Schwann cells with sheathed neurites and ganglions, and relatively few collagen fibers (Fig. 1E). Some Schwann cells and collagen fibers interlaced linearly, curvilinearly, and/or nodularly, and scattered against the myxoid stroma background (Figs. 2E and 3D). On T1-weighted images, these four tumors had homogeneously low signal intensity and the whorled appearance was not definitively observed in any tumor (Figs. 1A, 2A, and 3A). On T2-weighted images, the tumors were inhomogeneous but with predominantly markedly high signal intensity (Figs. 1B, 2B, and 3B), and a whorled appearance, which corresponded to interlacing bundles of Schwann cells and collagen fibers on histologic specimens, was observed sporadically within these tumors (Figs. 2B and 3B). These four tumors were inhomogeneous on post-contrast T1-weighted images, with mixed slight (or no) and moderate enhancement (Figs. 1C, 2C, and 3C) which corresponded chiefly to the myxoid stroma and the components of fibers and cellularity, respectively.

In five tumors, histologic examination revealed numerous Schwann cells with sheathed neurites and ganglions, abundant collagen fibers, and scanty myxoid stroma (Fig. 4D). Four of these five tumors had homogeneously low signal intensity (Fig. 4A) and one, which had a fat component within the tumor, had mixed low and intermediate signal intensity on T1-weighted images. Four of the five tumors had mixed intermediate and high signal intensity (Fig. 4B) and one had high signal intensity on T2-weighted images. Post-contrast T1-weighted images showed minimally inhomogeneous moderate enhancement in two (Fig. 4C), minimally inhomogeneous slight enhancement in two, and inhomogeneous moderate enhancement in one tumor. The degree of enhancement heterogeneity in these five tumors was less than that in the four tumors with a large amount of myxoid stroma. Linearly and thickly interlacing bundles of Schwann cells and collagen fibers were observed in only one tumor and had a whorled appearance on T1- and T2-weighted images. Post-contrast T1-weighted images were only partially enhanced in this region. Histologically, the bundles of Schwann cells and collagen fibers of this tumor were not different from that of other tumors.

In the remaining tumor, striking degeneration and hemorrhage were observed. Furthermore, vessels were relatively numerous as compared with other tumors. Neuroblasts, however, which suggest the potential of malignancy, were not observed at histologic examination (Fig. 5E). This tumor had mixed low and intermediate signal intensity on T1-weighted images and was inhomogeneous but predominantly

intermediate signal intensity on T2-weighted images. Post-contrast T1-weighted images showed inhomogeneous moderate enhancement (Figs. 5A, 5B, and 5C).

Dynamic enhancement pattern

On dynamic MR studies, all but one tumor lacked early enhancement, however enhancement gradually increased (Fig. 2D). The single exception was the above-mentioned degenerative tumor with a relatively early enhancement pattern, followed by partial washout of contrast material (Fig. 5D).

DISCUSSION

Ganglioneuroma is a rare benign tumor arising from sympathetic ganglia. Early detection, however, is important because complete resection results in a cure and the tumor rarely undergoes malignant transformation (2-6). Ganglioneuromas occur in all age groups but are more common before the age of 40 y, and are most often located in the posterior mediastinum, followed by the retroperitoneum and cervical region (9). These characteristics of age and anatomic distribution are consistent with those of our patients, that is, 7 of 10 patients were less than 40 y of age, and 8 tumors arose in the posterior mediastinum or retroperitoneum.

On T1- and/or T2-weighted images, the capsule is theoretically identified as a low intensity ring around the tumor. In the present study, however, T1- and T2-weighted images were not sensitive for this finding because the capsules were too thin to be observed. Moreover, ganglioneuromas do not occur in the parenchymal organs such as the liver and thyroid gland, so there is no parenchymal tissue to serve as a foil for the capsule. By contrast, the post-contrast T1-weighted image was more sensitive for viewing the capsule.

Ganglioneuromas were previously reported to have homogeneously low signal intensity on T1-weighted images and inhomogeneously high signal intensity on T2-weighted images (3,4,7,8). In the present study, ganglioneuromas had homogeneously low signal intensity on T1-weighted images, with the exception of the two tumors with hemorrhage or fat components, which had mixed low and intermediate signal intensity. On T2-weighted images, however, the tumors could be classified roughly into two types, markedly high signal intensity tumors and intermediate to high signal intensity tumors. Histologic examination confirmed that the amount of myxoid stroma, collagen fibers, and cellular components varied in ganglioneuroma. Comparison of tumor signal intensity on T2-weighted images with pathologic findings showed a good correlation in all tumors, except the degenerating tumor. A large amount of myxoid troma with relatively few cellular components and collagen fibers was observed in the tumor with markedly high signal intensity, while there was an abundance of cellular components and collagen fibers with relatively scarce myxoid stroma in the tumor with intermediate to high signal intensity. Accordingly,

the proportion of myxoid stroma to cellular components and collagen fibers influenced the tumor signal intensity on T2-weighted images to a large extent. Ganglioneuromas show different degrees of contrast enhancement (1,7): some show no enhancement, while others show inhomogeneous moderate or marked enhancement. In the present study, tumors showed inhomogeneous moderate (eight cases) or slight (two cases) enhancement. Comparison of tumor contrast enhancement with histologic findings revealed that the intensity of enhancement corresponded well to the histologic component and the degree of enhancement heterogeneity was also consistent with that of histologic heterogeneity. This finding supports the conclusion that different enhancement is due to variations in the myxoid stroma volume and in the amount of cellular components and collagen fibers. Despite the small number of patients in this series, the good correlation between MR imaging and histology suggests that histologic features can be estimated in the preoperative evaluation by analyzing the tumor signal intensity and the tumor enhancement.

One of the MR imaging characteristics of ganglioneuroma is a whorled appearance. Based on the results of a previous MR-pathologic correlation study that included two ganglioneuromas (8) and the results of the present study, this appearance is caused by interlacing bundles of Schwann cells and collagen fibers within the tumor. Five tumors had this appearance on T2-Weighted images in contrast to only one on the T1-weighted images. This might be because the difference of signal intensity between the myxoid stroma and the areas of interlacing bundles of Schwann cells and collagen fibers is greater on T2-weighted images. The tumor with a whorled appearance on T1-weighted images had thicker interlacing bundles of Schwann cells and collagen fibers than other tumors. Therefore, the visibility of a whorled appearance is also thought to be influenced by Its thickness. In this tumor, however, the area of the thicker interlacing cellular components and fibers was not completely enhanced on post-contrast T1-weighted images. The cause is not known. Histologically, this area was not different from that of other tumors. The timing of the scan might also influence the contrast enhancement. If post-contrast scans were performed after 10 min, better enhancement might be observed.

In all tumors, except one with degeneration, lack of early enhancement but gradually increasing enhancement was observed. In a previous study that included five ganglioneuromas examined with dynamic MR imaging, the same enhancement pattern was reported (1). Consequently, this pattern can be considered as characteristic of ganglioneuroma. The early enhancement is thought to be due to relative hypervascularity and capillary permeability. By contrast, delayed enhancement is caused by slow diffusion of the contrast medium into the extravascular space (1). Therefore, fibrous tissue having a large extravascular space and low blood supply demonstrates a delayed and prolonged enhancement. The single exceptional enhancement pattern was relatively early enhancement, followed by partial washout of

the contrast material. Based on previous reports (1) and our own experience, this enhancement pattern is observed in neuroblastoma, ganglioneuroblastoma, or other malignancies. There was no evidence to suggest malignancy, however, at histologic examination. Early enhancement might correlate with the relatively numerous vessels found within this tumor.

The differential diagnosis of ganglioneuroma includes neuroblastoma, ganglioneuroblastoma, neurofibroma, schwannoma, adrenal adenoma, adrenocortical carcinoma, and pheochromocytoma (1,2,5-8). Neuroblastomas and ganglioneuroblastomas have similar signal intensity compared to ganglioneuromas (7). Dynamic MR studies cannot be easily applied in younger cases, although there is usually marked early enhancement in neuroblastomas and ganglioneuroblastomas (1). Neuroblastomas and ganglioneuroblastomas are more aggressive tumors than ganglioneuromas, and the majority of them usually have an irregular contour, sometime with invasion to adjacent organs and encasement of vessels (2,4,7). Neuroblastomas are often associated with metastases to bone, regional lymph nodes, liver, and skin (9), while ganglioneuromas are not. Furthermore, neuroblastomas and ganglioneuroblastomas occur in a younger age group and the pattern of calcification on computerized tomography is more commonly amorphous and coarse rather than discrete and a punctate pattern observed in ganglioneuroma (1,2).

The most problematic differentiation is between ganglioneuroma and schwannoma or neurofibroma. It is difficult to differentiate these tumors with signal intensity characteristics alone. Schwannomas reveal late enhancement similar to that of ganglioneuroma, and curvilinear or nodular low intensity regions composed of collagenous fibrous tissue are observed within neurofibroma as well (8,10-12). Schwannomas and neurofibromas, however, are predominantly round and might produce bony erosion or destruction, whereas the majority of ganglioneuromas are flat and elongated and usually do not result in bony changes (2-9,13). Moreover, cystic degeneration frequently noted in schwannomas might be helpful in making the distinction (10-11), because it is not found in ganglioneuromas. On the other hand, neurofibromas are nonencapsulated tumors (5), and the possibility of neurofibroma can be excluded if the findings suggest the presence of a capsule.

Adrenal adenomas show mild early enhancement and quick washout, and pheochromocytomas and adrenocortical carcinomas reveal strong early enhancement and slower washout (14-15). Furthermore, local invasion into vascular structures is present in more than 50% of adrenocortical carcinoma cases (6).

The results of the present study suggest that the MR features of ganglioneuroma are well correlated with histologic findings. Ganglioneuroma shows different signal intensity and signal homogeneity, which depend on the amount and distribution of myxoid stroma, fibers, and cellular components. Ganglioneuroma usually demonstrates lack of early enhancement but gradually increasing enhancement on contrast-enhanced dynamic MR imaging. When a well-encapsulated mass with this enhancement

pattern is found in the posterior mediastinum, retroperitoneum, or cervical region, ganglioneuroma should be included in the differential diagnosis.

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