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Scientific Research

Contrast Enhancement of Posterior Mediastinal Ganglioneuromas—Correlation between the Level of Enhancement and Histopathological Features

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Abstract

Purpose: Relationship between CT or MR images and histological findings, especially vascularity, has not been adequately evaluated. The purpose of this study was to investigate correlation between contrast enhancement on CT and MRI and histological findings in posterior mediastinal ganglioneuromas. Materials and Methods: Contrast-enhanced (CE) CT (n = 11) and CE MRI (n = 5) of 12 patients with ganglioneuroma were reviewed. The attenuation, signal intensity, and dynamic enhancement pattern of the tumors were evaluated. The vascularity was histologically evaluated by the numbers of vessels. Results: Enhancement on CE-CT was none, mild, moderate, and high enhancement in 5 (45%), 2 (18%), 3 (27%), and 1 (9%) of the 11 lesions, respectively. Dynamic MRI showed mild, moderate and high enhancement in 3 (60%), 1 (20%) and 1 (20%) cases, respectively. The level of contrast enhancement correlated well only with the number of capillary vessels (r = 0.79, P = 0.0037). Conclusion: The posterior mediastinal ganglioneuromas sometimes show insufficient enhancement particularly on CE-CT. The level of enhancement might correlate with the amount of capillary vessels.

Keywords

Ganglioneuroma; Enhancement; CT; MRI; Mediastinum

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1. Introduction

Ganglioneuromas are neoplasms that are derived from the sympathetic ganglia and usually occur in the posterior mediastinum. There have been a few studies that evaluated contrast enhancement of posterior mediastinal ganglioneuromas and correlated it with histological findings [1]-[3]. To our knowledge, relationship between computed tomography (CT) or magnetic resonance (MR) images and histological findings, especially vascularity, has not been adequately evaluated. The aim of this study was to correlate contrast-enhanced (CE)-CT and CE-MR findings with histological findings such as density of various kinds of blood vessels in 12 cases with ganglioneuroma.

2. Materials and Method

The local institutional review board approved the retrospective evaluation of the data and waived informed consent for that analysis. We enrolled 12 cases of ganglioneuroma (4 men and 8 women, aged 7 - 62 years; mean: 37 years) seen between 1985 and 2007 in our institution from patient lists of Departments of Thoracic Surgery and Pediatric Surgery, and reviewed their CT and MR images (MRI). In all of them, the masses were found incidentally with no symptoms. All lesions arose in the paravertebral region, *i.e*., in the posterior mediastinum according to the classification by Felson [4]. Histological diagnoses were confirmed by complete surgical resection in all patients.

Overall, 4 cases had both CT and MRI examinations, 7 had only CT and 1 had only MRI. CT examinations with and without contrast were reviewed in 11 tumors. CT scanners and protocols were variable because of the long study period. CT images with 3, 5 and 10 mm thickness without interval were obtained in 4, 2 and 5 tumors, respectively, except for one patient with no CT images. Dynamic (early and late phases) and conventional CE-CT was performed in 4 and 7 patients, respectively.

A 300 mgI/ml non-ionized contrast medium (iohexol [Omnipaque 300, Daiichi-Sankyo, Tokyo, Japan], iopamidol [Iopamiron 300, Bayer Schering Pharma, Berlin, Germany] or iomeprol [Iomeron 300, Bracco-Eisai, Tokyo, Japan]) was injected through the antecubital vein. In 4 cases with dynamic study, the dose of contrast medium was 2 mL/kg (100 mL at maximum) and the injection duration of 50 seconds was used with a scan delay time of 30 (early phase) and 100 (late phase) seconds. In remainder 7 cases, the same dose and the injection duration of 60 seconds was used with a scan delay time of 60 seconds. CT attenuation of the neoplasms was classified visually as follows: low (lower than that of muscles); intermediate (equal to that of muscles); and high (higher than that of muscles). The region of interest was drawn at the area showing the strongest enhancement with largest size on unenhanced and enhanced images avoiding the beam-hardening artifacts and the areas with necrosis. On CE-CT images at the early and/or late phases, the degree of CT enhancement was evaluated visually and objectively by the change in the CT number (none, <5 HU; mild, $\geq$5 and <10 HU; moderate, $\geq$10 and <50 HU; and high, $\geq$50 HU) and the distribution of contrast material (homogeneous or heterogeneous) was also evaluated subjectively.

MRI studies included unenhanced T1-, T2- and fat-suppressed T2-weighted spin-echo images (T1-weighted images, T2-weighted images and FS-T2-weighted images) and CE images in 5 cases. CE-MR images were obtained at 10 minutes or longer after gadolinium with diethylenetriamineepentaacetic acid (Gd-DTPA) administration with a scan time of approximately 17 seconds under breath holding. Because of the long study period, several MR imagers (0.5- or 1.5-T systems) were used. Trans-axial images of 10 mm or thinner thickness with an interval of 20% were obtained in all patients. MR signal intensity (SI) of the neoplasms was classified by the SI of the major component of each neoplasm visually as follows: low (equal to or lower than that of muscles on both T1-weighted and T2-weighted images); intermediate (equal to that of bone marrow on both T1-weighted and T2-weighted images); and high (between those of bone marrow and fat on T1-weighted images, or between those of bone marrow and cerebrospinal fluid on T2-weighted images). The degree of MR enhancement and distribution were visually judged as none, mild, moderate or high and homogeneous or heterogeneous, respectively. The finding of necrosis was judged to be present when an area of scant enhancement was observed within an area of enhancement.

All CT and MR images were independently interpreted by 3 thoracic radiologists (26, 7, and 3 years of clinical experience, respectively). We resolved discrepancies among the 3 radiologists by consensus.

An experienced pathologist reviewed all cases and confirmed the diagnosis using the slide preparations stained by hematoxylin and eosin at a maximum cross section of the resected specimen. Then, the correlation

between the image findings and pathological features was discussed among the pathologist and radiologists. The pathological methods and findings evaluated in this study were the same for all. The evaluated pathological findings were the presence of large arteries and large veins (classified as either observed or not observed), the number small arteries (number/1cm^2), small veins (number/1cm^2) and capillary vessels (number/10 high-power field (HPF)). Spearman's rank-correlation coefficient was used to correlate the CT enhancement using the visual criterion with the number of vessels.

3. Results

CT and MR features together with surgical and pathological findings in the 12 ganglioneuromas are shown in **Tables 1** and **2**. CT attenuation was relatively low (25-54 HU, mean 36 HU) on unenhanced CT (**Table 1**). On CE-CT, 5 (45%), 2 (18%), 3 (27%) and 1 (9%) of the 11 neoplasms showed no, mild, moderate and high enhancement, respectively. Among the 4 neoplasms scanned with dynamic CE-CT protocol, 1 (25%), 2 (50%), 0 (0%) and 1 (25%) showed no (**Figure 1**), mild (**Figure 2**), moderate (**Figure 3**) and high (**Figure 4**) enhancement, respectively. In 3 (75%) and 1 (25%) of the 4 cases, there was no and moderate enhancement at early phase, respectively. The 1 (33%) and 2 (67%) of 3 cases with no enhancement at early phase showed no and mild (5 and 7 HU) enhancement at late phase (**Figure 2**). One case with a moderate enhancement at early phase gradually showed high enhancement at late phase (**Table 1**). There were 4 cases for which pre- and post-contrast CT numbers could not be calculated. All 4 cases showed homogeneous and no enhancement by the visual criterion (**Figure 1**). All the 7 neoplasms showing no (5 cases) or mild (2 cases) enhancement appeared as a homogeneous internal structure on enhanced CT.

The presence and numbers of the each vessel are summarized in **Table 2**. There was no correlation between degrees of CT enhancement and the presence of large vessels (large artery: $r = 0.13$, $P = 0.71$; large vein: $r = 0.58$, $P = 0.060$). The Spearman's rank-correlation coefficient between CT enhancement and the number of capillary vessels, small veins and small arteries was 0.79 ($P = 0.0037$), 0.14 ($P = 0.67$) and −0.020 ($P = 0.95$), respectively. Thus, only the number of capillary vessels showed a strong correlation with the degree of CT enhancement (**Figure 5**).

On MRI, the SI and homogeneity of the ganglioneuromas were variable. T1-weighted images showed intermediate or low SI, and T2-weighted images usually showed heterogeneous intensity. On MRI, CE-T1-weighted images showed a heterogeneous enhancement in all 5 patients and easily diagnosed as a solid lesion. The degree of enhancement was mild, moderate and high in 3 (60%), 1 (20%) and 1 (20%), respectively. One case (case 3) showed a discrepancy between the findings of CT and MRI showing scant and high contrast enhancement, respectively (**Tables 1-3**).

There were 2 patients (cases 2 and 12) who had both dynamic CE-CT and enhanced MRI. Both studies showed a similarly mild enhancement; however, enhancement on MRI was heterogeneous and was confirmed

Table 1. CT Features.

Patient	CT number (HU)			Enhancement		Slice
No./sex/age (years)	Pre-contrast	Early phase	Late phase	Homogeneity	Grade	Thickness (mm)
1/F/62	N/A	N/A	N/A	Homo	None	10
2/M/45	35	38	42	Homo	Mild	3
3/F/16	50	N/A	46	Homo	None	3
4/F/54	25	N/A	55	Hetero	Moderate	5
5/M/57	54	N/A	82	Homo	Moderate	10
6/F/20 (MRI alone)	N/A	N/A	N/A	N/A	N/A	N/A
7/M/57	N/A	N/A	N/A	Homo	None	10
8/F/12	N/A	N/A	N/A	Homo	None	10
9/F/36	28	28	28	Homo	None	3
10/M/7	36	N/A	53	Hetero	Moderate	10
11/F/15	28	49	82	Hetero	High	3
12/F/62	35	35	40	Homo	Mild	5

Homo = Homogeneous, Hetero = Heterogeneous, N/A = Not available.

Table 2. Grade of contrast enhancement on CT and numbers of vascularities of the tumor.

Patient						Enhancement	
No.	A	B	C	D	E	Homogeneity	Grade
1	0	0	0	13	21	Homo	None
2	0	0	3	8	44	Homo	Mild
3	1	0	6	38	34	Homo	None
4	1	1	4	22	43	Hetero	Moderate
5	0	0	3	46	48	Homo	Moderate
6 (MRI alone)	0	0	4	7	14	N/A	N/A
7	0	0	5	8	42	Homo	None
8	0	0	8	9	13	Homo	None
9	1	0	3	23	22	Homo	None
10	0	0	6	19	45	Hetero	Moderate
11	1	1	5	11	44	Hetero	High
12	0	1	6	13	30	Homo	Mild

A: large arteries, B: large veins, observed = 1 or not observed = 0. C: small arteries (number/1cm^2); D: small veins (number/1cm^2); E: capillary vessels (number/10 HPF).

Table 3. MRI features.

	T1WI		T2WI		FS-T2WI		Enhanced T1WI		Slice
No.	Homogeneity	SI	Homogeneity	SI	Homogeneity	SI	Homogeneity	Enhancement	Thickness (mm)
2	Homo	Low	Homo	IM-high	N/A	N/A	Hetero	Mild	5
3	Hetero	Low	Hetero	Low-high	Hetero	Low-high	Hetero	High	5
4	Hetero	IM-high	Hetero	IM	Hetero	IM	Hetero	Moderate	9
6	Homo	Low-IM	Hetero	Low-high	Hetero	Low-high	Hetero	Mild	8
12	Hetero	IM	Hetero	Me-high	N/A	N/A	Hetero	Mild	7

T1WI = T1-weighted image, T2WI = T2-weighted image, FS-T2WI = fat-suppressed T2-weighted image, SI = signal intensity, IM = intermediate, Homo = homogeneous, Hetero = heterogeneous, N/A = not available.

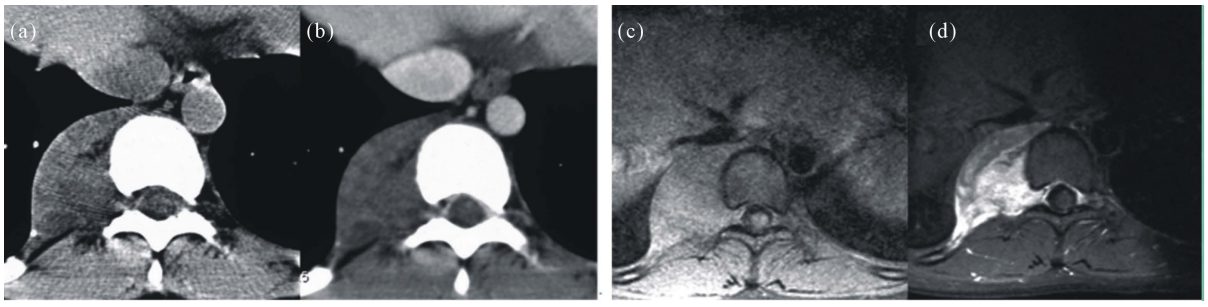

Figure 1. A 16-year-old woman with a ganglioneuroma in the right para-vertebral space (case 3). Axial (a) non-contrast CT shows a well-demarcated 50 HU mass with a band-like shape, fat-attenuation component and a punctate calcification. Axial (b) contrast enhanced CT shows no obvious enhancement (46 HU) on delayed phase scanned with a delay time of 100 sec after administrating contrast material. Axial (c) T1-weighted MR image (T1WI) shows a mass with a low signal-intensity similar to that of adjacent muscles. Axial (d) Post-contrast T1 weighted MR image with Gd-DTPA shows a heterogeneous high enhancement. The degree of contrast enhancement on MRI is more apparent than that on CT. The scores of each vessel are as follows; LA: 1, LV: 0, SA: 6, SV: 38, and CV: 34.

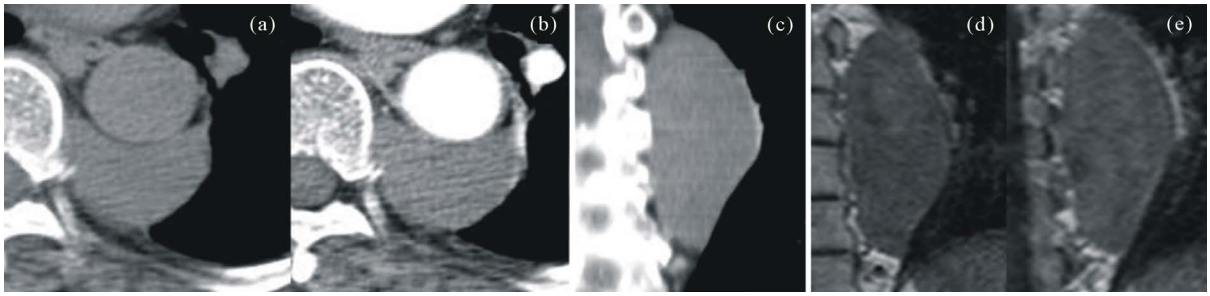

Figure 2. A 62-year-old woman with a ganglioneuroma in the left para-vertebral space behind the descending aorta (case 12). Axial (a) non-contrast CT image shows a crescent-shaped mass behind the descending aorta with a CT attenuation of 35 HU. Axial (b) contrast enhanced CT image shows little enhancement from 35 to 40 HU. Coronal (c) contrast enhanced CT image shows an oblong-shaped mass in cranio-caudal direction. Coronal (d) T1-weighted image shows a homogeneous low signal intensity mass. Coronal (e) enhanced T1-weighted MR image shows a heterogeneous and mild enhancement that is consistent with solid lesion. The scores of each vessel are as follows; LA: 0, LV: 1, SA: 6, SV: 13, and CV: 30.

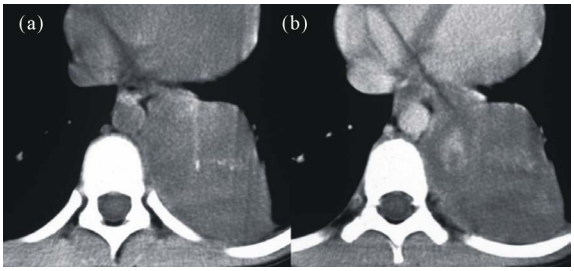

Figure 3. A 7-year-old boy with a ganglioneuroma in the left para-vertebral space (case 10). Axial (a) non-contrast CT image shows a homogeneous low attenuation (36 HU) mass with the punctate calcifications. Axial (b) contrast-enhanced CT image at a delayed phase of 100 sec after administrating contrast material shows a heterogeneous moderate enhancement of 53 HU at maximum. The scores of each vessel are as follows; LA: 0, LV: 0, SA: 6, SV: 19, and CV: 45.

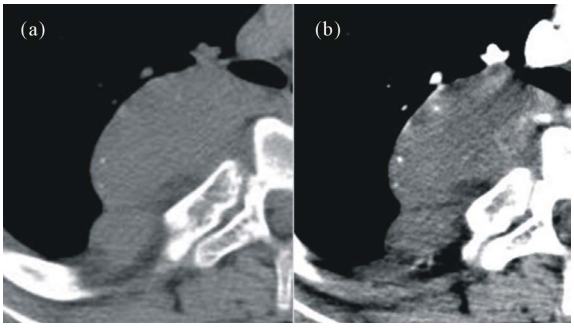

Figure 4. A 15-year-old woman with a ganglioneuroma in the right para-vertebral space (case 11). Axial (a) non-contrast CT image shows a homogeneous low attenuation (28 HU) mass with punctate calcifications in the right para-vertebral space. There is a tapered termination to the thoracic cage (tail-like extension). Axial (b) contrast-enhanced CT image at a late phase shows a heterogeneous contrast enhancement. A part of the mass shows a high enhancement (from 28 to 82 HU). There are several large vessels at the margin of the mass. The scores of each vessel are as follows; LA: 1, LV: 1, SA: 5, SV: 11, and CV: 44..

easily as showing a solid component. There were additional 2 cases (cases 3 and 4) who had both conventional delayed-phase CE-CT and MR. In case 3, enhancement on MR was heterogeneous and high compared to that on CT showing no enhancement. In case 4, enhancement on MR was moderate and heterogeneous, which was similar to that on CE-CT.

4. Discussion

Ganglioneuroma is a rare benign tumor arising from sympathetic ganglia. Early detection seems to be important

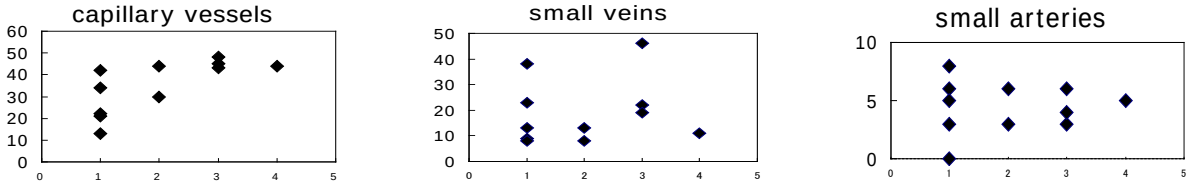

Figure 5. Relationship between the grade of contrast enhancement on CT and scores of small arteries, small veins and capillary vessels. Spearman's rank-correlation coefficient between CT enhancement and the number of capillary vessels, small veins and small arteries was 0.79, 0.14 and −0.02, respectively. The numbers of capillary vessels shows a strong correlation with the degree of CT enhancement (P = 0.003).

because complete resection usually results in a cure and the tumor rarely undergoes malignant transformation [1]. Ganglioneuromas occur in all age groups but are more common before the age of 40 years and the median age at diagnosis is approximately 7 years. The tumors are most often located in the posterior mediastinum, followed by retroperitoneum and cervical region [1], [5]. Ganglioneuroma averages 8 cm in diameter and may appear encapsulated, although a true capsule is infrequent. The tumors are firm, and white to yellow in color.

Although ganglioneuroma tends to be relatively homogeneous, the imaging characteristics of ganglioneuroma are similar to those of ganglioneuroblastoma and neuroblastoma; hence, they cannot be discriminated by imaging evaluation save for the presence of metastasis, which is quite rare in ganglioneuroma. Chest radiographs typically show a posterior mediastinal mass, which may cause rib spreading and foraminal erosion. On CT, calcifications are seen in approximately 20% - 60% of ganglioneuroma; calcifications are typically fine and speckled but may be coarse [5], [6]. A tail-shaped edge was recently observed as an interesting feature of this entity [6]. Fat is seen in approximately 30% [6]. On MRI, ganglioneuromas might show low SI on T1-weighted images and heterogeneous high SI on T2-weighted images. Several reports indicate that relatively high heterogeneous SI on T2-weighted images suggests ganglioneuroma; the appearance is presumed to be caused by a combination of myxoid material and relatively low amounts of ganglion cells [5]. An interesting finding of whorled appearance on T1-weighted and, more commonly, T2-weighted images within the tumor that corresponds to the microscopic interlacing patterns of Schwann cells and collagen fibers has been reported [5].

CE-CT showed mild to moderate enhancement, but cases showing no enhancement were reported to be not rare (6 of 13 cases; 46%) [6]. The homogeneous, relatively low attenuation and non-enhanced CT findings might lead to a miss-interpretation as a cystic lesion. In this study we showed a strong correlation between the numbers of capillary vessels and the grade of CT enhancement.

The enhancement on MRI varies from mild to marked. The early enhancement at dynamic CE-MRI has not been typical in ganglioneuroma [5]. It might accumulate contrast material over time [5]. The delayed-phase CE-MRI after dynamic study requires a longer period (about 10 minutes) after contrast material injection compared to CT (100 sec in this study), and this might be a major reason for the observation that MRI could be superior to CT to demonstrate contrast enhancement of ganglioneuromas.

On CT too, ganglioneuroma is usually enhanced gradually and the images scanned at delayed timing might be useful to confirm the degree and patterns of enhancement. Because the contrast resolution of CT among the soft tissues is inferior to that on MRI, the increased amount of contrast medium and/or elevation of injection rate should be essential to improve the diagnostic accuracy. The differential diagnosis of ganglioneuroma in the posterior mediastinum includes various kinds of cysts such as neuroenteric, coelomic cyst and foregut cyst, extra-medullary hematopoiesis and neurogenic tumors including neuroblastoma, ganglioneuroblastoma, neurofibroma, schwannoma, paraganglioma, and pheochromocytoma.

Malignant neurogenic tumors like neuroblastoma and ganglioneuroblastoma show a more aggressive nature than ganglioneuromas, and the majority of them usually have an irregular contour, occasionally with invasion to adjacent organs and encasement of vessels [5]. Neuroblastoma and ganglioneuroblastoma often develop metastases to the bone, regional lymph nodes, liver and skin, whereas ganglioneuromas do not. On dynamic CE-MR studies, there is usually marked early enhancement in neuroblastomas [1]-[3]. Furthermore, neuroblastomas and ganglioneuroblastomas occur in a younger age group, and the pattern of calcification on CT is more commonly amorphous and coarse rather than the discrete and punctuate pattern observed in ganglioneuromas [1].

The most problematic differential diagnosis would be among ganglioneuroma, schwannoma and neurofibroma. It is sometimes difficult to differentiate these tumors with SI characteristics on MRI alone. Schwannomas

reveal late enhancement similar to that of ganglioneuromas with areas of histological Antoni B type component, and curvilinear or nodular low intensity regions composed of collagenous fibrous tissue are observed within neurofibroma as well. Schwannomas and neurofibromas, however, are predominantly round and might produce a bony erosion or destruction, whereas the majority of ganglioneuromas are flat and elongated and usually do not produce bony changes. Moreover, the cystic degeneration frequently noted in schwannomas might be helpful in making the distinction, because it is not found in ganglioneuromas. On the other hand, neurofibromas are non-encapsulated, and the possibility of neurofibroma can be excluded if a capsule is present [1]. We suggest that the findings of scant enhancement without cystic change might become clear using contrast study.

The limitation of our study is that the sample size was small, and scan protocol was not standardized because ganglioneuroma is a relatively rare tumor and it takes a long time to collect a sufficient number of this tumor. In association with the fact, slice thickness of the images was variable. However, we think that this limitation had little effect on evaluation of contrast enhancement of the entire tumors, although further investigation with the standardized protocol might be desirable.

5. Conclusion

As shown in this study, ganglioneuromas sometimes show the CT findings similar to those of cystic lesions. The improvement of the scan protocol such as a longer scan delay and/or increased amount of contrast media or further examination using MRI would be required in some situations. The results of the current study suggest that ganglioneuromas usually demonstrate no or little early enhancement but gradually increasing enhancement on dynamic CE-CT according to the degree of capillary vessels. CE-MRI clarified the enhancement in all such 5 cases and the degree of contrast enhancement became various.

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