RESEARCH ARTICLE

Differential Diagnosis of CT Images in Children with Neuroblastomas and Ganglioneuroblastomas

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Abstract

Objective: To investigate the differential features of CT images in children with neuroblastomas (N) and ganglioneuroblastomas (G). Materials and Methods: Clinical data of 12 children in group G and 15 in group N undergoing CT examination and definitely diagnosed by pathology were retrospectively analyzed. The focal conditions were observed and compared in the two groups, including location, size, boundaries, morphology, enhanced degree and mode, abdominal vascular involvement, presence or absence of spanning the midline, infiltration of peripheral organs, angiography manifestations in tumors or surroundings, presence or absence of calcification and vascular tumor emboli as well as metastases of distal organs and lymph nodes. Results: In group N, the incidence of tumors in the adrenal area was conspicuously higher than in group G ($P<0.05$), while that of tumors with regular morphology and clear boundaries was significantly lower than in group G ($P<0.01$); Angiography manifestation rate and incidences of vascular embedding, lymph node metastasis, infiltration and organic metastasis in group N were all markedly higher than in group G ($P<0.05$). There was no statistical significance between the two groups in terms of focal size, presence or absence of calcification and spanning the midline, and enhanced degree and mode, as well as vascular tumor emboli ($P>0.05$). Conclusions: Mostly located in adrenal areas and with vascular embedding as a primary manifestation, the neuroblastoma extremely readily metastases to lymph nodes and other organs as well as infiltrating local tissues, with dilation on angiography frequent in or around the tumors. With vascular displacement as a primary manifestation, ganglioneuroblastoma has a regular morphology and clear boundaries.

Keywords: Neuroblastoma - ganglioneuroblastoma - CT images - lymph node metastasis - children

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Introduction

Deriving from immature embryonic cells of adrenal medulla or paravertebral sympathetic ganglion, neuroblastoma is the most common extracranial malignant solid tumor in children. With higher malignancy than nephroblastoma and hepatoblastoma, it can be easily misdiagnosed due to non-specific symptoms (Heczey et al., 2013; Morgenstern et al., 2013). As a sort of rare mixed-type malignant tumor, ganglioneuroblastoma originates from sympathetic ganglionic cells of neural crest, and its differentiated degree is between benign ganglion cells and malignant neural mother cells (Angelini et al., 2014). Both neuroblastoma and ganglioneuroblastoma pertain to peripheral neuroblastic tumors, so their signs and clinical symptoms are similar, but malignant degree and prognosis are greatly different (Duijkers et al., 2012). Hence, preoperative differential diagnosis is of great significance for selection of treatment methods and prognostic evaluation. This study analyzed the CT image features of children respectively with neuroblastoma and ganglioneuroblastoma and investigated their CT differential key points so as to provide some evidences for clinical diagnosis.

Materials and Methods

General data

The clinical data of 12 children with ganglioneuroblastoma and 15 with neuroblastoma undergoing CT examination and definitely diagnosed by pathology in our hospital from Oct., 2009 to Oct., 2013 were retrospectively analyzed. There were 7 males and 5 females in the children with ganglioneuroblastoma selected as group G. They were 8 months to 10.0 years old, with the median age of 3.0 years. There were 8 males and 7 females in the children with neuroblastoma selected as group N. They were 3 months to 6.5 years old, with the median age of 2.0 years. There were 10 children suffering from abdominal pain, 12 from abdominal lumps, 1 from diarrhea and 1 from exophthalmos in the two groups. Additionally, 3 cases were occasionally found due to other diseases.

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Table 1. Comparison on the Features of CT Plain Scan Images in Both Groups [*n* (%)]

Groups	*n*	Morphology		Location		Boundary		Calcification		Spanning the midline	
		Regular	Irregular	Adrenal area	Paravertebral are or spinal proparea	Clear	Vague	Yes	No	Yes	No
Group N	15	4 (26.7)**	11 (73.3)	13 (86.7)*	2 (13.3)	5 (33.3)**	10 (66.7)	8 (53.3)	7 (46.7)	6 (40.0)	9 (60.0)
Group G	12	8 (66.7)	4 (33.3)	7 (58.3)	5 (41.7)	9 (75.0)	3 (25.0)	8 (66.7)	4 (33.3)	4 (33.3)	8 (66.7)

Compared with group G, *$P<0.05$, **$P<0.01$

Table 2. Comparison on the Features of CT Enhanced Scan Images in Both Groups [*n* (%)]

Groups	*n*	Enhanced degree			Enhanced mode		Vascular relationship		Angiography manifestation in tumor or surrounding the tumor	
		Mild	Moderate	Significant	Uniform	Nonuniform	Displacement	Embedding	Yes	No
Group N	15	1 (6.7)	5 (33.3)	9 (60.0)	1 (6.7)	14 (93.3)	5 (33.3)	10 (66.7)*	8 (53.3)*	7 (46.7)
Group G	12	3 (25.0)	4 (33.3)	5 (41.7)	3 (25.0)	9 (75.0)	8 (66.7)	4 (33.3)	3 (25.0)	9 (75.0)

Compared with group G, *$P<0.05$.

Methods

CT scan: The children in supine position were scanned by American GE Lightspeed 16-layer spiral scanner. Before examination, those crying and screaming children were given 10% chloral hydrate for sedation, 0.25~0.50 mL/kg. Scanning parameters: 120~200 mV tube current, 100~120 kV tube voltage, 1.000~1.375 screw pitch, scanning-layer thickness and reconstruction-layer thickness being 5.00 mm and 1.25 mm, respectively. Meanwhile, 300 mg I/mL contrast agent iohexol was injected in bolus by scalp veins or forearm veins for enhanced scan, with 0.8~2.5 mL/s flow rate, and the dosage was 1.2~2.0 mL/kg body mass. The images at arterial and venous phases were achieved 15~20 s and 50~60 s after injection.

Image analysis: Two professional radioautography diagnostic doctors read the films and came to an agreement. The observation contents were as follows: focal location, size, boundary, morphology, enhanced degree and mode, abdominal vascular involvement, presence or absence of spanning the midline, infiltration of peripheral organs, angiography manifestation in tumor or surrounding the tumor, presence or absence of calcification and vascular tumor embolus, metastases of distal organs and lymph nodes. According to the major focal location, the region where focuses were located was divided into spinal proparea, paravertebral area and retroperitoneal adrenal area. The focal boundary was split into clear and vague in terms of presence or absence of fat space between focuses and peripheral tissues and organs, and size was measured with the longest diameter of the biggest cross section as criteria. Morphology fell into regular (round and quasi-circular) and irregular. With the muscles in abdominal wall as reference, the enhanced degree of tumor parenchyma was divided into mile (lower than muscular strengthened degree), moderate (similar to muscular strengthened degree) and conspicuously enhanced (higher than muscular strengthened degree). Spanning the midline meant the focus surpassed the contralateral edge of spinal cord; vascular displacement meant the vessels were directly or indirectly displaced, and vascular embedding meant the vessels were completely embedded by the focus.

Statistical data analysis: SPSS 13.0 statistical software was applied to analyze the data. The measurement data were compared with normality test first, and t test was used for comparison among groups if the data were normal distribution. The enumeration data were compared with x^2 test. $P<0.05$ was considered to be statistically significant.

Results

Comparison on the biggest tumor diameters in two groups

The biggest tumor diameter in group N was 2.5~10.5 cm, averagely (5.8±2.6) cm; the biggest tumor diameter in group G was 1.8~9.6 cm, averagely (4.9±2.1) cm. There was no statistical significance between two groups by comparison to the biggest tumor diameters ($P>0.05$).

Comparison on the features of CT images in two groups

Plain-scan image: In group N, the tumors were located in adrenal area in 13 cases; 10 cases had the tumors with vague boundary and irregular morphology, and some of superficial and big phyllodes were like multi-nodular fusion; tumor calcification and spanning the midline occurred in 8 and 6 cases, respectively. In group G, the tumors were located in retroperitoneal adrenal area in 7 cases; 9 and 8 cases had the tumors respectively with clear boundary and regular morphology; tumor calcification and spanning the midline occurred in 8 and 4 cases, respectively. In group N, the incidence of tumor in adrenal area was conspicuously higher than in group G ($P<0.05$), while that of tumor with regular morphology and clear boundary was significantly lower than in group G ($P<0.01$). Significant differences were not presented in two groups by comparison to the conditions of calcification and spanning the midline ($P>0.05$) (Table 1).

Enhanced-scan image: The CT value of parenchyma in 27 children with peripheral neuroblastic tumor was 22~45 HU. The parenchyma part of tumor body was reinforced evidently at arterial phase of enhanced scan, and CT value was increased approximately 17 HU on average; the parenchyma part of tumor body was enhanced continuously at venous phase, and CT value was increased about 19 HU on average, with similar range to arterial phase. Nonuniform enhancement was predominant in both groups, and different sizes of low-density areas without enhancement appeared inside. Angiography in

Table 3. Comparison on the Malignant Degrees of CT Images in both Groups [*n* (%)]

Groups	*n*	Lymph node metastasis		Vascular tumor embolus		Infiltration and organic metastasis	
		Yes	No	Yes	No	Yes	No
Group N	15	8 (53.3)*	7 (46.7)	1 (6.7)	14 (93.3)	7 (46.7)*	8 (53.3)
Group G	12	3 (25.0)	9 (75.0)	1 (8.3)	11 (91.7)	2 (16.7)	10 (83.3)

Compared with group G, *P<0.05

tumor or surrounding the tumor in linear or areatus line appeared among 11 cases, in which thin and small vessels in linear or areatus line arose in 3 cases and punctiform and linear enhanced angiography in 8 cases. In group N, peripheral great vessels were embedded by tumors in 10 cases, including embedment of renal veins and arteries (6 cases), celiac trunk and its branches (6 cases), abdominal aorta (6 cases) accompanied by movement forward (3 cases), inferior vena cava (3 cases) as well as superior and inferior mesenteric arteries (5 cases). In group G, peripheral great vessels were displaced by tumors in 8 cases. Angiography manifestation rate and incidences of vascular embedding in group N were markedly higher than in group G (P<0.05), and there was no statistical significance between two groups in terms of enhanced degree and mode (P>0.05) (Table 2).

Comparison on the malignant degrees of CT images in two groups

In group N, 8 cases suffered from lymph node metastasis, manifesting a swelling soft tissue shadow surrounding the renal pedicle and abdominal aorta; 7 cases encountered infiltration and organic metastasis, in which 3 cases suffered from renal invasion, 1 from invasion of psoas major muscle and lumbar metastasis, 1 from intrapulmonary invasion accompanied by skull metastasis, 1 from liver metastasis and 1 from femoral metastasis. The incidences of lymph node metastasis, infiltration and organic metastasis in group N were all notably higher than in group G (P<0.05), and there was no statistical significance between two groups with regard to the vascular tumor embolus (P>0.05) (Table 3).

Discussion

Neuroblastoma, a sort of embryonal tumor, is one of the most commonly-encountered malignant tumors in childhood and easily occurs in children less than 10 years old. It can be found at any part of adrenal medulla and sympathetic plexus distribution, especially at retroperitoneal site (Gheytanchi et al., 2014; Louis et al., 2014; Wang et al, 2014). Ganglioneuroblastoma is a rare malignant tumor between neuroblastoma and ganglioneuroma. Its major clinical manifestation is long-term intractable diarrhea, mostly accompanied by metabolic acidosis, malnutrition, hypokalemia and abdominal distension. Ganglioneuroblastoma is misdiagnosed easily due to non-conspicuous abdominal pain at an early stage if it is not identified accurately, consequently affecting the prognosis (Keating et al., 2005). Ganglioneuroma, neuroblastoma and ganglioneuroblastoma all derive from developmental neural cells of sympathetic nervous system, but their differentiated degrees and biological behaviors are not consistent completely (Kubota et al., 2000). Ganglioneuroma belongs to benign tumors, frequently occurring in the young and adult, whereas both neuroblastoma and ganglioneuroblastoma pertain to malignant tumors, tending to occur in the children and teenagers (Otal et al., 2001; Nasseh et al., 2013). A lot of studies have revealed that CT scan can clearly show the focal location, size, morphology, internal structure, density and relationships with peripheral organs, and thus it is of great importance for preoperative qualitative diagnosis, selection of therapeutic regimens and prognostic evaluation (Liu et al., 2013; Sharp et al., 2013). Hence, this study primarily explored the differences between neuroblastoma and ganglioneuroblastoma from the differential perspective of CT images.

The study demonstrated that the enhanced degree of tumor body was significantly associated with its microvessel density (Qin et al., 2013). In this study, nonuniform enhancement was respectively presented in 14 cases (93.3%) of group N and 9 cases (75.0%) in group G, and different sizes of low-density areas without enhancement appeared inside in both groups, illustrating that hemorrhage and necrosis easily occur in peripheral neuroblastic tumors. Ganglioneuroblastoma is frequently found in the posterior of peritoneum, and some experts have pointed that it is generally located in the retroperitoneal paravertebral sympathetic chain. Jay et al. found that among the children, about 1/3 of retroperitoneal ganglioneuroblastomas occurred in paravertebral ganglion, approximately 2/3 in adrenal medulla (Jay et al., 2006). In this study, ganglioneuroblastomas of 5 cases (41.7%) and 7 cases (58.3%) occurred in paravertebral area or spinal proparea and adrenal area, respectively, similar to the research results of Jay et al. Neuroblastoma is characterized by no envelope, mostly infiltrative growth and vague boundary, whereas ganglioneuroblastoma generally has complete or incomplete false fibrous envelope, and its boundary is more explicit. Vague or no fat space between the tumor focus and peripheral organs indicates that the tumor has malignant biological tendency. In this study, neuroblastomas of 11 cases had irregular morphology, and fat space with peripheral tissues and organs appeared in 5 cases, while ganglioneuroblastomas of 4 cases had irregular morphology, and fat space with peripheral tissues and organs arose in 9 cases.

Neuroblastoma is mostly infiltrative growth and has stronger invasion. Its focuses can infiltrate into peripheral great vessels, and the growth between spinal cords and in the posterior of abdominal aorta can embed and displace the abdominal aorta forward (Kiyonari et al., 2014). However, ganglioneuroblastoma is mainly expansive growth. Although it is closely adjacent to peripheral tissues, the boundary is more explicit. In this study, peripheral great vessels were embedded by tumors in 10 cases (66.7%) in group N and displaced by tumors in 8 cases (66.7%) in group G, indicating that the major manifestations of neuroblastoma and ganglioneuroblastoma are separately embedment and displacement of peripheral great vessels. When tumor growth accelerates and only dependence on the initial vessels of tumor cannot meet the growth demand, compensatory blood supply of peripheral vessels makes vessels broaden, thereby leading to the manifestation of angiectasis in tumor or surrounding the tumor in linear or areatus line (Sutton et al., 2009). In this study, angiography manifestation rate in group N was markedly higher than in group G, showing that the blood supply of neuroblastoma is more abundant. Additionally, the incidences of lymph node metastasis, infiltration and organic metastasis in group N were all notably higher than in group G, suggesting that metastases of lymph nodes and organs as well as infiltration to local tissues and organs easily occur in neuroblastoma.

To sum up, mostly located in adrenal area and with vascular embedding as primary manifestation, neuroblastoma is extremely easy to encounter metastases of lymph nodes and organs as well as infiltration to local tissues and organs, and dilated angiography frequently appears in tumor or around the tumor in linear or areatus line. With vascular displacement as primary manifestation, ganglioneuroblastoma has a regular morphology and clear boundary.

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