Image defined risk factors using MDCT, Are they a good predictor of surgical outcomes in abdominal neuroblastoma regardless of the disease stage?

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Aims and objectives

Background:

Neuroblastoma is one of the most common malignances in children during early childhood [1]. It arises from primitive neuroblasts of neural embryonic crest and can occur anywhere within the sympathetic nervous system [2]. The most common site of the primary tumors is intraabdominal and half of the intra-abdominal neuroblastoma arise from the adrenal medulla [3].

Therapeutic management depends on the tumor stage. It can be surgical or chemo-radiotherapy. Surgery is usually reserved to localized abdominal neuroblastoma where immediate complete resection of the tumor could be done with no need for subsequent therapy or near complete resection followed by adjuvant therapy in some cases [1]. The role of surgery in metastatic disease is still debatable with some authors reported that there is no advantages in terms of survival probability in patients with metastatic disease who underwent complete surgical excision while other studies noted that gross resection of the tumor led to improved clinical outcomes in terms of the local control of the disease and survival rate [4, 5].

Image defined risk factors (IDRFs) are risk factors that have been recently used in the new international neuroblastoma risk group classification system which is basically an image based staging system for neuroblastoma [6].

The image defined risk factors for abdominal neuroblastoma as defined by the international neuroblastoma risk group (INRG) are:

- Tumor infiltrating the porta hepatis and/ or the hepatodudenoanal ligament.
- Tumor encasing branches of the superior mesenteric artery at the mesenteric root.
- Tumor encasing the origin of the celiac axis, and/ or of the superior mesenteric artery.
- Tumor invading one or both renal pedicles.
- Tumor encasing the aorta and/ or vena cava.
- Tumor encasing the iliac vessels.
- Pelvic tumors crossing the sciatic notch.
• Intraspinal tumoral extension with more than one third of the spinal canal in the axial plane is invaded.

• Infiltration of adjacent organs and structures including the diaphragm, kidney and the liver. [6]

**Purpose:**

To evaluate if the IDRFs detected by MDCT are good predictors of surgical outcomes in abdominal neuroblastoma regardless of the disease stage in terms of rate of complete surgical resection and the occurrence of surgery related complications.
Methods and materials

Patient group:

Between April 2014 and August 2015, After the approval of the local ethical committee and informed written consent of the patients' parents or their legal guardians. We prospectively enrolled 20 cases with abdominal neuroblastoma, proved with Tru cut needle biopsy, and who would undergo surgery.

Patient characteristics were: 12 males, 8 females, mean age 2.9 ± 2.3 years.

Six of the patients were with localized disease (30%) while 14 of the patients had metastatic disease (70%).

Examination protocol:

Pre-operative contrast enhanced CT was done using a GE bright speed (16 row) CT scanner, single scan phase using the following parameters: 120KV, smart mA (100 - 440), rotation time 0.75 sec, Pitch 1.75:1, speed 35 mm/rotation. Detector width 1.25 mm X 16 row.

Axial images were taken with thickness of 5 mm and interval of 5 mm then reconstructed into 1.25 mm thickness and 0.6 mm interval for multiplanar reformats.

IV contrast administration of non ionic contrast material (Iopromide 300 mg Iod/mL, Ultravist®, Schering, Berlin, Germany) with dose of 2 ml/Kg (Maximum of 50 ml) administrated by power injector at a rate of 2 ml/sec.

Bolus tracking was used with ROI placed over the proximal abdominal aorta and bolus tracking threshold of +100 HU (Above the baseline HU). Scan delay BT100+ 35 second.

Image assessment:

All the studies were examined by two independent radiologists and the presence of any of the following IDRFs was reported:
- Invasion of one or both renal pedicles.

- Encasement of any of the main vascular structures including the aorta, IVC, celiac axis, superior mesenteric artery and the iliac vessels.

- Infiltration of the adjacent organs, mainly the kidney, liver and spleen.

- Intra spinal tumor extension.

**Statistics:**

- Patients were assigned to two groups: group 1 consisted of patients with no IDRFs reported in the pre-operative CT, group 2 consisted of patients with at least one of the IDRFs reported in the pre-operative CT.

- Operative notes and surgery related complications were recorded.

- Statistical analysis using Pearson's chi square test. The presence of one or more of the IDRFs was correlated with the extent of tumor resection and rate of surgery related complications.

- P-values of less than 0.05 were regarded as significant.
Results

Of the 20 cases, at least one IDRF was reported in 11 cases representing 55% (Group 2) and none of the IDRFs were reported in 9 representing 45% (Group 1).

The image defined risk factors that were reported are: Infiltration of the porta hepatis (1), encasement of the celiac axis (2), Infiltration of the renal pedicle (5), Encasement of the iliac vessels (1), Intraspinal extension (1), Infiltration of the adjacent organs (1).
**Fig. 1:** Axial Contrast enhanced CT image in a 6 years old male patient with right supra renal neuroblastoma. The mass is seen infiltrating the right kidney and the right renal pedicle (IDRF).

**References:** South Egypt Cancer Institute - Assiut University - Asyut/EG

**Fig. 2:** Axial contrast enhanced CT image in a 1.5 years old female patient with pelvic neuroblastoma that shows intraspinal extension and involves more than one third of the spinal canal (IDRF).

**References:** South Egypt Cancer Institute - Assiut University - Asyut/EG
**Fig. 3:** Coronal reformatted image in a 1.5 years old male patient that shows left supra renal mass encasing the left renal artery (IDRF).

**References:** South Egypt Cancer Institute - Assiut University - Asyut/EG
Fig. 4: Coronal reformatted image in a 6 years old patient with right supra renal neuroblastoma that infiltrates the right diaphragmatic crus (IDRF).

References: South Egypt Cancer Institute - Assiut University - Asyut/EG

Complete surgical excision was achieved in all the cases of group 1. While in group 2, complete surgical excision was achieved in only 5 cases (45.5 %) but incomplete excision was done in 6 cases (55.5 %).

The rate of complete surgical excision was significantly higher in the absence of the IDRFs (P<0.03).
Surgery related complications was documented in 5 cases of group 2. But none of the surgery related complications were documented in any of the cases of group 1.

The surgery related complications that were documented are: Lymphorrhea (2), Nephrectomy (1), Nephrectomy and splenectomy (1) and intestinal fistula (1).

Of the 5 cases with surgery related complications, renal pedicle infiltration was reported in three of them (60%).

The occurrence of surgery related complications was not significantly related to the mere presence of the IDRFs. (P < 0.43).

However, the infiltration of the renal pedicle was the only single IDRFs with significantly higher rate of surgery related complications. (P < 0.04).
Images for this section:

**Fig. 1:** Axial Contrast enhanced CT image in a 6 years old male patient with right supra renal neuroblastoma. The mass is seen infiltrating the right kidney and the right renal pedicle (IDRF).

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Fig. 2: Axial contrast enhanced CT image in a 1.5 years old female patient with pelvic neuroblastoma that shows intraspinal extension and involves more than one third of the spinal canal (IDRF).

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Fig. 3: Coronal reformatted image in a 1.5 years old male patient that shows left supra renal mass encasing the left renal artery (IDRF).

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Fig. 4: Coronal reformatted image in a 6 years old patient with right supra renal neuroblastoma that infiltrates the right diaphragmatic crus (IDRF).

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Conclusion

IDRFs are good predictors of surgical outcomes in abdominal neuroblastoma regardless of the disease stage as their presence was associated with lower rate of complete surgical resection.

Renal pedicle infiltration was the only single IDRF with significantly higher rate of surgery related complications but the mere presence of the IDRFs didn't show significant relation with the rate of the surgery related complications.

When comparing our results with the literature, we couldn't find much as IDRFs were originally developed as part of the new international neuroblastoma risk group image based staging system and not as independent surgical risk factors. However, Simon et al. [7], performed a retrospective study on patients with stage 4 neuroblastoma and age of 18 months or older at diagnosis and they concluded that IDRFs are predicative for the extent of operative resection but wasn't associated with the frequency of complications.

Limitations

The limitations of our study were the small number of cases and that most of our cases were with metastatic disease and that was due to the fact that patients with neuroblastoma usually present late to our center with higher stage of the disease. Finally, we recommend additional studies with larger number of cases.
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