Chyle leak following surgery for abdominal neuroblastoma

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ABSTRACT

Background: The incidence and optimal management of postoperative chylous leak of neuroblastoma is inadequately documented. We analyzed the risk factors, management, and the implication of chyle leak following surgery for abdominal neuroblastoma.
Methods: One hundred sixty patients who underwent surgery for abdominal neuroblastoma between September 2004 and August 2014 were evaluated. To find the oncological implication we evaluated the delay in starting further treatment, local control, event free and overall survival.
Results: Chyle leak was the most common complication (20%). The median measure of leakage was 100 ml/day and it persisted for a median of 12 days. All patients were managed conservatively except one who needed exploration for wound dehiscence. Number of lymph nodes resected was the only factor associated with the risk of chyle leaks ($p = 0.013$). Adjuvant chemotherapy was not delayed in any patient because of chyle leaks per se and the local control, event free and overall survival were not different for patients with and without chyle leak.
Conclusion: Chylous leakage is a common postoperative complication of abdominal neuroblastoma, predisposed by the number of lymph nodes resected. It responds to conservative management and does not compromise further the oncological treatment and outcome hence; it should not be a deterrent to complete surgery.

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Surgical intervention forms an important part of the therapeutic plan for neuroblastoma. However, surgery can be formidable considering the proclivity of these tumors to encase important vascular structures, which makes the resection technically challenging, and often associated with complications [1–3]. The commonest complications from neuroblastoma surgery include vascular injury, nephrectomy, infections, organ dysfunction etc. [2]. Chyle leak because of disruption of retroperitoneal lymphatic channels is a possibility, however, its incidence and management after surgery for abdominal neuroblastoma is inadequately documented [4,5]. We analyzed our observations to find risk factors and the optimal management of chyle leaks following resection of abdominal neuroblastoma. Second, we also evaluated the impact of chyle leaks on further therapy, local control, and outcome.

1. Materials and methods

All patients who underwent surgery for abdominal neuroblastoma between September 2004 and August 2014 in a single tertiary cancer center were included in this study. Following a thorough clinical evaluation, histological confirmation of disease was achieved with an image-guided biopsy of the primary lesion. Metastatic work-up included a meta-iodobenzylguanidine (MIBG) scan, bone marrow studies, and a bone scan. Positron emission tomography (PET) scan was also performed in some patients. The patients were stratified into low, intermediate, and high-risk groups according to the Children Oncology Group (COG) risk categories [6]. Patients with low-risk disease, considered resectable, underwent upfront surgery and those with features of unresectability and all with intermediate or high-risk stratification received preoperative chemotherapy. All treatment decisions were taken in a multidisciplinary tumor board meeting.

The corresponding author (SSQ) performed or supervised all the surgeries. None of the patients underwent laparoscopic resection or diagnostic laparoscopy before exploration. The operative technique is

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described previously [7]. Concisely, a transverse supraumbilical or a thoracoabdominal incision was utilized based on the site and extent of disease. The operative goal was complete resection of the tumor and the involved or suspicious regional lymph nodes, without removal or injury to other structures. A combination of sharp and blunt tissue dissection was performed with no specific preference for using monopolar or bipolar electrocautery. Feeding tumor blood vessels and the visible lymphatic channels were secured with hemoclips, which were preferred over ties owing to the ease of application without undue stretches over the lymphatics. Areas of diffuse lymphatic ooze were under run, with silk sutures. Tissue glue was not used in any patient. Since the lymphatics are not very obvious, they were not ligated prophylactically and neither was the cysterna chyli. An abdominal drain was placed in all patients in anticipation of the abdominal distension and possible respiratory distress from the ascites resulting from peritoneal surface transudation because of prolonged exposure coupled with the ileus. The drains were removed five days after surgery unless significant drain output or chyle leak was present. Enteral nutrition was commenced on the second postoperative day and was discontinued if there was abdominal distension or vomiting. Patients were discharged from the hospital a day after the drain removal and were reviewed two weeks later.

Chyle leak was diagnosed on clinical suspicion in patients having a high drain output with change in color of the drain fluid to milky white. Biochemical confirmation of chyle with drain chylomicrons or lymphangiography to find site of the leak was not performed in any patient. Conservative management of chyle leaks included fat free/low fat diet of medium chain triglyceride (MCT) and continuous drainage with the intra-abdominal drain. Total parenteral nutrition (TPN) or somatostatin analogue was not offered to any patients. The drain was removed when the volume reduced to less than 50 cc/day and the color appeared serous after normal diet was commenced. Prophylactic antibiotics because of the presence of abdominal drain were not used during the duration of chyle leaks. Adjuvant therapy, when indicated was initiated in the postoperative period, even in patients with chyle leaks usually 10 days after the surgery. Delay in therapy was defined as noninstitution of adjuvant chemotherapy within 2 weeks of the surgery.

The resected specimen and the lymph nodes were labeled and sent separately for histopathological examination. The total number of lymph nodes resected was determined by the pathologist during grossing of the specimen.

Data were analyzed using SPSS software (version 20 for Windows; SPSS, Chicago, IL). Local control (LC) was calculated from date of diagnosis to date of local recurrence or local progression regardless of metastatic disease status at the time in order to better characterize our ability to control local disease. Overall survival (OS) was calculated from the date of diagnosis to date of death from any cause or last follow-up. Event free survival (EFS) was calculated from the date of diagnosis to the date of relapse at any site or death for any reason or last follow-up. The chi-square test was used to compare proportions and risk factors were compared using the log-rank test. A p value less than 0.05 was considered significant. Following factors were studied to find the risk of chyle leaks: gender, age (less or more than 1 year), tumor site, stage (stage 1, 2 and 4S or stage 3 and 4), and risk group. In addition, the timing of surgery (upfront or post chemotherapy), side (right or left), approach, completeness of resection, operative time, blood loss and the number of lymph nodes dissected were analyzed.

2. Results

One hundred sixty patients with abdominal neuroblastoma were included in this study. The median age of the patients was three years (range 1 month–28.2 years). Most patients had stage IV disease (50%) arising from the adrenal gland (Table 1). Up-front surgery was performed in 19 patients while 141 underwent surgery after

Table 1
Characteristics of all patients.

Characteristics	Chyle leak (n = 32)	No chyle leak (n = 128)	p Value
Gender			
Male	19 (59.3%)	79 (61.7%)	0.84
Female	13 (40.6%)	49 (38.2%)	
Age at diagnosis			
Median (years)	3	3	0.23
Range (years)	0.5–15.7	0.1–28.2	
<1 year	6 (18.7%)	14 (10.9%)	
>1 year	26 (81.2%)	114 (89%)	
Primary site			
Adrenal	20 (62.5%)	71 (55.4%)	0.55
Nonadrenal	12 (37.5%)	57 (44.5%)	
Stage			
Stage 1/2/4S	5 (15.6%)	21 (16.4%)	1
Stage 3/4	27 (84.3%)	107 (83.5%)	
Risk group			
Low	3 (9.3%)	19 (14.8%)	0.57
Intermediate	10 (31.2%)	31 (24.2%)	0.26
High	19 (59.3%)	78 (60.9%)	0.68
Surgery			
Upfront	2 (6.2%)	17 (13.2%)	0.36
Postchemotherapy	30 (93.7%)	111 (86.7%)	
Side			
Right	11 (34.3%)	63 (49.2%)	0.16
Left	21 (65.6%)	65 (50.7%)	
Approach			
Abdominal	13 (40.6%)	63 (49.2%)	0.32
Thoracoabdominal	19 (59.3%)	65 (50.7%)	
Resection type			
Gross total resection	24 (75%)	109 (85.1%)	0.19
≤95% resection	8 (25%)	19 (14.8%)	
Operative time			
Median (hours)	5.07	4.17	0.49
Range	2.15–10	1.15–12	
Blood loss			
Median (ml)	240	210	0.63
Range	40–3200	20–4200	
Nodes dissection			
Median	11.5	8	**0.013**
Range	0–59	0–47	**0.03**
<5 nodes	6 (18.7%)	51 (39.8%)	
>5 nodes	26 (81.2%)	77 (60.1%)	
Hospital stay			
Median (days)	12.5	7	<**0.001**
Range	6–32	4–12	
Local control	83.2%	86.6%	0.66
Event free survival	51.3%	45.2%	0.48
Low risk	100%	100%	-
Intermediate risk	77.1%	60.2%	0.44
High risk	29.4%	25.6%	0.54
Overall survival	59.6%	48.6%	0.18
Low risk	100%	100%	–
Intermediate risk	90%	62.7%	0.2
High risk	39%	31.5%	0.63

Bold values indicate significance at p<0.05.

preoperative chemotherapy. Abdominal approach was used in 78 and thoracoabdominal in 82 patients. Gross total excision was achieved in 133 (83.1%) patients and 19 patients (11.9%) underwent excision of more than 95% of the disease. Less than 95% excision or biopsy was performed in remaining eight patients. Lymph nodes were excised in 144 patients. Chyle leak was documented in 32 (20%) patients. The median measure of leakage was 100 ml (range, 30–800 ml) per day and the chyle leak persisted for a median of 12 days (range, 5–32 days). Only 10 patients had a leak of over two weeks. Other postoperative complications included wound infection in six patients, fever in five, intestinal obstruction in three, neurological lesion in three and acute renal failure, renal infarct and nerve entrapment in one patient each. The duration of hospital stay was significantly longer in patients that developed a chyle leak (median 12.5 days, range 6–31 days) as compared to those who did not have chyle leak (median