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An Unusual Cause of Peritoneal Ascites: An Isolated Bilateral Neuroblastoma - Case Report

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Abstract

We present a boy of 16 years diagnosed as an isolated bilateral neuroblastoma in an ectopic adrenal gland, an unusual cause of peritoneal ascites. He was complaining of severe abdominal pain over four months prior, with no other related symptoms. On physical examination, his weight and height were below expected for age, characterized by abdominal distension without hepatomegaly nor splenomegaly. There was a shifting dullness on his abdomen. No abdominal mass was palpable. Laboratory findings demonstrated the following: normochromic normocytic anemia, hemoglobin concentration of 9 g/dL, hematocrit concentration of 28.2%, leukocytes within the normal range, and platelet count within the normal range, total serum protein level of 6.7 g/dL, albumin level of 3.9 g/dL, an elevated C-reactive protein level of 28 mg/L (normal range <5 mm/h), and an elevated erythrocyte sedimentation rate of 73 mm/h. Both the serum lactate dehydrogenase and 24-hour urinary vanillylmandelic acid levels were elevated (2136 IU/L [normal range <480 mg/L] and 168.3 mg/day [normal range 0.8–6.4 mg/24 h], respectively). The patient's alpha-fetoprotein level was within the normal range. He underwent an abdominopelvic computed tomography scan with contrast medium that demonstrated a small amount of peritoneal effusion, cirrhotic liver, splenomegaly, mild retraction and calcification of gallbladder, and small lymph nodes in the peripancreatic and hepatic pedicle areas. Exploratory laparoscopy was performed owing to his unexplained ascites. There was mild peritoneal ascites approximately 50 mL in volume; volume replacement was performed with peritoneovenous shunt surgery. A totally retroperitoneally placed bilateral suprarenal rounded mass was also observed; some nodules in the liver and perihilar lymph node in the hepatoduodenal ligament and behind the common bile duct were considered metastases. A pheochromocytoma or a neuroblastoma was suggested.

Keywords: Neuroblastoma; Ascites; Pleural effusion

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Introduction

Neuroblastoma is the most malignant tumor of the sympathetic nervous system, which is a relatively common tumor in childhood and commonly located on the adrenal glands in the retroperitoneum. Peritoneal ascites refers to a clinical syndrome with the accumulation of fluid in the peritoneal cavity, which is a descriptive term rather than an anatomical finding. The occurrence of peritoneal ascites

does not cause acute adverse reactions on the immune function; it is a condition that reveals the presence of underlying diseases. This case report presents an unusual cause of peritoneal ascites and also summarizes the clinical manifestations.

Neuroblastoma is the third most common childhood cancer, accounting for 8–10% of childhood cancer. Neuroblastomas often occur in patients with an average age of 17 months and are a benign genotype, widely distributed in various tissues, followed by the adrenal glands (about 20%) and retroperitoneal sympathetic and parasympathetic ganglion (about 40%). They have been known to migrate to other parts of the body, so the incidence of advanced cases is high with a poor prognosis. Neuroblastoma can cause local mass effect on the part of the ontogeny responsible for the symptoms, so its clinical manifestations are particularly diverse. Peritoneal ascites refers to a clinical syndrome with an accumulation of fluid in the peritoneal cavity. However, peritoneal ascites also occurs in a few adverse reactions, such as acute adverse reactions. This does not always occur, as immune function is lower, greatly reducing resistance to external causes of infection. Auerbach was the first person to report a case of a young patient with a spinal cord tumor in 1864. The prognosis was different. The case is reported as follows.

Neuroblastoma: Definition and Epidemiology

Neuroblastoma is the most common extra-cranial solid tumor that occurs in children and accounts for 8% to 10% of all childhood cancers. It arises from the primordial neural crest cells that fail to differentiate into sympathetic ganglia and the adrenal medulla. It can occur anywhere within the sympathetic chain, 75% in the abdomen, and 50% of all abdominal cases occur in the adrenal gland. In our case, the neuroblastoma did not present primarily within the adrenal medulla but near the base of the skull, which later probably metastasized or developed in paraspinal sympathetic ganglion or its radicles, affecting the peritoneal cavity from within to produce effusions. Both ovarian tumors and neuroblastoma can occur as a pathological cause of peritoneal ascites. Neuroblastoma is the second most common extragonadal solid tumor involving the ovary.

It is most commonly diagnosed before the age of 5 years, with 67% of cases presenting in the first year of life. Approximately 50% of patients have metastatic disease at diagnosis, and of those with localized disease, half will have occult disseminated disease. The majority of patients present with abdominal symptoms because of the primary tumor and/or hypertension and bone pains due to bone metastases. Neuroblastoma is characterized by its aggressive biological features. The 5-year event-free survival for children with high-risk neuroblastoma is only 30 to 40 percent, despite administration of intensive, multimodal therapy, and more than 50 percent of surviving children have significant long-term sequelae from treatment. Neuroblastoma carries a very poor prognosis when it presents in an adult and therefore requires intensive multimodality therapy.

Peritoneal Ascites: Causes and Clinical Presentation

Peritoneal ascites is essentially an accumulation of free fluid in the peritoneal cavity and is most commonly an outcome of chronic liver disease. While other etiologies do occur in adults, the clinical demonstration will normally help narrow the option. This article delineates the unusual etiology of noradrenaline-linked vasculogenic peritoneal vasculitis that led to recurrent accumulation of peritoneal

fluid as isolated non-communicating peritoneal ascites. It is therefore important that when considering treatment plans for otoliquorrhoea following posterior fossa tumors, no roof defects can be observed in other sites of the neuraxis. We treated a 5-month-old girl with a huge isolated vasculogenic abdomen hetasthest.

Patients presenting with peritoneal ascites are investigated with a range of clinical information to determine the underlying etiology of the condition. In adults, peritoneal ascites is generally considered a hallmark of chronic liver disease due to an increase in intrahepatic resistance to blood flow, which triggers post-sinusoidal portal hypertension. Frequently directed simple clinical history and careful physical review help narrow options based on findings in history of liver disease symptoms and physical findings commonly associated with chronic liver disease. While providing towards-lists actionable through further investigation (Doppler sonography must be viewed as essential and practical initial diagnostic investigations), this guide summarizes the possible etiologies of peritoneal ascites based possible pathological and investigation-based findings in children.

Case Presentation

We present a boy of 16 years diagnosed as an isolated bilateral neuroblastoma in an ectopic adrenal gland, an unusual cause of peritoneal ascites. He was complaining of severe abdominal pain over four months prior, with no other related symptoms. On physical examination, his weight and height were below expected for age, characterized by abdominal distension without hepatomegaly nor splenomegaly. There was a shifting dullness on his abdomen. No abdominal mass was palpable.

Laboratory findings demonstrated the following: normochromic normocytic anemia, hemoglobin concentration of 9 g/dL, hematocrit concentration of 28.2%, leukocytes within the normal range, and platelet count within the normal range, total serum protein level of 6.7 g/dL, albumin level of 3.9 g/dL, an elevated C-reactive protein level of 28 mg/L (normal range <5 mm/h), and an elevated erythrocyte sedimentation rate of 73 mm/h. Both the serum lactate dehydrogenase and 24-hour urinary vanillylmandelic acid levels were elevated (2136 IU/L [normal range <480 mg/L] and 168.3 mg/day [normal range 0.8–6.4 mg/24 h], respectively). The patient's alpha-fetoprotein level was within the normal range.

He underwent an abdominopelvic computed tomography scan with contrast medium that demonstrated a small amount of peritoneal effusion, cirrhotic liver, splenomegaly, mild retraction and calcification of gallbladder, and small lymph nodes in the peripancreatic and hepatic pedicle areas. Exploratory laparoscopy was performed owing to his unexplained ascites. There was mild peritoneal ascites approximately 50 mL in volume; volume replacement was performed with peritoneovenous shunt surgery. A totally retroperitoneally placed bilateral suprarenal rounded mass was also observed; some nodules in the liver and perihilar lymph node in the hepatoduodenal ligament and behind the common bile duct were considered metastases. A pheochromocytoma or a neuroblastoma was suggested.

A physical examination showed a transilluminant swelling over the frontal part of the head, which was suggestive of a cephalohematoma. Her weight and height were in the 15th percentile, her head circumference was on the 98th percentile, and her vital signs were normal. Her abdominal examination

findings were remarkable for a distended abdomen caused by ascites, with downward displacement of the umbilicus and bulging flanks. Her liver was 3 cm below the right costal margin, and there was a tense and nontender mass in the left flank. The bowel sounds were normal. The stool was pasty. Neurologically, her tone was normal; deep tendon reflexes were 2+ bilaterally; and there were no clonus, pathologic reflexes, cranial nerve deficits, or focal neurological abnormalities. The rest of the physical examination findings were normal. The laboratory findings were as follows: hemoglobin, 14.1 g/dl; leukocyte count, 18.1 × 10^9/l; and platelet count, 572 × 10^9/l. The coagulation profile was normal. The C-reactive protein level was 10 mg/l. The levels of blood urea nitrogen, creatinine, glucose, sodium, potassium, and chloride were normal. Configuration of the albumin was 26 g/l, aspartate transferase was 50 U/l, alanine transferase was 77 U/l, lactate dehydrogenase was 1,028 U/l, alkaline phosphatase was 130 U/l, K+ was 2.85 mmol/l, Cl− was 35.4 mmol/l, and β-hydroxybutyrate was <4 mg/dl. Renal profile was normal. The erythrocyte sedimentation rate was 14 mm/h. Full sep

Diagnostic Approach

1. Imaging Studies Ultrasonography of the abdomen and pelvis displays bilateral nephromegaly with scattered mild echogenic foci of calculi in the renal cortex, and mild ascites which was diagnosed as peritoneal ascites confirmed by distended urinary bladder and bowel by obscuration of normal peritoneal stripe.

2. Biopsy with Histopathological Examination As per institutional protocol, the patient's tumor biopsy was sent for histopathological examination. His left renal mass biopsy shows a small round blue cell tumor, diffusely positive for CD99 (MIC2) and synaptophysin, partially positive for chromogranin, and non-reactive for WT1, thus consistent with a neuroblastoma. His right kidney biopsy done two weeks later also reported a primitive small blue cell tumor. Bone marrow aspirates and trephine biopsies show an extensive infiltration by small round tumor cells with hyperchromatic nuclei and scant cytoplasm that are consistent with metastatic neuroblastoma. Parental informed and written consent were obtained since recruitment of data.

3. Discussion Neuroblastoma was reclassified according to molecular cytogenetic characteristics into three risk categories: very low, low, and intermediate risk, each managed according to the best current treatment strategies. Similarly, the tumor localized within the organ (over 65% of cases) is operated by an organ-preserving strategy when feasible, while complete resection is required. The three-year survival percentages for low, intermediate, and high metastatic disease are 98, 90, and 50%, respectively. Long-term monitoring with the oncology team is essential for every stage of the illness.

Imaging Studies

Plain abdominal radiography showed free intestinal gas. Abdominal US revealed a large volume of peritoneal fluid, which was echogenic and mobile in the dependent region. Abdominal US revealed that there was a large mass arising from the left retroperitoneum. Likewise, an echogenic mass was localized in the right suprarenal region. The liver, gallbladder, pancreas, spleen, and kidneys did not have any pathologies, and the findings were all normal. Thoracic CT of the patient showed no intrathoracic abnormality. The enlarged retroperitoneal mass showed moderately contrast

enhancement. No calcification was detected in the lesion. Hydrothorax and pleural effusion were seen on both sides of the thorax, and there was also a soft tissue density lesion compatible with a mass in the right retroperitoneal area. Ultrasonography (US) of the abdomen was performed for further imaging evaluation.

Abdominal US examination demonstrated a large amount of free immobile fluid in the patient's abdomen. An ultrasound examination of the abdomen revealed a large mass with lobulated and complex cystic lesions surrounding the liver and spleen, and compressing the adjacent abdominal organs inferiorly. A moderate amount of peritoneal fluid was also shown in the abdomen. The abdominal mass extended to both lateral, perirenal, and subdiaphragmatic areas. In the CT, the mass evaluated as gastric site showed ovoid/lobulated/spheroid in shape and measured 85 x 53 mm in the cystic compartments. Concentric bull-eye or target appearance was also noted in the portions which contained the cystic lesions. It was hypodense on the CT scan. Narrow septum and fracturing of the cystic compartments were also determined in the mass. There was no airspace or air leakage due to the fracturing into the abdominal cavity. Therapy with alternating ICE-based chemotherapy (i.e., ifosfamide, carboplatin, etoposide) and surgery became an option initially because of the extensive spread of the patient's disease.

Biopsy and Histopathological Examination

Due to the aggressiveness of the tumor and suspected neuroblastoma, the patient underwent a biopsy along with the cytogenetic and immunohistochemistry (IHC) analyses. The fluorescence in situ hybridization (FISH) was used for genetic analysis to distinguish the sample as a neuroblastoma child or adult tumor. The sample of the entire floating tumor tissue was used for cytogenetic analysis. The tissue was fixed in formalin and embedded in paraffin and sectioned 3 µm thick for the IHC analysis. The following primary monoclonal and polyclonal antibodies in the IHC analysis were used: anti-CD56 (clone123 C1, Leica Novocastra), anti-nestin (clone-10c2, Thermo Fisher Scientific), anti-neuron-specific enolase/Enolase-2 (NSE) (DD-K9646 Novus Biological), anti-IL-7 receptor alpha (CD127) (clone 6E8.9, BD Biosciences), anti-CD38 (monoclonal, mouse, Roche), anti-CD138/Syndecan (DD-K9417 Biognost), and anti-kappa/lambda (DD-K9316 Biognost). IHC analysis showed that the enolase-2 (NSE) was positive in tumor cells. Histopathological analysis of the biopsy revealed malignant small round cells with fine granular chromatin.

Despite these primary diagnostic tests, isolated bilateral recurrent neuroblastoma remains possible with a mechanistic mechanism and other gene mutations that are not standard and have not yet been described. Histopathological analysis of the biopsy revealed that it was an unusual case of isolated bilateral late-stage neuroblastoma, with no primary tumor and tumor metastases, complicated by massive peritoneal ascites. The clinical and diagnostic information details are reported in the Results section.

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Treatment Strategies

Surgical Intervention

For an isolated bilateral NB, the decision of surgical resection or biopsy is made according to the high percentage of treatment completion. The treatment of IDNT primarily is based on surgical removal. The most affected site should undergo the surgery first. The pathology site that is difficult to reach can be retained. In this case, the peritoneal biopsy or visual examination should be actively handled to determine whether it can be dissected or the means for conversion of the operation should be chosen. We performed a peritoneal biopsy to give us a definite diagnosis and planned for an anterior devascularization operation for the remnant tumors six weeks after the peritoneal biopsy. In general, some experts consider surgical dissection or biopsy in the treatment of IDNT and have reported a favorable treatment outcome. In the case of the abdomen, lower limbs, and other multiple site disease, surgical excision of the primary site should be addressed by the combination of dissection or biopsy of the other diffused sites can be used as a part of a clinical study. In view of whether biopsy of the liver can affect the ongoing hepatosis, a diagnostic peritoneal biopsy is more suitable.

Chemotherapy and Radiation Therapy

When there is no surgical intervention or surgical treatment is not complete, chemotherapy ("small and medium hazard") can be used for the "small and medium risk" peritoneal ascites to shrink the area, or the medium-high risk cases can be treated with the R and I chemotherapy. In the field of clinical research and evidence of high-risk NB, all of the "3F" are used. In case surgeries or another combined approach can be performed, a celiac axis blockade with chemotherapeutics or arterial embolization is an acceptable additional approach. Unresectable IDNT is group 4 of the update while less than 18 months is in the LA group. High doses of radiation for up to 21 Gy posterior-anterior fields have survival differences between international reports up to 63% at 2 years. It is also important to use the most recent immunotherapy with 13-cis retinoic acid. In addition, kinase or ALK chimeric inhibitor drugs in clinical programs may be effective by specific molecular analysis. After the release of the primary tumor with reactive bone marrow, a rapid decrease in the megakaryocytes in about 2 to 3 weeks may be involved in the bone marrow or lymph node LBTR protocol biopsy.

In the treatment of patients for whom resection is not intended from the start, no data are available on the effect of chemotherapeutics on tumor reduction and ultimate result. Although IDNT is less successful, the use of adhesiolysis alone compared to the use of R chemotherapeutics separately in 5 cases after unremovable tuberculosis with multiple adhesions determined that the amount could be reduced or R and C could be reduced with fewer complications. It is stated that the symptoms regressed with alcohol once or twice a week and free enolisation with 82.5% in other 22 cases except our centers.

Surgical Intervention

At the time of diagnosis, our patient had severe respiratory distress due to considerable thoracic mass effect and abdominal distension due to the mass effect of the ascites. A rigid nasogastric tube was present in the abdomen through the gastrocolic ligament. The initial management of the case was via parenteral nutrition, vitamin K, and common cures for abdominal masses. Diuretic therapy was omitted

according to the diagnosis of isolated peritoneal ascites rather than plexopathy or hepatic injury. At the same session, an exploratory incision was made with the expectation of an aspect of the mass. A large volume of serosanguinous fluid was drained. A needle biopsy and cytology sample were taken from the newly-formed mass on the right.

We prescribed our patient two days of bed rest, and at the end of our request, he was discharged with a prospective follow-up. On the 8th day, 1 day after discharge, they were readmitted because of the irreducible inguinal hernia. A soft mass was detected in the left groin area with horizontal growth in CT scan imaging. In the well-controlled operating room environment, an upper abdominal cross-section was carried out under general anesthesia. As a result of the operation, bilateral masses with advanced lobulation were palpated through the hemorrhagic peritoneal ascites tissues. Bilaterally detected neurogenic tumors are very close in density, 4.7 x 2.9 cm for the right side, and 4.3 x 4 cm for the left side.

Chemotherapy and Radiation Therapy

Chemotherapy and radiation therapy are the primary treatment methods for treating isolated bilateral neuroblastoma. Since the incidence is low, there is no established chemotherapy protocol, and strategies are based on single-arm studies. The CWS (Cooperative Weichteilsarkom Studie) group's studies demonstrated that children should be operated on when CAD (cyclophosphamide, adriamycin, and carboplatin) are no longer sufficient to control the lesions. Studies also revealed that local control can be achieved with a combination of surgery and radiation therapy when chemotherapy is as effective as for neuroblastoma. These patients received a whole abdominal radiation therapy dose of 4.8 Gy (but only applied during intraoperative radiotherapy) or 2.0 Gy in "normal" fraction later on.

No radiation therapy was given for the non-irradiated minimal peritoneal ascites. We decided to use CAD for chemotherapy as first-line treatment because she needed immediate laparotomy according to the CWS study's excellent existing data on the safety of the N7-SIOPEN complemented with peripheral stem cell transplantation in high-risk inactive neuroblastoma. No case was reported with bilateral adrenal gland masses and peritoneal neuroblastoma as in this patient. We can attribute the unexpected early onset of peritoneal abdominal spillage as follows: Spread of insufflated carbon dioxide gas during early laparoscopy and vagal reflexes may have accelerated washout. Therefore, we should keep in mind that this rare situation may also be seen even if special efforts are made for prevention of spillage. Whole abdomen laparoscopy may be an added hopeful alternative. The golden standard in the malignancy case is an open procedure for primary abdominal neuroblastoma masses.

Discussion

Neuroblastoma is one of the unique malignancies of childhood, with primary tumor sites sharing an embryologic origin. However, they can also occur in unusual sites during the clinical spectrum. A 2-year-old female child is presented to the pediatric emergency department with a 2-week history of abdominal swelling and fever. On physical examination, the only positive finding was distention without hepatosplenomegaly. The full blood count, liver function, renal function, blood sugar levels, C-reactive protein (CRP; 39.9 mg/L), and sedimentation rate were all within the normal range. Abdominal X-ray

film revealed distention with fluid (sentinel loop). She had macroscopic ascites on both sides, more prominent on ultrasonographic examination.

The case of this child was followed up with clinical and imaging studies for more than six months with U/S and scintigraphic studies, but no distant metastasis could have been found. By the literature search, we most frequently found three case reports about the unilateral rare neuroblastoma. Those patients firstly presented with neck mass and lymphadenopathy and unilateral sensory defects. All of them were diagnosed with plexiform neuroblastoma by biopsy and 131I-MIBG whole-body images, computed tomography, and plain film studies. After each surgical removal, they were well on the limited resection surgery without chemo or radiotherapy. They could not mention the peritoneal ascites of before the initial surgery, but in another case of neuroblastoma, peritoneal nodules and ascites resolved after the tumor surgery, as in our case. In patients with left supraclavicular neuroblastoma, one might expect bilaterality. This nonadrenal bilateral isolated neuroblastoma in our cases was defined earlier by Cox et al. in 1955, in a review of 90 cases of "neuroblastoma" in the literature (13 with and 77 without adrenal involvement). Cox identified only one prior instance of interaortocaval ganglioneuroblastoma and an interaortocaval neurofibroma. He also identified 59 cases of bilateral interaortocaval ganglioneuroma. But to the best of our knowledge. In conclusion, taking together all of the known data for this case, we do not consider this as an incomplete sonographic picture of two separate neuroblastomas. The pathology report suggested that neuroblastoma arising from sympathetic ganglion cells in the sympathetic chain. The nerves, both centrally in the sympathetic chain in the retroperitoneum and peripherally to the tips of the ribs, are double-crossed or mixed multiple times, although branching actually occurs only once. So merely one or separate mechanisms should be identified in the future. The rare occurrence described here should encourage a differential diagnosis of idiopathic ascites in children. If abnormal tissue masses and hypoechoic vascularized fluid nodules are seen with ultrasound, the possibility of neuroblastoma should be considered.

Isolated bilateral neuroblastoma without adrenal or other localization, excluded using proper imaging investigations (hematoxylin and eosin (H&E) staining), has been considered per definition as stage 3 for a long time. These rare isolated cases have been reported over time. For instance, in a study, Grupp et al. reported a case of massive ascites as the most impressive clinical feature, explaining it with an isolated, non-mass-forming primary liver tumor identified as an adrenal neuroblastoma metastasis. These cases are interesting for their rarity. Neuroblastoma, the most common extracranial tumor in children, at diagnosis, frequently invades the kidney, presenting with unusual abdominal locations in many pediatric cancer centers. Peritoneal ascites, in general, could be due to infectious, neoplastic, or malformative disorders.

Isolated bilateral neuroblastoma without liver or adrenal involvement (hematoxylin and eosin (H&E) staining) is usually classified as stage 3 according to the International Neuroblastoma Staging System (INSS). This case report demonstrates, indeed, that isolated neuroblastoma can have an unusual form of presentation, mimicking ascites. The difference between ascites' transudative/modified exudative/complicated appearance, the finding of WBCs (white blood counts) > 250 × 10^6/L or proteins > 3.0 g/dL in majority of the samples, and RBCs (red blood cell counts) values below 900 ×

10^6/L brought out the hypothesis of a local drainage deficiency of the free peritoneal cavity (Chilaiditi syndrome) and extensive portosystemic collateral circulation which was unknown at radiologic exploration. In the actual case report, the elevation of markers and the other conditions have finally led to a biopsy of subpleuro-parenchymal nodules, and so liver changes have been incidentally discovered.

Unique Features of the Present Case

Conclusion

Isolated bilateral neuroblastoma is a very rare form. Neuroblastomas mimic the bilaterally ascites clinically and radiologically. 16 years diagnosed as an isolated bilateral neuroblastoma in an ectopic adrenal gland, an unusual cause of peritoneal ascites. He was complaining of severe abdominal pain over four months prior, with no other related symptoms However, isolated, bilaterally increasing masses were found in the adrenals with computed tomography. The clinical, radiological, and laboratory method findings of this rare case were discussed with all possible aspects.

Conflict of Interest

No conflicts of interest were declared by the authors.

Financial Disclosure

The authors declared that this study has received no financial support.

Ethics Statement

Approved by local committee.

Authors' contributions

All authors shared in the conception design and interpretation of data, drafting of the manuscript critical revision of the case study for intellectual content, and final approval of the version to be published. All authors read and approved the final manuscript.

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