CASE REPORT

Anesthetic management in children with giant nephroblastoma. Presentation of a case

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Abstract

Introduction. Nephroblastoma is the most common abdominal solid tumor in childhood. The first description of this type of tumor was due to Hunter in 1793. In 1899, Max Wilms Max Wilms (1867–1918), also a surgeon, described a tumor that he called nephroblastoma, which later became known as Wilms tumor. It occurs most frequently in the first five years of life.

Objective. Present the anesthetic management during surgery in a child with giant nephroblastoma.

Clinical case. Two-year-old male patient weighing 10 kg, who began with abdominal pain three months before admission. Upon palpation, the abdomen was soft, depressible, and slightly painful. Deep palpation on the right flank revealed a non-mobile, painful mass of hard consistency, approximately 25 cm in diameter, with regular outlines and smooth surface. Laboratory tests showed lymphopenia, mild eosinophilia and iron deficiency anemia in the hemogram. Abdominal ultrasound showed a round, solid-looking image that measures approximately 30cm in diameter at the lower pole of the right kidney. The anesthetic plan for the laparotomy consisted of multimodal anesthesia. Prolonged surgery requires vigorous intravascular volume replacement with crystalloids, colloids, and blood. Right nephrectomy and resection of a 3.7 kg giant tumor mass were achieved. During the postoperative period, the patient presented several complications: such as hemodynamic instability, oliguria, hypoglycemia, seizures, and hypoproteinemia. The strict follow-up and timely treatment of each complication made it possible to discharge the patient from the hospital on the eighth postoperative day.

Conclusions. The anesthetic management of this type of patients is a great challenge, more so considering the poor working conditions due to the lack of both equipment and medicines in this country; but the multimodal anesthesia technique is effective and safe for achieving success.

Key words

Wilms tumor, nephroblastoma, multimodal anesthesia.

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■ INTRODUCTION

Childhood nephroblastoma called Wilms tumor is the most common childhood kidney tumor. It is the fifth childhood tumor in incidence, and the first among childhood abdominal solid tumors. The first description of a tumor of this type was due to Hunter, who in 1793 dissected and preserved a bilateral infant tumor. In 1899, Max Wilms (1867–1918), also a surgeon, described for the first time seven children affected by a tumor that he called nephroblastoma, which has later come to be known as Wilms tumor. The tumor is considered embryonic as it derives from remains of the primitive metanephric blastema.(1,2)

Nephroblastomatosis represents a complex of pathological entities defined by the persistence of nephrogenic elements after nephrogenesis (beyond the 36th week of gestation), which retain the ability to evolve towards nephroblastoma. (3)

Clinical manifestations in 90% of cases, present as an abdominal mass, which is why it is frequently discovered after palpation of an asymptomatic tumor by a family member, or by the doctor in a routine examination. Another of the most frequent symptoms is arterial

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hypertension (increased renin in plasma) which occurs in 25% of the cases. Also, within the clinical picture, there is gross hematuria, fever, nausea, vomiting, decreased appetite, weight loss, constipation and stomach pain.

The diagnosis must be based on clinic and imaging studies. Abdominal ultrasound is the study for initial evaluation, which usually shows a solid mass, and is also useful to assess the presence of compromise of the renal or cava vein, in addition to the liver and other abdominal structures.

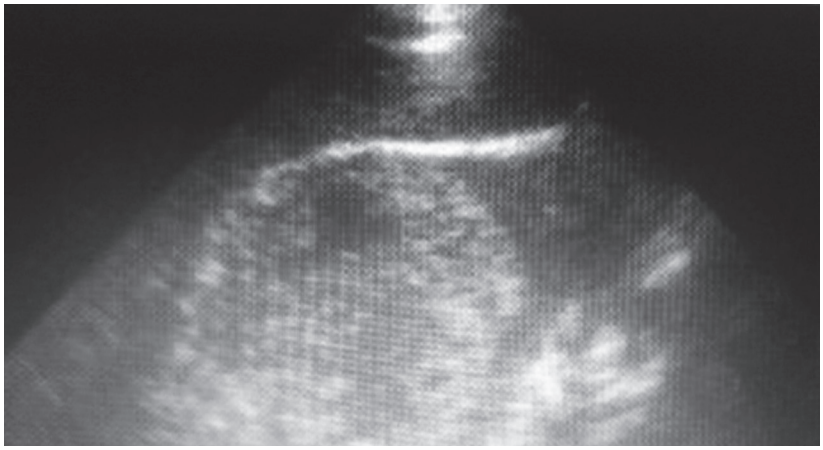

Figure 1. Abdominal ultrasound, showing image of a solid mass in the lower pole of the right kidney.

Computed tomography and MRI better assess the primary tumor; determining retroperitoneal involvement of lymph nodes, and other abdominal structures. Arteriography should be carried out, when parenchymal conservative surgery is planned as in bilateral cases. Other necessary studies, such as CT or chest x-ray, assess lung involvement, since this organ is the most frequent location of distant metastasis.(4–7)

■ PRESENTATION OF THE CASE

A two-year-old male patient, DJ, weighing 10 kg is brought for consultation. The mother refers that he began with abdominal pain three months before. She took him to several health care centers, in which an accurate diagnosis was not provided. The day before admission, the mother noticed an increase of volume in the right flank, when bathing him.

Physical examination

On superficial palpation of the abdomen, it was soft, depressible and slightly painful; on deep palpation, on the right flank, there was a non-mobile, painful, mass of hard consistency, approximately 25 cm in diameter, with regular contours and a smooth surface. This mass extends from the anterior axillary line to the posterior axillary line. Fist percussion on the right flank is positive. Vital signs were: respiratory rate: 32 x min, heart rate: 110 x min, temperature 36.8 °C, weight: 10kg, height 80 cm.

Complementary exams

Lymphopenia, mild eosinophilia, and iron deficiency anemia were observed in the blood tests.

Abdominal ultrasound showed a round, solid-looking image of approximately 30cm diameter over the lower pole of the right kidney.

An abdominal CT scan was performed, which showed a hypodense mass in the lower pole of the right kidney with a diameter of 20 cm x 12 cm, displacing the kidney in a posterior and cephalic direction. No alterations were observed in the liver, retroperitoneum and adrenal glands. The diagnosis is highly suggestive of Wilms tumor. The chest CT scan was not suggestive of metastasis (Figure 1).

The case remained hospitalized for approximately 15 days, until it was discussed collectively with professionals from the West Africa College of Surgeons, who were performing scheduled surgical sessions in this institution and a decision is made to perform laparotomy, with possible radical right nephrectomy and tumor exeresis.

Anesthetic management

Pre-anesthetic consultation to evaluate clinical condition is carried out. Fasting regimen was indicated. Two peripheral venous lines were placed with 20G and 24G Teflon cannulas. The anesthetic plan consists of multimodal anesthesia in which combination of general endotracheal anesthesia and caudal epidural anesthesia was applied.

Premedication with atropine at 0.01mg/kg administering 0.1mg and dexamethasone 1.5mg intravenously was performed for general anesthesia.

Induction of anesthesia was done using propofol at 2mg/kg, administering 20mg IV of a mixture of oxygen and 0.7 vol % isofluorane. Once sleep induction was achieved, succinylcholine was administered at 1mg/kg, using 10mg IV to facilitate airway access.

Endotracheal intubation is performed by laryngoscopy with a Miller 2 spatula; a 4.5 endotracheal tube with cuff is placed without difficulty. Mechanical Artificial Ventilation by coupling to a Rimas2000 mechanical ventilator, tidal volume 8ml/kg, 20 rpm frequency, I:E ratio of 1:2, FiO 2 0.5 is done. For maintenance, a mixture of 0.5 oxygen and air, isofluorane 0.9vol% and three doses of fentanyl, an initial one before the incision of the skin at 1mcg/kg, 10mcg, and two subsequent doses of 0.5mcg/kg, 5mcg, IV with a 1 hour interval between doses; 4 doses of Pancuronium, initial dose 0.8mg, two subsequent doses of 0.4mg and a final dose of 0.2mg IV, with an interval of approximately 120 minutes between doses.

A caudal No. 19 epidural catheter is inserted 13 cm from the skin without complications for regional anesthesia administration with local anesthetics of the bupivacaine

type 0.5% at 1mg/kg, which considerably reduced the need for anesthetics during the intraoperative period and a second dose of 0.5mg/kg before the end of the intervention, that is, 8 hours apart with the aim of contributing to postoperative analgesia.

Due to the complexity of the intervention, the intra-operative period was prolonged for 8 hours, with important body fluid losses, including considerable blood losses that led to hemodynamic instability. Vigorous intravascular volume replacement with crystalloids, colloids and blood was performed. A total of 1280 ml Ringer lactate type crystalloids, 140 ml of 4% Gelofusine type colloids and 120 ml of whole blood were used. In addition, it was necessary to use vasoactive drugs such as adrenaline type infusion, initially 0.05 mg/kg and an increase to 0.07 mg/kg was necessary until stabilization of the hemodynamic parameters.
During the surgical act, right nephrectomy was performed; this kidney was removed with a total tumor mass of 3.7kg (Figure 2).

POSTOPERATIVE PERIOD

During the postoperative period (Figure 3), several complications emerged, including hemodynamic instability with oliguria in the first hours after surgery. At 24 hours, an episode of hypoglycemia with a glycemia of 2.6 mmm/l led to a scenario of seizures and hypoproteinemia with poor fluid distribution. Strict surveillance of all parameters and timely treatment of each complication were maintained and it was possible to successfully complete this phase of treatment with hospital discharge on the eighth postoperative day.

Figure 3. The child on the 6th postoperative day.

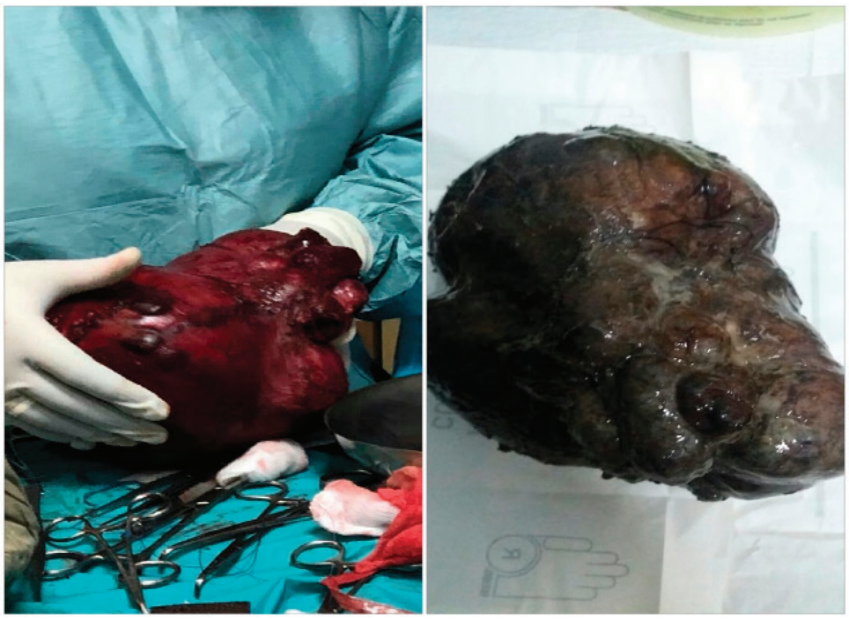

Figure 2. Right kidney removed with total tumor mass.

■ DISCUSSION

The tumor in our patient is the most common urogenital neoplasm in childhood. Twenty-one percent are diagnosed during the first year and fifty percent before the third year, matching the age of this boy, with a male/female ratio of 0.78 to 1.

The National Wilms Tumor Study Group (NWTSG) staging system is widely used:
I. Tumor limited to the kidney and completely excised, the capsule is intact, there is no rupture during excision; category to which the case presented belongs to.

II. Cancer spread through the renal capsule, local seeding. The tumor can be biopsied.

III. Residual non-hematogenous tumor, limited to the abdomen, presence of lymph node involvement and peritoneal seeding, beyond the surgical margin.

IV. Hematogenous metastasis, to the lung, liver, bone, brain, and other organs.
V. Bilateral involvement at the time of diagnosis.

Several factors intervene in the survival of the patient, the main ones are:
• the degree of differentiation, the stage, and size of the tumor and, the age of the child;
• the possibility of completely removing the tumor by surgery that was possible in this child;
• whether the cancer is newly diagnosed or recurrent

• whether there are abnormal chromosomes or genes, and
• whether the patient is treated by pediatricians who are experts on this pathology.

The survival rate for Wilms tumor is more than 90% five years after disease diagnosis, due to the advances in surgical techniques, and in chemo and radiotherapy treatments.

Surgery is the most suitable treatment against Wilms tumor. Initially in most children radical nephrectomy with a transperitoneal approach is considered. The current NWTSG recommendation is to consider partial surgery for patients with bilateral Wilms tumor.(8–11)

The anesthetic management of abdominal tumors in childhood can be perfectly performed with the combination of general anesthesia with regional anesthesia techniques, which means that after the induction by general anesthesia, the regional technique is carried out to maintain adequate intraoperative and postoperative analgesia, since there is an optimal control of pre- and post-stimulus pain, allowing rapid recovery of the child's primary functions such as feeding and ambulation. Planning this type of multimodal anesthesia must have clearly defined objectives, since the success of the procedure and the child's well-being are essential.(12)

■ CONCLUSIONS

The use of the multimodal anesthesia technique in this type of pediatric patient is extremely useful, providing excellent surgical conditions and postoperative analgesia; but we must bear in mind that this type of anesthesia needs adequate equipment and resources to assure success.

Manejo anestésico del niño con nefroblastoma gigante. Presentación de un caso

Resumen

Introducción. *El nefroblastoma es el tumor abdominal sólido más frecuente en la infancia. La primera descripción de este tipo de tumor se debió a Hunter en 1793. En 1899, el cirujano Max Wilms describió un tumor al que llamó nefroblastoma, que más tarde se conocerá como tumor de Wilms. Ocurre con mayor frecuencia en los primeros 5 años de vida.*

Objetivo. *Presentar el manejo anestésico durante la cirugía en un niño con nefroblastoma gigante.*

Caso clínico. *Paciente masculino de 2 años de 10 kg de peso que tres meses antes del ingreso debuta con dolor abdominal. El abdomen a la palpación es suave, deprimible y levemente doloroso; a la palpación profunda en el flanco derecho se detecta una masa no móvil, dolorosa, de consistencia dura con aproximadamente 25 cm de diámetro, contornos regulares y superficie lisa. Las pruebas complementarias de laboratorio muestran: linfopenia, eosinofilia leve y anemia ferropénica en el hemograma. La ecografía abdominal muestra una imagen redondeada de aspecto macizo que mide aproximadamente 30 cm de diámetro en el polo inferior del riñón derecho. El plan anestésico aplicado para realizar la laparotomía consiste en anestesia multimodal. La cirugía prolongada requiere un reemplazo vigoroso del volumen intravascular con cristaloides, coloides y sangre. Se logró nefrectomía derecha y resección de una masa tumoral gigante de 3,7 kg. Durante el postoperatorio, el paciente presentó varias complicaciones: como inestabilidad hemodinámica, oliguria, hipoglucemia, convulsiones, hipoproteinemia. El seguimiento estricto y el tratamiento oportuno de cada complicación hicieron posible el alta hospitalaria al octavo día posoperatorio.*

Conclusiones. *El manejo anestésico de este tipo de pacientes es un gran desafío, sumado a las malas condiciones del hospital por la falta tanto de equipos, como de medicamentos en este país; pero la técnica de anestesia multimodal es eficaz y segura para lograr el éxito.*

Palabras clave

Tumor de Wilms, nefroblastoma, anestesia multimodal.

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Hidden' genes could be key in development of new antibiotics

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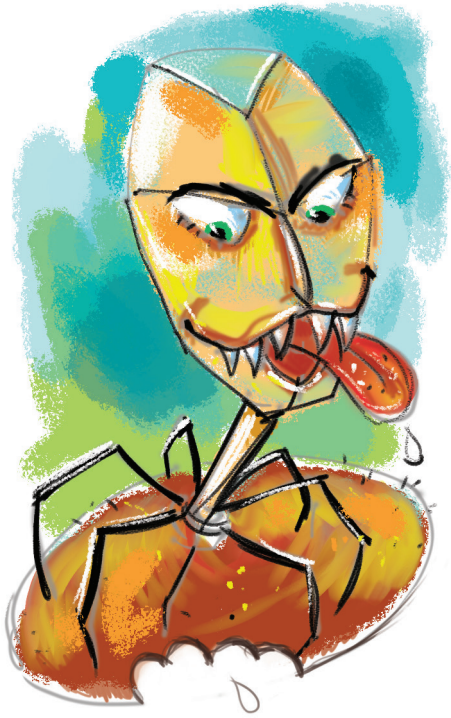

A study from the Center for Phage Technology of Texas A&M's College of Agriculture and Life Sciences and AgriLife Research, shows how the "hidden" genes in bacteriophages -- types of viruses that infect and destroy bacteria -- may be key to the development of a new class of antibiotics for human health. Antibiotic-resistant bacteria pose an increasing threat to human health, creating an urgent need for the development of novel antibiotics.

"There has been an increased interest in bacteriophages and their potential as antibacterial agents to fight pathogenic bacteria," Center for Phage Technology director Ryland Young, Ph.D., who supervised the study research said that "there has been an increased interest in bacteriophages and their potential as antibacterial agents." In large part due to the ability of the 'lysis genes' of the phage that cause cellular breakdown in the bacterial host." They also release new "progeny" phage virions that are genetically and structurally identical to the parent virus.

"Small phages, such as the ones in this study, make a single protein which causes host lysis," Young said. "Basically, the virus produces a 'protein antibiotic' that causes lysis in the same way antibiotics like penicillin do -- by disrupting the multistage process of cell wall biosynthesis. When the infected cell tries to divide, it blows up because it can't create the new cell wall between the daughter cells."

He said these small lysis proteins can be the model for a completely new class of antibiotics.

The study focuses on characterizing the lysis genes of leviviruses, bacteriophages containing small single-stranded RNA genomes with only three to four genes. Tens of thousands of leviviruses have been discovered. Among the known levivirus genes is Sgl (single gene lysis). Sgl encodes a protein that induces cellular breakdown of bacteria.

Many leviviruses contain Sgl genes, but these have remained "hidden" because they are small, extremely varied and can be embedded within other genes. "We wanted to discover these 'hidden' lysis genes in single-stranded RNA phages, as well as understand how their structure and evolution could benefit development of new, more effective antibiotics," said Karthik Chamakura, Ph.D., a postdoctoral research associate and the study's first author.

Researchers identified 35 unique Sgls that produced lytic or destructive effect on E. coli bacteria, Chamakura said. The team also determined that each of these Sgls could potentially represent a distinct mechanism for the lysis of host cells.

Single-stranded RNA phages have high mutation rates. "High mutation rates allow these phages to infect new species of bacteria," he explained. "In order to escape the new hosts, the phages have to either change the existing Sgl gene or evolve a new Sgl. In spite of a very short total length of genomic RNA, these phages can encode two or more Sgls or proto-Sgls for the lytic activity to destroy multiple bacterial hosts."

Another far-reaching aspect of the study was that a large proportion of the Sgls found in the investigation had originated and evolved within the gene for the phage replication protein, or Rep.

A disproportionate number (22 of the 35) of Sgls or Sgl candidates were found embedded within the Rep gene," Chamakura said. "Overlaying the location of Sgl genes on the respective Rep sequences revealed that most of the Sgl genes evolved in less conserved regions of Rep. The study also revealed that closely related phages showed significant evidence of de novo gene evolution.

"This indicated some of these Sgls did not evolve from existing genes but were essentially made from scratch in sections of the genome that do not code for any functional molecules," Chamakura said. "Therefore, a single-stranded RNA phage might have two or more lysis genes at different stages of gene evolution."

"Through the analysis of a relatively minuscule sample of the total leviviral universe, we have uncovered a diversity of small peptides that carry out a critical function in the life cycle of RNA viruses," Chamakura said. "We have also shown leviviruses readily evolve Sgl genes and sometimes have more than one per genome. And because these genes share little to no similarity with each other or to previously known Sgl genes, they rep resent a rich source for potential protein antibiotics."

He said the study should also be useful in helping to uncover small genes and their biological functions in RNA viruses of more complex organisms -- such as plants and animals -- as well as provide a good model for studying how new genes evolve.

"Further research could include exploiting these peptides for identifying targets for antibiotic development," he said.

Original Source: Texas A&M AgriLife Communications.
Reference: Chamakura KR, Tran JS , O'Leary C, Lisciandro HG, Antillon SF, Garza KD, et al. Rapid de novo evolution of lysis genes in single-stranded RNA phages. Nature Communications, 2020; 11 (1) DOI: 10.1038/s41467-020-19860-0