17 Anesthesia

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17.1 Introduction

Wilms' tumor (WT) is the commonest abdominal malignancy in the pediatric population. While these tumors are mostly unilateral, 5% are bilateral, and a smaller percentage of patients (~1%) have intravascular extension of tumor to the inferior vena cava (IVC) and sometimes to the right atrium.

In about 10% of cases, the tumor manifests in conjunction with syndromes such as Beckwith–Wiedemann, Soto's, Denys–Drash, WAGR, and trisomy 18 [1].

Asymptomatic abdominal mass is the most regular presentation of WT. Abdominal pain occurs in 25% of patients [2], while fever, hypertension, and gross hematuria happen in 5–30% of patients. Some patients with intra-tumor hemorrhage may present with anemia and hypotension [3]. Respiratory symptoms in lieu of lung metastases are seen in those with advanced disease.

In addition to general considerations of pediatric anesthesia, WT may pose additional issues due to its occasional massive size, vascular invasion, bilateral disease, and hypertension. Minimal invasive surgery, though seldom used, may add another dimension because of space constraints, pneumoperitoneum, and virtually a compartment syndrome like picture.

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As perioperative physicians, it is our utmost duty to give a child diagnosed with WT a pain-free and unperturbed ride through his/her medical treatment and surgery.

17.2 Preoperative Concerns and Optimization

Children with WT may require anesthesia at several stages of their management process, including that for diagnostic radio-imaging studies- Computerised tomography (CT) or magnetic resonance imaging (MRI) much before being planned for any surgical procedure. A detailed preoperative assessment of the child forms the basis for the anesthetic plan.

Most children with untreated WT are systemically well and asymptomatic. However, malnutrition and concomitant infective pathologies in low-middle-income countries may compromise the general condition of the child. Maintaining good nutrition throughout the course of treatment is gaining acceptance nowadays.

History regarding previous anesthetics exposure, any prolonged hospitalization, intensive care unit (ICU) stay, family predisposition to anesthetic problems like malignant hyperthermia, known allergies, any coexisting medical problems, and current medications must be elicited. Information elicited from the history should lead the physical examination of the child.

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Respiratory signs and symptoms should be elucidated in suspected metastasized disease and the chest X ray/CT chest reviewed. Rarely, pulmonary function tests may be required to know the extent of the pulmonary involvement due to metastases [4].

A baseline blood pressure reading is mandated.

Reviewing a recent complete blood count and serum electrolytes is desirable by the anesthesiologist. Blood dyscrasias, most commonly anemia or thrombocytopenia, occur from occult tumor bleeding into the abdominal cavity. WT being a renin secreting tumor, secondary hypertension is common which causes electrolyte and acid base disturbances. Nevertheless, most cases reveal a normal renal function. In addition, preoperatively, a coagulation profile must be reviewed, and availability of cross-matched blood and blood products should be ensured at the time of surgery.

In cases of syndromic WT, it is essential to do a thorough physical examination for features that may have anesthetic implications. Children with overgrowth syndromes may require airway equipment of a size different from that predicted by weight or age. Among the overgrowth syndromes, Simpson–Golabi–Behmel and Beckwith–Wiedemann syndrome feature hypotonia, macroglossia, and hyperinsulinism, while Soto's syndrome is linked with marked hypotonia and congenital heart disease mandating an additional echocardiographic evaluation [5]. The patients with trisomy 18 (Edward's syndrome) have varied anomalies that include micrognathia (possible difficulty in intubation) and cardiac anomalies like ventricular septal defects and patent ductus arteriosus, once again mandating an essential cardiology clearance. Early renal impairment and secondary hypertension often develop in patients with Denys–Drash syndrome.

Since atrial tumor thrombus may remain asymptomatic, the anesthesiologist should look for any established IVC thrombus by CT angiography or echocardiography.

Some patients are given pre-nephrectomy chemotherapy (ChT) to shrink the size of the tumor in SIOP protocol which is becoming more popular in the developing world. Initial ChT regimens include Vincristine, which might cause the syndrome of inappropriate antidiuretic hormone secretion and Actinomycin-D which damages the liver and impairs hematopoietic function, increasing the risk of coagulopathy. Children with metastatic disease receive Doxorubicin which potentially causes myocardial damage, resulting in acute cardiomyopathy and cardiac dysrhythmias, thus necessitating an echocardiographic evaluation to assess myocardial contractility.

More than 50% of patients planned for surgical resection of WT present with hypertension. The etiology of hypertension is attributed to an increased plasma concentration of renin produced by perivascular spaces surrounding the tumor [6], and the areas of kidney cortex entrapped within it. Normally, renin produced by the juxtaglomerular apparatus acts on circulating angiotensinogen, converting it to angiotensin I. In the lungs, angiotensin I is converted to angiotensin II by angiotensin converting enzyme (ACE). Angiotensin II, a potent arteriolar vasoconstrictor, causes hypertension. Hypertension in a case of WT may be labile and severe, the results of which include left ventricular hypertrophy and intravascular volume contraction. Electrolyte disturbances may additionally occur due to renal potassium wasting induced by aldosterone and fluid retention due to hyperreninemia [7, 8]. This may also cause patients to develop lethal congestive heart failure [9].

Centrally acting sympatholytics like methyldopa and clonidine decrease the stimuli for renin formation [10].

Captopril, which is an ACE inhibitor, is particularly effective in treating hypertension preoperatively. It has a plasma half-life of 2 h and a clinical half-life of 4 h; hence the last dose should not be given within 4 h of tumor removal to prevent rebound hypertension [11, 12].

Saralasin, a synthetic angiotensin II receptor partial agonist, has also been used to control severe hypertension in WT [9, 13].

Non-selective beta-adrenergic blockers should be used with caution in patients with uncontrolled hypertension, as the mechanism of the hypertension is not affected by beta blockade and may in turn get exacerbated due to inhibition of the beta-

adrenergic vasodilatory mechanism [9]. Also non-selective beta blockers prevent the reflex increase in heart rate that develops as a compensatory response to sudden hypotension caused by the labile nature of a renin secreting WT in an event of decreased renin secretion. However, propranolol in the dose of 2 mg/kg/6 h (up to a maximum dosage of 6 mg/kg/6 h) is often used in the perioperative management of hypertension.

In the control of preoperative blood pressure various combinations of labetalol, hydralazine, diazoxide, and prazosin have been proven ineffective [11, 12, 14]. Diuretics also fail to affect the mechanism of hypertension in these patients and may in turn worsen electrolyte disturbances.

Adequate preoperative control of blood pressure lessens the incidence of perioperative hemodynamic instability due to fluctuating renin concentrations [15], since preoperative optimization ensures a good cardiac output in the intraoperative period by decreasing the preload and afterload.

17.3 Intraoperative Management

The challenges of anesthetizing pediatric patients with WT are primarily those pertaining to lengthy transabdominal retroperitoneal surgery in small children and infants: fluid balance, thermoregulation, ventilating the child/infant with raised intra-abdominal pressure, intermittent IVC compression, and potential risk of major hemorrhagic complications. One may also encounter the consequences of paraneoplastic phenomena such as coagulopathy and hypertension, tumor thrombus extension to proximal IVC or right atrium, and preoperative or past treatment with ChT.

Though the neoadjuvant ChT used for a fresh case of WT is nearly bereft of any major side effects, some of the patients of recurrent WT would receive high-dose intensive ChT and stem-cell rescue before the surgeon decides to excise the locally relapsed tumor or the systemic metastases. These patients would be prone to develop mucositis, which is characterized by painful, erythematous and ulcerative lesions. This may cause airway bleeding secondary to tissue friability and supraglottic edema resulting in a difficult airway situation. It is usually seen 7–10 days after the start of ChT and remains for 1–2 weeks. Ideally, the surgery should be delayed in such a case, but if there is rare indication for an early surgery after such an intensive ChT, then the anesthesiologist must be very careful intubating such children.

Choice of anesthesia is to be guided by preoperative history and clinical examination findings. Option regarding pain management is to be discussed with the parents. While epidural anesthesia at the lower thoracic levels is a wonderful option for intraoperative and postoperative pain relief, it may be difficult to perform in infants especially those in the initial few months of life. Ultrasound guided epidural anesthesia is a good alternative in such cases.

Adequate nil per oral status must be ensured. The child may be premedicated with Syrup Midazolam (0.5 mg/kg) in preoperative room. Allowing parents/caretakers in at least the preoperative room, if not in the operation theatre (OT) during induction (as done in the western world), could allay child's fears and family's anxiety.

In OT, all standard monitors must be attached. Induction of anesthesia is done with sevoflurane along with 100% fractional concentration of oxygen if intravenous (IV) line is not available initially and the child does not allow placement of IV line. If an IV line is available, IV induction may be done with inj. Fentanyl (2 μg/kg) and inj. Thiopentone (5–7 mg/kg). Inj. Vecuronium (0.1 mg/kg) or inj. Rocuronium (0.6 mg/kg) may be used for muscle relaxation. The child is then intubated with an appropriate-sized endotracheal tube decided according to the age of the patient. A naso-gastric tube is inserted.

If difficult intubation is anticipated, a check laryngoscopy may be done before the administration of a muscle relaxant and Cormack-Lehane (CL) grading assessed. Also, adequate chest rise is ensured by bag and mask ventilation before any muscle relaxant is given.

An arterial line is inserted because of the potential risk of hemodynamic instability during tumor handling, sudden hypotension, and the usual presence of hypertension in these children. Core temperature monitoring is mandatory, as

a warning for both impending hypothermia and hyperthermia if forced air warming techniques are used. The standard practice entails careful positioning, padding of pressure areas, and eye protection.

It is desirable to secure at least two large bore IV cannulas in upper limbs specially if intraoperative inferior vena cava clamping is anticipated. If a difficult IV cannulation is anticipated, placing a central line is a wise option since resection of a large WT is a major surgery involving massive fluid shifts; the central line shall prevent panic moments in case of intraoperative hemorrhage, which may necessitate massive blood and volume transfusion.

After induction and intubation, an epidural catheter is placed by loss of resistance (LOR) technique or ultrasonographically guided in a case of difficult anatomy. A functional epidural catheter reduces the requirement for IV opioids which reduces the chances of post-op respiratory depression.

A urinary catheter must also be placed; urine output is constantly monitored throughout the surgery.

Maintenance of anesthesia is ensured with 2% sevoflurane, regular top ups/infusion of muscle relaxant and fentanyl. For epidural infusion, the common practice is an infusion of 0.125% bupivacaine at the rate of 0.2 mg/kg/h for neonates and 0.4 mg/kg/h for older children.

Goal-directed therapy, titrated according to hemodynamic response, is adopted for administration of IV fluids with an average fluid administration (balanced salt solution) at the rate of 10–20 ml/kg/h during anesthesia [16]. Rarely, a background infusion of glucose (1–2.5%) may be given at the rate of 10 ml/kg/h in younger children and those children prone to hypoglycemia. In surgeries spanning over many hours, blood sugar levels must be measured, and glucose administration adjusted accordingly.

It is often difficult to ensure adequate ventilation is a case of WT because the intraabdominal pressure is typically raised owing to the large size of the tumor. Small tidal volume breaths with a respiratory rate kept on the higher side shall ensure adequate respiratory exchange of gases. The pressure-controlled mode of ventilation is preferred with a vigilant eye on the peak airway pressures to prevent barotrauma and further compromise in ventilation. Also, epidural analgesia plays a significant role here by reducing the intra op requirement of opioids thereby preventing post op respiratory depression.

In 1% cases, where the tumor may extend to the IVC and right atrium a transesophageal echocardiography or Doppler probe is placed to assess the cardiac output.

Intraoperative fluctuations in blood pressure are frequently encountered during tumor handling. If a rapidly shooting blood pressure cannot be brought under control by maneuvers such as increasing the depth of anesthesia or administering opioids, drugs such as phenoxybenzamine, phentolamine, sodium nitroprusside, and Esmolol are used for control of the same.

Episodes of hypotension are also not a rarity. It occurs frequently due to IVC compression by the surgeon or an episode of sudden blood loss. Blood loss must be replaced with crystalloids or blood products as appropriate. Colloids are generally avoided as a replacement for blood loss since studies have shown that colloids potentially cause renal tubular damage via hyperosmotic mechanisms [17]. More often than not blood pressure is immediately restored upon asking the surgeon to stop the surgery for a little while, and to release the retractors that may be causing a possible IVC compression.

Blood gas analysis may be performed at regular intervals. Analysis of blood gas allows us to note changes over time. Serial values of central venous oxygen saturation ($ScVO_2$) may be used as a fast indicator and base excess and lactate concentration as slow indicators of tissue perfusion. In case of a negative trend in these parameters, countermeasures are taken accordingly, before a pathological level is reached.

Hypothermia needs to be avoided both intra- and in the immediate postoperative period. If epidural anesthesia is not being used, local anesthetic (0.125% bupivacaine) should be infiltrated at the incision site (taking care not to exceed the highest permissible dose according to the weight of the child).

Once the surgery is over, an arterial blood gas assessment is done. If the acid base gas (ABG) picture shows conditions conducive to extubation, reversal of the child is attempted with Inj. Glycopyrrolate (0.01 mg/kg) and injection neostigmine (0.05 mg/kg). An antiemetic is also given in older children to prevent postoperative nausea and vomiting. Once the child is extubated, he/she is shifted to the postoperative recovery room. The epidural if inserted is generally kept in situ for postoperative pain relief.

In a situation where extubation is not possible due to reasons such as massive blood loss, acidosis, or inadequate reversal, the child is shifted to the intensive care unit (ICU) and is kept under continuous supervision until it is possible to wean him/her off the ventilator.

17.4 Anesthesia for Special Circumstances

17.4.1 Anesthesia in a Case of Tumor Extension to the Right Atrium

Neoadjuvant ChT is almost necessarily given in all cases of tumor extension to the IVC or right atrium, to shrink the tumor which shall enable surgery without the requirement of cardiopulmonary bypass. However, in some cases, hemodynamic instability caused by the tumor invasion into the right atrium that presses onto the tricuspid valve requires an upfront emergency surgery.

Cardiopulmonary bypass (CPB), with or without circulatory arrest, is used frequently to facilitate the resection of the tumor thrombus extending into the suprahepatic IVC and right atrium (Daum stages III and IV). CPB requiring the use of a median sternotomy, atriotomy, and systemic anticoagulation is associated with significant morbidity from the systemic inflammatory response provoked by the the extracorporeal circuit. There is higher incidence of neurological dysfunctions, systemic inflammatory response syndrome (SIRS), and coagulopathies in such cases. CPB prolongs the operative time, exposing the patient to risk of acidosis, hypothermia, blood transfusion, and cardiac arrest.

In addition to the challenges posed by a regular nephrectomy in a pediatric patient, the anesthesiologist shall have to deal with a plethora of other anesthetic challenges of cardiopulmonary bypass specifically during the transition period, while going into bypass circuit and coming off bypass. Normally the nephrectomy is done prior to intracardiac removal of the tumor with the help of extracorporeal CPB, since systemic anticoagulation that is a necessity for CPB predisposes the patient to unanticipated bleeding, if nephrectomy is planned post bypass in the same sitting. Adequate anticoagulation should be ensured before going on bypass by administration of Inj. heparin (3 mg/kg), titrated to point of care anticoagulant test values. The anticoagulation should be adequately reversed with Inj. protamine after the patient is off bypass, to minimize the chances of further bleeding.

The anesthesiologist should be adept in the management of myriad arrhythmias that are frequently encountered while the patient is coming off CPB. All antiarrhythmic drugs, inotropes, and a functional defibrillator should be ensured in the operation theatre before shifting the patient for surgery. Arterial blood gas should be done at frequent intervals and acidosis if any must be corrected aggressively.

Epidural is not to be put in patients planned for CPB due to risks of bleeding, and thrombus formation associated with systemic anticoagulation and analgesia is achieved mainly with IV opioids.

Since such patients are majorly electively mechanically ventilated postoperatively, postoperative respiratory depression due to opioids is of a lesser concern.

17.4.2 Anesthesia in Bench Surgery

Bench surgery involves the removal of the diseased kidney from its bed while ligating the renal vein, artery, and ureter (close to the bladder), excision of the tumor(s) on the removed kidney in cold preservation solution extracorporeally and transplanting the residual kidney back into the iliac fossa in the same patient.

Apart from the routine anesthetic concerns, our main goal during this surgery is to maintain adequate renal perfusion. Thus, a high normal BP and a central venous pressure (CVP) of 8–12 cm of water is ensured with the help of generous IV hydration before the renal artery is clamped. Ischemic injuries to the kidney are prevented by mannitol infusion [18].

During the bench surgery (extracorporeal surgery interval), our aim is to prevent fluid overload. During that period, CVP is kept on the lower side.

Just before the anastomosis and release of the clamp, CVP is increased and a higher BP maintained to provide necessary perfusion to the transplanted kidney [19, 20].

Furosemide is given to ensure diuresis and to improve graft viability. Oxygen consumption in the renal tubules is also lowered by furosemide thus reducing the chances of any ischemic kidney injury [21].

17.4.3 Anesthesia for Laparoscopic Nephrectomy

Laparoscopy surgery is restricted to only small tumors to be performed by surgeons with reasonable degree of expertise and experience in laparoscopic procedures; a low threshold to conversion to an open procedure is emphasized. General anesthesia with endotracheal intubation without the use of nitrous oxide is ideal as with any major laparoscopic operation. The major concerns are hypercapnia due to abdominal insufflation with carbon dioxide and hypoventilation. Increased intraabdominal pressure caused by pneumoperitoneum causes the diaphragm to displace cephalad resulting in decreased compliance and decreased functional residual capacity. Increased airway resistance increases peak pressure and plateau pressures thereby resulting in an increased work of breathing. Therefore, pressure-controlled ventilation is the preferred mode. Normocapnia is ensured by keeping a high respiratory rate with lower pressure limits and thus lower tidal volume. Care should be taken to monitor the rate of insufflation of gas into the peritoneal cavity. To minimize the cardiorespiratory adverse effects of pneumoperitoneum, insufflation pressures should be limited to 5–10 mmHg in neonates and 10–12 mmHg in older children [22]. Gas embolism is a known complication of any laparoscopic surgery, and the anesthesiologist should be observant of any sudden fall in end tidal carbon dioxide, sudden hypotension, arrhythmias, or desaturation. The treatment would then consist of desufflating the abdomen, ventilation with 100% oxygen, trying to break the air embolus by cardio-pulmonary cerebral resuscitation, and aspirating the embolus through central venous line by Durant's maneuver [23].

Ports sites should be infiltrated with local anesthetic at the end of the operation to provide adequate pain relief. Regional anesthesia such as an epidural catheter may be used for intra op and post op analgesia specially if the Pfannenstiel incision is of a bigger size.

Although both laparoscopy and retroperitoneoscopy have been used for the radical nephrectomy, the latter is associated with increased CO_2 absorption and pulmonary hypertension in children [24]. This may have central nervous system and cardiorespiratory consequences during and after the operation.

17.5 Postoperative Concerns

Once the child is extubated and shifted to the post op recovery room, care must be taken to ensure a pain-free postoperative period to restore normalcy in the child's life as fast as possible. A complete hemogram is done to assess the actual blood loss during the procedure. Blood products are transfused based on reports of the postoperative hemogram.

The epidural catheter, if in situ, is followed up regularly by an anesthesiologist with regular top ups of injection bupivacaine or bupivacaine infusion administered as per patient's requirement. A Prothrombin Time-International Normalized Ratio (PT-INR) report is mandatory before taking out the epidural catheter, and care is taken to ensure that the catheter tip is intact while it is being taken out.

If there is no epidural catheter in situ, other modes of postoperative analgesia must be considered like opioids or even simpler steps such as round the clock dosage of paracetamol goes a long way in ensuring adequate pain relief. If the child is receiving opioid analgesia, vigilant monitoring of his vitals and respiratory parameters must be ensured.

The child must be encouraged to do incentive spirometry to ensure full recovery of his/her pulmonary functions.

17.6 Conclusions

Nephrectomy in the twenty-first century remains a potentially challenging case for any anesthesiologist, more so in children. Comprehensive imaging, multidisciplinary team discussion, and preoperative optimization are frequently necessary across diverse specialities. A good coordination between the surgeon, anesthesiologist, oncologist, and a meticulous planning backed by a harmonious teamwork shall ensure that every child with WT leaves the hospital with a smile and carries good will for his treating doctors in the years to come.

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