

Pleuropulmonary Blastoma

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Pleuropulmonary blastoma (PPB) is a dysontogenetic neoplasm of childhood that involves lung and/or pleura. There is an increased incidence of neoplasias and dysplasias among young relatives of children with PPB. Pathophysiologically, PPB evolves from a cystic to solid state over time. It is subclassified as type I (purely cystic), type II (both cystic and solid elements), and type III (completely solid). Type II and type III may be associated with metastasis, with the brain being the most common metastatic site. The absence of epithelial malignancy in PPB is a feature that distinguishes it from the adult-type pulmonary blastoma. The clinical presentation includes signs and symptoms associated with various respiratory disorders. To make a definitive diagnosis of PPB, an examination of the cystic fluid or solid tumor is required. Treatment for PPB consists primarily of surgery and chemotherapy. Nursing care is directed toward maintaining normal respiratory and neurological function, maintaining normal fluid and electrolyte balance, minimizing side effects associated with treatment, and providing education for the family.

Key words: pleuropulmonary blastoma, pathophysiology, diagnosis, treatment, nursing care

In 2006, a 4-year-old female patient presented to the emergency department with increasing cough, chest pain, and tachypnea. Physical examination findings included the absence of right-sided breath sounds and the presence of a right-larger-than-left chest asymmetry.

A chest X ray (CXR) (Figure 1) revealed a pulmonary mass occupying a large portion of the right hemithorax. A subsequent computed tomography (CT) (Figure 2) scan showed that the mass extended to the anterior, middle, and posterior mediastinum with almost complete atelectasis of the right lung. There was a left mediastinal shift and compression of the right mainstem bronchus, right pulmonary artery, right atrium, and vena cava. Following a biopsy, the mass was initially thought to be embryonal rhabdomyosarcoma, but the final diagnosis was pleuropulmonary blastoma (PPB). Imaging studies were negative for metastatic disease.

The child's medical history is significant for pneumonia with invasive group A *Streptococcus pneumoniae*, an illness that necessitated a pediatric intensive care unit (PICU) stay during infancy. In addition, asthma was diagnosed at 8 months of age. The family history is negative for childhood neoplasias and dysplasias. The only adult family member known to have cancer was a great-grandmother with colon cancer.

After the child received 2 fractions (400 cGy) of emergent radiation therapy, her respiratory status showed significant improvement and chemotherapy was started. The chemotherapy consisted of cycles of vincristine, actinomycin D, and cyclophosphamide with mesna alternating with doxorubicin and cisplatin. (Note: This chemotherapy regimen is no longer recommended

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Figure 1. Initial Chest X Ray Showing a Pulmonary Mass Occupying a Large Portion of the Right Hemithorax

for PPB.) Granulocyte colony-stimulating factor was given with each cycle of chemotherapy. Following 4 cycles of chemotherapy and a modest decrease in tumor size, surgery was performed. A right middle lobectomy and excision of extensive mediastinal tumor left only a small area of tumor along the vena cava that could not be safely removed. Postoperatively, a course of radiation therapy to the right chest (5040 cGy) and 4 additional cycles of chemotherapy were given.

Shortly after beginning the first cycle of chemotherapy, the child developed hypoxia and significant respiratory distress. She required intubation and was transferred to PICU, where her care was provided for the next 6 weeks. The hematology/oncology team collaborated with the PICU team, and scheduled chemotherapy treatments were given during the weeks of intensive care. One week after leaving PICU, the child was discharged from the hospital. She returned for scheduled appointments for chemotherapy, surgery, and radiation therapy, completing treatment 8 months after diagnosis.

Unfortunately, after the child was off treatment for 7 months, imaging studies showed recurrent chest disease. There was still no evidence of metastatic dis-

ease. Chemotherapy treatment resumed using a phase I study for children with refractory solid tumors. Six months into this treatment there is little change in the chest disease, but clinically the child is doing well.

Features of Pleuropulmonary Blastoma

Pleuropulmonary blastoma is a rare dysontogenetic neoplasm that involves lung and/or pleura. Historically, it was known as pulmonary blastoma of childhood, but with increased knowledge about the tumor and the characteristics that distinguish it from pulmonary blastoma in adults, it came to be known as pleuropulmonary blastoma (PPB) (Manivel et al., 1988). PPB is diagnosed primarily in children less than 5 years of age.

Worldwide, there are about 300 known cases of PPB (Priest et al., 2007). Although uncommon, PPB is a significant diagnosis not only for patients but also for family members. The incidence of familial PPB and other neoplasias and dysplasias in those with PPB and their young, close relatives is approximately 25% (Boman et al., 2006; Pai et al., 2007). Renal abnormalities,

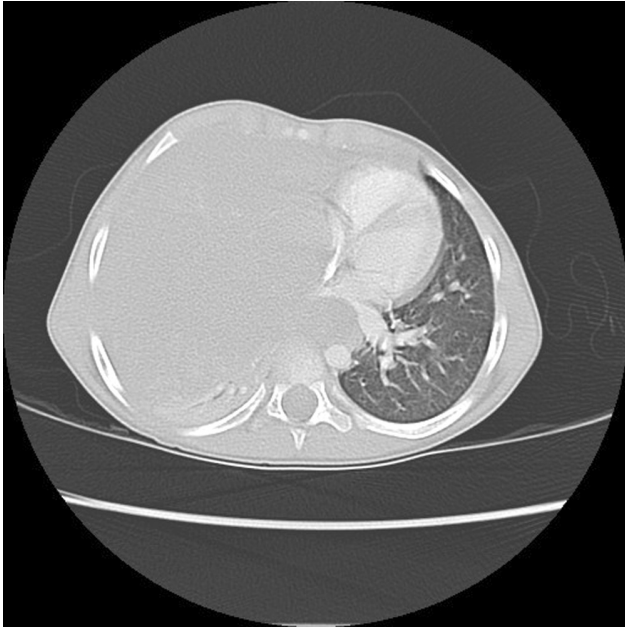


Figure 2. Initial Computed Tomography Scan Showing Extension of the Pulmonary Mass to the Anterior, Middle, and Posterior Mediastinum

especially cystic nephroma, appear to be common in families with PPB and are associated with an increased incidence of bilateral pulmonary cysts and/or tumors in those with PPB (Boman et al., 2006). Other findings in families with PPB include medulloblastoma, germ cell tumor, and hematologic and thyroid malignancies (Orazi et al., 2007; Priest et al., 2007).

Cytogenetic abnormalities, particularly gains in chromosome 8, are regularly identified in PPB tissue. However, a specific inherent genetic abnormality that predisposes families to PPB and associated neoplasias and dysplasias has yet to be discovered (Boman et al., 2006; Taube et al., 2006; Vargas, Nosé, Fletcher, & Perez-Atayde, 2001).

Pathophysiology and Prognosis

An unusual feature of PPB is that it evolves from a cystic to solid state over time. This progression is subclassified as type I, followed by type II and then type III (Dehner, Watterson, & Priest, 1995; Priest et al., 2006). Type I PPB is purely cystic, is diagnosed at a median age of 10 months, and has a survival rate of 80% to 85%. If it recurs, it is usually as type II or type III PPB. Type II PPB is composed of both cystic and solid elements and

is diagnosed at a median age of 34 months. Type III PPB is completely solid and is diagnosed at a median age of 44 months. Type II and type III PPB have a survival rate of 45% to 50% (Priest et al., 2007).

Histologically, PPB is a heterogeneous malignancy that may include features associated with other tumors of early childhood, such as embryonal rhabdomyosarcoma, Wilms tumor, and malignant germ cell tumor. Like the adult-type pulmonary blastoma, PPB is associated with an immature stroma and a blastematos appearance. However, unlike the adult-type tumor, there is no epithelial malignancy associated with PPB (Manivel et al., 1988).

Type I PPB consists of a single cyst or, more commonly, multilocular cysts with thin septa. Beneath a benign ciliated respiratory epithelial lining, the cysts contain cambium-like areas with proliferation of primitive mesenchymal cells. Herein, foci of rhabdomyoblasts are often noted, but the blastematos cells of PPB differentiate it from rhabdomyosarcoma. The location of type I PPB appears to be confined to pulmonary parenchyma and/or visceral pleura (Pai et al., 2007; Priest et al., 2006).

Type III PPB is a completely solid tumor with blastematos and sarcomatos characteristics. At times, hemorrhagic and necrotic areas may be seen. The histologic components of type III PPB generally include blastematos islands, cartilaginous nodules, rhabdomyoblasts, and anaplastic cells (Priest et al., 2006; Taube et al., 2006). As with cystic PPB, the presence of primitive blastematos cells within the solid tumor diagnoses PPB (Al-Backer, Puligandla, Su, Anselmo, & Laberge, 2006).

Type II PPB has both cystic features as seen in type I PPB and solid characteristics similar to those associated with type III PPB. The location of type II and type III PPB often extends beyond the pulmonary parenchyma and visceral pleura to involve parietal pleura, mediastinum, and diaphragm. Unlike type I PPB, both type II and type III PPB may be associated with metastasis, with the brain being the most common metastatic site. PPB may also spread to bones, lymph nodes, liver, pancreas, kidneys, and adrenal glands (Al-Backer et al., 2006; Priest et al., 2007).

Clinical Presentation

The clinical presentation for PPB includes signs and symptoms associated with various respiratory

disorders—cough, tachypnea, chest pain, respiratory distress, and diminished or absent breath sounds over affected lung fields. Also, there may be abdominal pain, fever, anorexia, fatigue, and general malaise. Initially, it may be thought that the child has a lower respiratory tract infection.

When metastatic disease to the brain is present, there may be increased intracranial pressure and changes in neurological status. Signs and symptoms include nausea, vomiting, lethargy, seizures, hemiparesis, and altered vision (Priest et al., 2007). Metastasis to other areas may lead to signs and symptoms associated with abnormalities in the affected organs and systems of the body.

Diagnostic Evaluation

Initial diagnostic studies include a thorough history for the child and family as well as a complete physical examination. CXR is an early imaging study. When significant respiratory compromise is present initially or when clinical symptoms persist and follow-up CXR shows no improvement, a CT scan is done. Common radiographic findings include partial or complete opacification of a hemithorax and deviation of the mediastinum to the contralateral side. A metastatic workup with type II and type III PPB may include CT scans or magnetic resonance imaging (MRI) of the brain as well as CT scans of the abdomen and pelvis and whole-body bone scan.

The diagnosis of PPB is often missed at first, because the clinical and radiographic findings are thought to indicate other respiratory disorders such as pneumonia or a benign congenital cyst, particularly a congenital cystic adenomatoid malformation, now referred to as a congenital pulmonary airway malformation, type 4 (Pai et al., 2007; Stocker, 2002; Vargas et al., 2006).

PPB is not definitively diagnosed by clinical and radiographic findings. To make a diagnosis of PPB, the cystic fluid or solid tumor must be examined. It is important that multiple areas of the specimen be histologically analyzed because the primitive blastemata cells that are diagnostic of PPB may be localized rather than uniformly distributed (Hill et al., 2008; Priest et al., 2006).

Treatment

The treatment plan for PPB generally includes both surgery and chemotherapy.

Surgery is the primary treatment for PPB, with the goal being resection of all tumor. Depending on the extent of disease, surgery may be a cystectomy, segmentectomy, lobectomy, or pneumonectomy. In some cases, only a biopsy is done initially. Second-look surgery is done when complete resection is not achieved with initial surgery. In addition, there is increasing recognition of the need for surgical resection of congenital cystic pulmonary lesions because it is difficult to distinguish between benign cystic lesions and type I PPB apart from pathologic examination (Al-Backer et al., 2006; Hill et al., 2008).

The International Pleuropulmonary Blastoma Registry is a primary resource for current chemotherapy recommendations for the treatment of PPB. Chemotherapy for type I PPB consists of VAC—vincristine, actinomycin D, and cyclophosphamide. In 2007, following dialogue among sarcoma experts in Europe and North America, the chemotherapy recommendation for type II and type III PPB was changed to IVADo—ifosfamide, vincristine, actinomycin D, and doxorubicin (International Pleuropulmonary Blastoma Registry, 2008).

Radiation therapy may be added for type II and type III PPB when residual disease is present. High-dose chemotherapy followed by autologous stem cell transplant may be considered for relapsed PPB (Kaneko et al., 2006).

The aggressive nature of PPB requires a strict surveillance schedule to detect progressive or recurrent disease early. It is recommended that CT scans of the chest, and CT scans or MRI of the brain, be done at 3-month intervals for at least 36 months following diagnosis (Indolfi et al., 2007; Priest et al., 2006; Priest et al., 2007).

Nursing Management

With PPB, as with other pediatric cancers, the care of the child and family progressing through the diagnostic workup, treatment, and follow-up requires interdisciplinary collaboration. The nurse should expect to work with specialists in pediatric oncology, surgery, pharmacology, respiratory therapy, dietary, social work, and child life.

Table 1. Antineoplastic Agents for PPB

Classification	Vincristine Mitotic inhibitor	Actinomycin D Antibiotic	Cyclophosphamide Alkylating agent	Ifosfamide Alkylating agent	Doxorubicin Anthracycline antibiotic
Alerts	Vincristine is a vesicant. If this drug infiltrates, be prepared to immediately implement your institution's protocol for management of vincristine extravasation. The maximum single dose for vincristine is 2 mg.	Actinomycin D is a vesicant. If this drug infiltrates, be prepared to immediately implement your institution's protocol for management of actinomycin D extravasation. Actinomycin D is not given during times of radiation therapy.	To decrease risk of urinary system toxicity, patient should meet the following prerequisites prior to infusing cyclophosphamide: <ul style="list-style-type: none"> • specific gravity less than 1.010 • urine output at least 3 mL/kg/h. Give mesna with cyclophosphamide to decrease risk of hemorrhagic cystitis.	To decrease risk of urinary system toxicity, patient should meet the following prerequisites prior to infusing ifosfamide: <ul style="list-style-type: none"> • specific gravity less than 1.010 • urine output at least 3 mL/kg/h. Give mesna with ifosfamide to decrease risk of hemorrhagic cystitis.	Doxorubicin is a vesicant. If this drug infiltrates, be prepared to immediately implement your institution's protocol for management of doxorubicin extravasation. The maximum cumulative dose for doxorubicin is decreased when mediastinal radiation is given.
Side effects	<ul style="list-style-type: none"> • Neuropathy (tingling/ numbness in hands and feet, jaw pain, leg pain, absent deep tendon reflexes, constipation, paralytic ileus, ptosis, foot drop, slapping gait, weakness) • SIADH • hair loss 	<ul style="list-style-type: none"> • Myelosuppression (anemia, neutropenia, thrombocytopenia) • stomatitis • nausea and vomiting • diarrhea • hepatotoxicity • hair loss • radiation recall 	<ul style="list-style-type: none"> • Myelosuppression (anemia, neutropenia, thrombocytopenia) • nausea and vomiting • hemorrhagic cystitis • hair loss • renal toxicity • hepatotoxicity • metallic taste in mouth • SIADH • cardiac toxicity with high doses 	<ul style="list-style-type: none"> • Myelosuppression (anemia, neutropenia, thrombocytopenia) • nausea and vomiting • hemorrhagic cystitis • hair loss • renal toxicity • hepatotoxicity • altered neurologic status (lethargy, confusion, hallucinations, seizures, coma) • cardiac toxicity with high doses 	<ul style="list-style-type: none"> • Myelosuppression (anemia, neutropenia, thrombocytopenia) • nausea and vomiting • anorexia • stomatitis • esophagitis • hair loss • cardiac toxicity • photosensitivity • radiation recall • reddish-orange-colored urine

NOTE: SIADH = syndrome of inappropriate antidiuretic hormone. Vincristine, actinomycin D, and cyclophosphamide (VAC) are given with type I PPB. Ifosfamide, vincristine, actinomycin D, and doxorubicin (IVADo) are given with type II and type III PPB.

Table 2. Nursing Care for the Child With Pleuropulmonary Blastoma

Objectives	Nursing Interventions
Maintain normal respiratory function	Assess breath sounds in all lung fields Assess work of breathing Monitor oxygen saturation Encourage use of incentive spirometer Collaborate with physician and respiratory therapist to provide supplemental oxygen as needed Report the following: Tachypnea Chest pain Respiratory distress Diminished or absent breath sounds Abnormal pulse oximetry readings
Maintain normal neurological function	Assess neurological status Report the following: Vomiting Seizures Lethargy Impaired arm/leg mobility Altered vision Altered mental status Altered sensation (eg, numbness) Changes from baseline neurological function
Maintain normal fluid and electrolyte balance	Administer prescribed intravenous fluids with chemotherapy Measure and assess intake and output Weigh and assess body weight Assess electrolyte values Report the following: Significant difference between intake and output Significant weight gain or weight loss Abnormal electrolyte values
Provide supportive care with emetic chemotherapy	Administer prescribed antiemetics prior to, during, and following emetic chemotherapy. Report episodes of emesis Collaborate with interdisciplinary team to improve antiemetic support when current plan is inadequate
Provide supportive care during myelosuppression	When anemia is present: Group patient care activities together to facilitate rest times for child Administer packed red blood cells as prescribed When thrombocytopenia is present: Provide a safe environment to protect child from injury and bleeding Restrict child from rough activities Administer platelets as prescribed When neutropenia is present: Provide a protective environment to decrease child's risk of infection Report signs of possible sepsis or septic shock: Hyperthermia Hypothermia Tachycardia Tachypnea Increased pulse pressure Hypotension (late sign) Administer antibiotics as prescribed for fever with neutropenia (presumed sepsis) When mucositis is present: Assess pain and note pain score at regular intervals Collaborate with interdisciplinary team to identify plan for pain management Administer prescribed analgesics to relieve pain and facilitate normal nutritional intake

During the diagnostic workup, nursing care includes developmentally appropriate preparation of the child and family for the diagnostic imaging studies and surgical procedures. This is often a stressful time, and the child and family generally value the nurse's informational and emotional support as they wait to be informed of test results and the child's diagnosis.

While the diagnostic workup is in progress, the nurse regularly assesses the child's overall physical status. Monitoring for hypoxia, increased work of breathing, and respiratory distress is imperative because the lungs and pleura are primary disease sites. The nurse must be alert for deficits and changes in the neurological system, because the brain is the most common site of metastatic disease with PPB.

Chemotherapy treatments usually begin soon after surgery and confirmation of the diagnosis of PPB. Nursing care includes preparation of the child and family for these treatments, safe administration of the prescribed antineoplastic agents, and monitoring of the child for side effects of treatment. (See Table 1 for information about antineoplastic agents used in the treatment of PPB.)

The child receiving treatment for PPB is at risk for respiratory and neurological compromise. In addition, chemotherapy frequently puts the child at risk for fluid and electrolyte imbalance, nausea and vomiting, and myelosuppression. Common objectives and interventions for nursing care of the child with PPB are derived from these risks (Table 2). Specific nursing interventions relating to such things as pain management, nutritional needs, and emotional support are likely to vary from child to child depending on extent of disease, treatment received, developmental level, and psychosocial needs associated with diagnosis, treatment, and response to treatment.

As with other pediatric cancers, ongoing care of the child with PPB is necessary to promptly detect progressive or recurrent disease. The nurse has a key role in teaching the family about the aggressive nature of PPB and the importance of regular follow-up care for the child. The family learns that in addition to physical assessments, follow-up care usually includes CT scans of the chest and CT scans or MRI of the brain every 3 months for at least 3 years from the date of diagnosis. Also, the family learns of the increased risk for neoplasias and dysplasias among their family members.

The International Pleuropulmonary Blastoma Registry has an informative Web site for health care professionals and families of children with PPB (www.ppbregistry.org). The "For Families" section has resources that the nurse may use to provide education about PPB and about how families may participate in increasing knowledge about this rare childhood tumor and its treatment.

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