

ONCOLOGY

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CHAPTER 153

Oncology Assessment

Childhood cancer is rare; only about 1% of new cancer cases in the United States occur among children younger than 19 years of age. However, cancer is the leading cause of disease-related death in children age 1–14 years. Acute leukemia is the most common childhood cancer, followed by central nervous system (CNS) tumors, lymphomas, and sarcomas of soft tissue and bone (Fig. 153.1). There is wide variability in the age-specific incidence of childhood cancers. Embryonal tumors, such as neuroblastoma and retinoblastoma, peak during the first 2 years of life; acute lymphoblastic leukemia peaks during early childhood (ages 2–4 years); osteosarcoma peaks during adolescence; and Hodgkin disease peaks during late adolescence (Fig. 153.2). The overall incidence of cancer among White children is higher than other ethnic groups and is approximately 50% higher than Black children in the United States.

HISTORY

Many signs and symptoms of childhood cancer are nonspecific. Although most children with fever, fatigue, weight loss, or limp do not have cancer, each of these symptoms may be a manifestation of an underlying malignancy. Uncommonly a child with cancer will have no symptoms at all. An abdominal mass may be palpated on routine examination, or a complete blood count (CBC) may be unexpectedly abnormal.

It is important to explore quality, duration, location, severity, and precipitating events of the chief complaint. A prominent lymph node that does not resolve (with or without antibiotics) may warrant imaging and/or a biopsy. A limp that does not improve within weeks should prompt a CBC and a radiograph. Fever, night sweats, or weight loss should raise the concern for lymphoma. In addition, it is important to obtain the birth history, medical and surgical history, growth history, developmental history, family history, and social history.

Cancer-predisposing genes (such as *TP53*) are mutated in approximately 9% of children and adolescents with cancer, even though family history in most patients does not predict an underlying predisposition syndrome. If known to have a

genetic susceptibility to cancer, the child should be screened appropriately (Table 153.1).

PHYSICAL EXAMINATION

Growth parameters and vital signs are important to obtain in all patients. Pulse oximetry should be obtained if respiratory symptoms are present. The general appearance of the patient should be noted, along with signs of pain, cachexia, pallor, and respiratory distress. Palpable masses should be measured, if possible. Lymphadenopathy and organomegaly should be quantified, if present. A thorough examination of the skin may reveal rashes, bruises, and petechiae. A genitourinary exam is important in any patient with unexplained findings. Careful neurologic and ophthalmologic examinations are crucial if headache or vomiting is present because the vast majority of patients with CNS tumors have abnormal neurologic examinations.

COMMON MANIFESTATIONS

The most common manifestations of childhood cancer are fatigue, anorexia, malaise, pain, fever, abnormal lump or mass, pallor, bruising, petechiae, bleeding, headache, vomiting, visual changes, weight loss, and night sweats (Table 153.2). Lymphadenopathy and organomegaly are common in leukemia, particularly with T-cell acute lymphoblastic leukemia (ALL) or lymphoma. Patients with solid tumors usually have a palpable or measurable mass. Children with retinoblastoma may have leukocoria or absence of the red reflex (which may be seen on a photograph). Other signs and symptoms may include limp, cough, dyspnea, cranial nerve palsies, and papilledema. In general, malignant masses are large/growing, firm, fixed, and nontender, whereas masses that are infectious or inflammatory in nature are relatively smaller/stable in size, softer, mobile, and tender to palpation.

DIFFERENTIAL DIAGNOSIS

Distinguishing a malignant process from another disease can be difficult. Ultimately, a tissue diagnosis (from bone marrow or solid tumor biopsy) with pathologic confirmation is required to confirm a diagnosis of cancer. Infection commonly masquerades as a potential malignancy. Epstein-Barr virus, cytomegalovirus, and mycobacterial infections

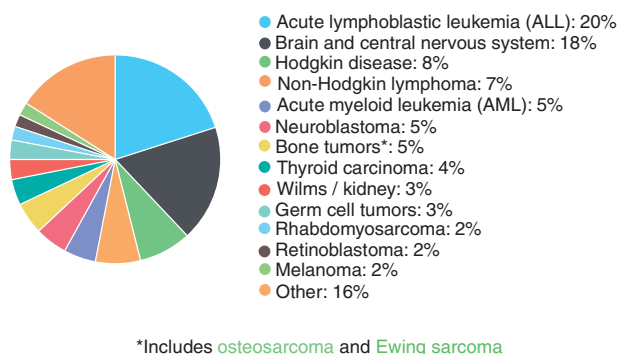


FIGURE 153.1 Number of childhood cancer diagnoses per year. Total = 15,780; age 0–19 years. (<http://curesearch.org/Number-of-Diagnoses>)

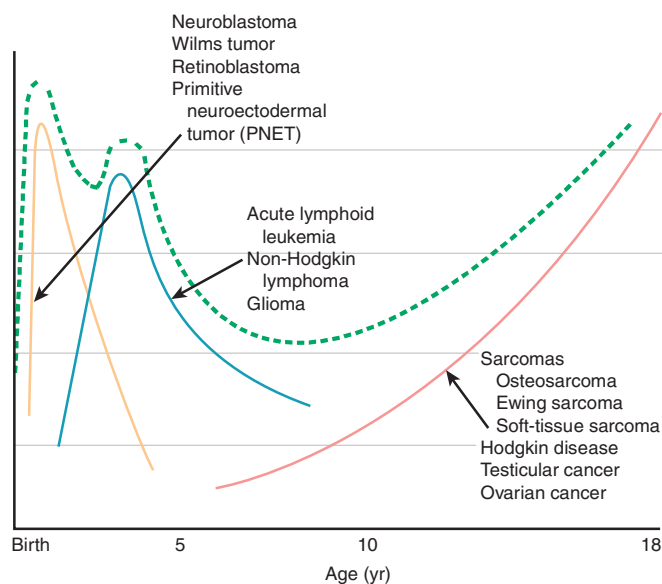


FIGURE 153.2 Incidence of the most common types of cancer in children by age. The cumulative incidence is shown as a dashed line. (Courtesy Archie Bleyer, MD.)

can mimic leukemia or lymphoma by causing fever, night sweats, lymphadenopathy, organomegaly, weight loss, and abnormal blood counts. Trauma may produce swelling that can mimic solid tumors. Idiopathic thrombocytopenic purpura and iron deficiency can produce thrombocytopenia and anemia, respectively. Immune deficiencies or irregularities (such as autoimmune hemolytic anemia, autoimmune neutropenia, or transient erythroblastopenia of childhood) can also produce cytopenias. Juvenile idiopathic arthritis and other collagen vascular disease can cause musculoskeletal pain, anemia, or thrombocytopenia, mimicking leukemia. Benign tumors are relatively common in children, including reactive adenopathy, mature germ cell tumors/hamartomas,

hemangiomas or other vascular tumors, mesoblastic nephromas, and bone cysts.

INITIAL DIAGNOSTIC EVALUATION

Screening Tests

A CBC with differential and review of the peripheral blood smear is the best screening test for many pediatric malignancies. Leukopenia (with or without neutropenia), anemia, or thrombocytopenia may be present in leukemia or any cancer that invades the bone marrow (e.g., neuroblastoma, rhabdomyosarcoma, and Ewing sarcoma). Leukemia may also produce leukocytosis, usually with blasts present on the peripheral blood smear. An isolated cytopenia (neutropenia, anemia, or thrombocytopenia) widens the differential diagnosis but still could be the only abnormal laboratory finding. Of note, a patient with leukemia may also have a normal CBC. Lactate dehydrogenase and uric acid are often elevated in fast-growing tumors (leukemia or lymphoma) and occasionally in sarcomas or neuroblastoma. In many cases, it is appropriate to assess electrolytes and renal and hepatic function in the screening process. Elevated blood pressure, if confirmed by repeat measurements, should prompt a urinalysis, as should the palpation of an abdominal mass. Serum (and/or cerebrospinal fluid) α -fetoprotein (AFP) and β -human chorionic gonadotropin (β -HCG) are screening tests (and tumor markers) for germ cell tumors. Serum AFP is also a tumor marker for hepatoblastoma. Urine homovanillic acid and vanillylmandelic acid are tumor markers for neuroblastoma.

Diagnostic Imaging

A chest x-ray (CXR) (posteroanterior and lateral) is the best screening radiographic study for a patient with suspicious cervical lymphadenopathy, fever, and weight loss. Mediastinal masses and pleural effusions can be detected on CXR. Abdominal signs or symptoms usually warrant an ultrasound or computed tomography (CT) scan. Persistent headaches or morning vomiting should prompt a CT scan or magnetic resonance imaging (MRI) of the head. For suspected bone tumors, plain radiographs are indicated and will usually reveal the lesion(s), if present, although radiographs may be normal when a bony pelvic lesion is suspected. CT or MRI should be obtained if radiographs are abnormal. Other imaging studies to delineate a mass and to search for suspected metastases are often indicated. Discussion with a radiologist is almost always helpful. Positron emission tomography (PET), usually combined with CT or MRI, is useful for staging and assessing response for lymphomas and sarcomas. Metaiodobenzylguanidine scans are useful for neuroblastoma. Table 153.3 shows the general use of diagnostic imaging following confirmation of a diagnosis of cancer, assessing the primary tumor and for metastases.

PEARLS FOR PRACTITIONERS

See *Oncology: Pearls for Practitioners* at the end of this section.

TABLE 153.1 Known Risk Factors for Selected Childhood Cancers

CANCER TYPE	RISK FACTOR	COMMENTS
Acute lymphoid leukemia	Ionizing radiation	Prenatal diagnostic x-ray exposure and therapeutic irradiation for cancer treatment increases risk.
	Race	White children have a twofold higher rate than Black children in the United States.
	Genetic conditions	Down syndrome is associated with an estimated 10- to 20-fold increased risk. Neurofibromatosis 1, Bloom syndrome, and ataxia-telangiectasia, among others, are associated with an elevated risk.
Acute myeloid leukemia	Chemotherapy and radiation therapy	Alkylating agents and epipodophyllotoxins increase risk, as does radiation therapy for other cancers.
	Genetic factors	Down syndrome and neurofibromatosis 1 are strongly associated. Familial monosomy 7 and several other genetic syndromes are also associated with increased risk.
Brain cancer	Ionizing radiation to the head	Radiation therapy for one brain tumor can lead to a secondary brain tumor.
	Genetic factors	Neurofibromatosis 1 is strongly associated with optic gliomas and, to a lesser extent, with other central nervous system tumors. Tuberous sclerosis and several other genetic syndromes are associated with increased risk.
Hodgkin disease	Family history	Monozygotic twins and siblings are at increased risk.
	Infections	Epstein-Barr virus and papillomaviruses are associated with increased risk.
Non-Hodgkin lymphoma	Immunodeficiency	Acquired and congenital immunodeficiency disorders and immunosuppressive therapy increase risk.
	Infections	Epstein-Barr virus is associated with increased risk in African countries.
Osteosarcoma	Ionizing radiation	Cancer radiation therapy and high radium exposure increase risk.
	Chemotherapy	Alkylating agents increase risk.
	Genetic factors	Increased risk is apparent with Li-Fraumeni syndrome and hereditary retinoblastoma.
Ewing sarcoma	Race	Incidence is about nine times higher in White children than in Black children in the United States.
Neuroblastoma	Genetic factors	Chromosome 6p22 variants and mutations in the <i>ALK</i> and <i>PHOX</i> genes are associated with increased risk.
Retinoblastoma	Genetic factors	Mutations in the <i>Rb</i> gene on chromosome 14
Wilms tumor	Congenital anomalies	Aniridia, Beckwith-Wiedemann syndrome, and other congenital and genetic conditions are associated with increased risk.
Renal medullary carcinoma	Sickle cell trait	Etiology is unknown.
Rhabdomyosarcoma	Congenital anomalies and genetic conditions	Li-Fraumeni syndrome and neurofibromatosis 1 are associated with increased risk.
Hepatoblastoma	Prematurity	Etiology is unknown.
	Genetic factors	Beckwith-Wiedemann syndrome, hemihypertrophy, Gardner syndrome, and familial adenomatous polyposis are associated with increased risk.
Hepatocellular carcinoma	Infections	Hepatitis B virus infection increases risk.
Malignant germ cell tumors	Cryptorchidism	Cryptorchidism is a risk factor for testicular germ cell tumors.

Modified from Scheurer ME, Lupo PL, Bondy ML. Epidemiology of childhood cancer. In: Pizzo PA, Poplack DG, eds. Principles and Practice of Pediatric Oncology. 7th ed. Philadelphia: Wolters Kluwer; 216:10.

TABLE 153.2 Common Manifestations of Childhood Malignancies

SIGN/SYMPTOM	SIGNIFICANCE	EXAMPLE
HEMATOLOGIC		
Pallor, anemia	Bone marrow infiltration	Leukemia, neuroblastoma
Petechiae, thrombocytopenia	Bone marrow infiltration	Leukemia, neuroblastoma
Fever, neutropenia	Bone marrow infiltration	Leukemia, neuroblastoma
SYSTEMIC		
Bone pain, limp, arthralgia	Primary bone tumor, metastasis to bone	Osteosarcoma, Ewing sarcoma, rhabdomyosarcoma, leukemia, neuroblastoma
Fever of unknown origin, weight loss, night sweats	Lymphoreticular malignancy	Hodgkin or non-Hodgkin lymphoma
Painless lymphadenopathy (especially in the cervical region)	Lymphoreticular malignancy, metastatic solid tumor	Leukemia, Hodgkin and non-Hodgkin lymphoma, Burkitt lymphoma, nasopharyngeal carcinoma, thyroid carcinoma
Cutaneous lesion	Primary or metastatic disease	Neuroblastoma, leukemia, Langerhans cell histiocytosis, melanoma
Abdominal mass	Abdominal/pelvic organ	Neuroblastoma, Wilms tumor, Burkitt lymphoma, hepatoblastoma, germ cell tumor
Hypertension	Sympathetic nervous system tumor	Wilms tumor, neuroblastoma, pheochromocytoma
Diarrhea	Vasoactive intestinal polypeptide	Neuroblastoma
Soft tissue mass	Local or metastatic tumor	Ewing sarcoma, osteosarcoma, neuroblastoma, rhabdomyosarcoma, germ cell tumor, thyroid carcinoma
Diabetes insipidus, galactorrhea, poor growth	Neuroendocrine involvement of hypothalamus or pituitary gland	Germ cell tumor, adenoma, craniopharyngioma, prolactinoma, Langerhans cell histiocytosis
Emesis, visual disturbances, ataxia, headache, papilledema, cranial nerve palsies	Increased intrathecal pressure	Primary brain tumor; metastasis
OPHTHALMOLOGIC		
Leukocoria	White pupil	Retinoblastoma
Periorbital ecchymosis	Metastasis	Neuroblastoma
Miosis, ptosis, heterochromia	Horner syndrome: compression of cervical sympathetic nerves	Neuroblastoma
Opsomyoclonus, ataxia	Paraneoplastic/immune	Neuroblastoma
Exophthalmos, proptosis	Orbital tumor	Rhabdomyosarcoma, neuroblastoma, lymphoma
THORACIC		
Anterior mediastinal mass	Cough, stridor, pneumonia, tracheal-bronchial compression	Germ cell tumor, T-cell lymphoma/leukemia, Hodgkin disease, primary mediastinal large B-cell lymphoma
Posterior mediastinal mass	Vertebral or nerve root compression; dysphagia	Neuroblastoma, ganglioneuroblastoma, ganglioneuroma

TABLE 153.3 Minimum Work-Up Required for Common Pediatric Malignancies to Assess Primary Tumor and Potential Metastases

MALIGNANCY	BMA/BX	CXR	CT SCAN	MRI	BONE SCAN, PET SCAN, OR PET-CT SCAN	CSF ANALYSIS	MARKER(S)	OTHER
Leukemia	Yes	Yes				Yes		
Non-Hodgkin lymphoma	Yes	Yes	Yes		Yes	Yes		
Hodgkin lymphoma	Yes	Yes	Yes		Yes			
CNS tumors				Yes		Yes		
Neuroblastoma	Yes		Yes		Yes		VMA, HVA	mIBG scan
Wilms tumor		Yes	Yes					
Rhabdomyosarcoma	Yes	Yes	Yes		Yes	Yes, for parameningeal tumors only		
Osteosarcoma		Yes	Yes (chest)	Yes (primary)	Yes			
Ewing sarcoma	Yes	Yes	Yes (chest)	Yes (primary)	Yes			
Germ cell tumors		Yes	Yes				AFP, β -hCG	Consider brain MRI
Liver tumors		Yes	Yes				AFP	
Retinoblastoma	$\pm$		Yes, if MRI not available	Yes (brain)	$\pm$	Yes		Rb gene analysis

*Individual cases may require additional studies.

AFP, α -fetoprotein; BMA/bx, bone marrow aspirate/biopsy; CNS, central nervous system; CSF, cerebrospinal fluid; CT, computed tomography; CXR, chest x-ray; β -HCG, β -human chorionic gonadotropin; HVA, homovanillic acid; mIBG, metaiodobenzylguanidine; MRI, magnetic resonance imaging; PET, positron emission tomography; Rb, retinoblastoma; VMA, vanillylmandelic acid.