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REVIEW PAPER

Oncological vigilance in pediatric practice

Karolina Gawle-Krawczyk, Paweł Łaguna

Department of Oncology, Pediatric Hematology, Clinical Transplantology and Pediatrics, University Pediatric Hospital, Medical University, Warszawa, Poland

ABSTRACT

Annually in Poland, malignant neoplasms are diagnosed in approximately 1100–1200 pediatric patients. 5-year overall survival is observed in 81.2% of patients, reflecting substantial progress in pediatric oncology that encompasses enhanced diagnostic capabilities, innovative therapeutic agents, multimodal treatment strategies, and optimized supportive care protocols. However, classical manifestations of malignancy frequently overlap with benign pathologies commonly encountered in the pediatric population, contributing to delayed diagnosis and increased treatment failure rates. Consequently, comprehensive physical examination with heightened oncological awareness is imperative during routine clinical encounters. This vigilant approach may facilitate early neoplastic detection at lower clinical stages, thereby significantly improving prognostic outcomes and decreasing therapeutic toxicity.

KEY WORDS:

neoplasms, lymphadenopathy, leukemia, oncological vigilance.

INTRODUCTION

In Poland, nearly 1,200 malignant neoplasms are diagnosed annually in the pediatric population [1]. While relatively uncommon in this population, it represents the second leading cause of pediatric mortality after accidents, trauma and toxicological events, and remains the predominant cause of disease-related mortality [2]. Hematologic malignancies, predominantly leukemias, constitute the largest proportion at 27% of all neoplastic disorders. Central nervous system (CNS) neoplasms represent the second most prevalent category [3], followed by neuroblastoma, which demonstrates the highest incidence among infantile malignancies. The epidemiological distribution of specific malignancies is comprehensively illustrated in Figure 1.

Current epidemiological data indicate that 70–80% of pediatric oncology patients achieve complete remission. However, it should be emphasized that despite these significant therapeutic advancements, the majority of cases are diagnosed with advanced-stage disease (stage III or IV) at initial diagnosis, correlating with increased therapeutic failure rates [4]. A primary diagnostic challenge in pediatric oncology is that clinical manifestation of malignancies is highly variable, with non-specific and ubiquitous symptoms. Classical manifestations of malignancy, including fever, lymphadenopathy, asthenia and cephalalgia, frequently overlap with numerous benign pathologies commonly observed in pediatric populations [4, 5]. Therefore, early detection of neoplastic disorders in pediatric patients necessitates comprehensive clinical assessment during routine clinical encounters, including infectious disease assessments, pre-vaccination screening, and developmental milestone evaluations. The evaluation protocol must encompass detailed medical history taking from parents and thorough physical examination including systematic lymph node palpation and abdominal examination. In male patients, testicular examination is man-

ADDRESS FOR CORRESPONDENCE:

Dr. Karolina Gawle-Krawczyk, Department of Oncology, Pediatric Hematology, Clinical Transplantology and Pediatrics, University Pediatric Hospital, Medical University, Warszawa, Poland,
e-mail: karolina.gawle@uckwum.pl

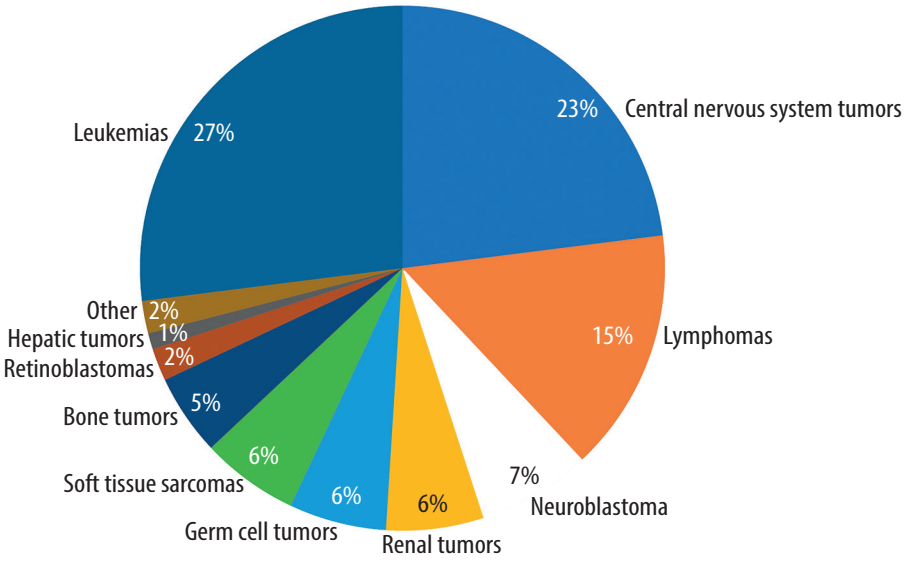

FIGURE 1. Incidence of pediatric malignancies in Poland (based on: Pediatrics. Wydawnictwo Lekarskie PZWL, Warszawa 2018)

datory as it may reveal signs of testicular leukemic infiltration or testicular tumors.

A comprehensive understanding of the symptoms associated with neoplasms and oncological vigilance in pediatric practice facilitates early disease detection and prompt referral to a specialized pediatric hematology and oncology center. The earlier the diagnosis is made and the appropriate treatment applied, the better the chances of improved prognostic outcomes and reduced treatment-related toxicity [4].

GENERAL SYMPTOMS AND MEDICAL HISTORY

Clinical evaluation of pediatric patients with confirmed malignancy reveals alarming symptoms in the majority of cases on both subjective assessment and physical examination. Neoplastic processes may demonstrate insidious progression giving rise to acute bone pain, often misattributed to trauma, or manifest themselves with recurrent headaches persisting over extended periods. Pyrexia, frequently misinterpreted as having an infectious etiology, may delay definitive diagnosis. Prolonged fever of unknown origin can indicate various malignant processes, with the highest prevalence observed in leukemia, lymphoma, and neuroblastoma [2, 6].

Multiple non-specific symptoms including fatigue, malaise, reduced physical activity, loss of appetite and unintentional weight loss, unrelated to acute infection, may be a manifestation of underlying malignancies [2, 6]. These systemic manifestations result from increased metabolic demands of rapidly proliferating neoplastic cells and may also arise from body hypoxia due to anemia.

Significant weight loss (exceeding 10% within 6 months), accompanied by diaphoresis (particularly nocturnal), cutaneous pruritus, and lymphadenopathy strongly suggest Hodgkin lymphoma [6, 7]. The constellation of pallor, asthenia, increased bruising tendency, epistaxis, and lack of appetite associated with anemia or a hemorrhagic diathesis is highly suggestive of leukemia, especially when accompanied by lower limb pain and abdominal distention. In such cases, complete blood count with peripheral blood smear microscopy provides definitive diagnostic evidence [6, 8].

During parental medical history taking, particular attention must be directed toward symptom chronology and severity. Certain malignancies, such as non-Hodgkin lymphoma, demonstrate aggressive progression with tumor mass doubling within 24 hours, potentially resulting in life-threatening complications. Conversely, other neoplasms may present with gradual symptom progression, such as progressive weight loss or nocturnal diaphoresis characteristic of Hodgkin lymphoma. Currently, it is estimated that 4–10% of cancers are associated with genetic predispositions to neoplasia. Therefore, thorough evaluation of the patient's medical history requires attention to disease burden, child's developmental history, and comprehensive family history focusing on oncological and genetic disorders.

The following sections detail the subjective symptomatology and physical manifestations of specific malignancies, categorized by affected organ systems.

LYMPHADENOPATHY

Lymphadenopathy is a prevalent clinical manifestation in the pediatric population. In the vast majority of cases, it is a benign condition affecting the cervicofacial region, being a sign of infection occurring in this area [9]. Reactive lymph nodes associated with respiratory tract infections typically present as discrete, tender lymph node enlargement without tendency to coalescence. Primary lymphatic infection manifests with pyrexia, lymph node tenderness on palpation, decreased nodal consistency and overlying cutaneous erythema. The presence of fluctuance suggests abscess formation.

In contrast, lymph nodes exceeding 2–3 cm in diameter, demonstrating firm consistency, absence of inflammatory characteristics (including tenderness and local hyperthermia), lack of cutaneous erythema, progressive enlargement despite antimicrobial therapy, and pathological vascularization patterns on ultrasonography warrant heightened oncological vigilance. An alarming symptom is the asymmetric appearance of a lymph node conglomerate in the supraclavicular fossa area, always suggestive of an underlying proliferative process [6, 7, 9]. An accompanying abdominal mass may suggest neuroblastoma or lymphoma [3]. The combination of hepatosplenomegaly with systemic manifestations including osseous pain, pallor, petechiae, and fever without evident infectious etiology, accompanied by generalized or localized lymphadenopathy, should prompt consideration of acute leukemia [2, 5]. Lymphatic metastases may occur in sarcomas or thyroid carcinoma [7]. All of these clinical presentations necessitate immediate referral to specialized pediatric oncology-hematology centers. Additional investigations helpful in the diagnosis of malignancy include complete blood count with microscopic smear, assessment of inflammatory parameters, lactate dehydrogenase test, ultrasound of lymph nodes and abdomen, and chest X-ray [2, 9].

CUTANEOUS MANIFESTATIONS

Pallor of the skin and mucous membranes may indicate anemia secondary to acute leukemia. Associated symptomatology includes palpitations, asthenia, and fatigue. The skin may also demonstrate symptoms of thrombocytopenia i.e. spontaneous or minor trauma induced ecchymoses, potentially accompanied by gingival bleeding or epistaxis. Petechial hemorrhages may also occur (Fig. 2), which may be subtle, necessitating meticulous examination of cutaneous surfaces and oral mucosa. Similar clinical manifestations may result from bone marrow metastases from various malignancies, including solid tumors, non-Hodgkin lymphoma, or Hodgkin lymphoma [2].

Expansion of leukemic cells can affect multiple tissues and organs, including skin and mucous membranes, more commonly in non-lymphoblastic acute leukemia (Fig. 3) [10]. Cutaneous manifestations demonstrate variable morphology, ranging from macular lesions and infiltrates to nodular formations, typically presenting with violaceous to brownish discoloration [11]. Another important skin symptom associated with malignancy is persistent skin itching leading to excoriations and scratches, suggesting Hodgkin lymphoma [6].

RESPIRATORY SYMPTOMS

Although cough etiology encompasses numerous pathologies, malignancy must be included in the differential diagnosis. Nonproductive cough or dyspnea persisting beyond three weeks, without apparent etiology or demonstrating therapeutic resistance, may indicate mediastinal neoplasia associated with Hodgkin lymphoma, non-Hodgkin lymphoma, leukemia (Fig. 4), or neuroblastoma, warranting comprehensive diagnostic evaluation. Initial imaging should include anteroposterior and lateral chest radiographs

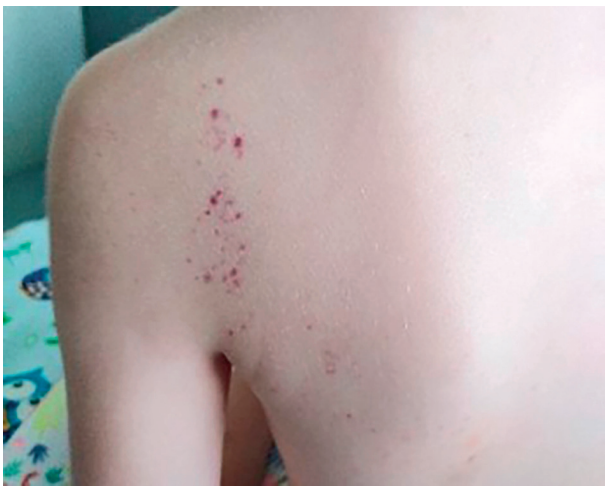

FIGURE 2. Petechiae as a manifestation of thrombocytopenia (own source)

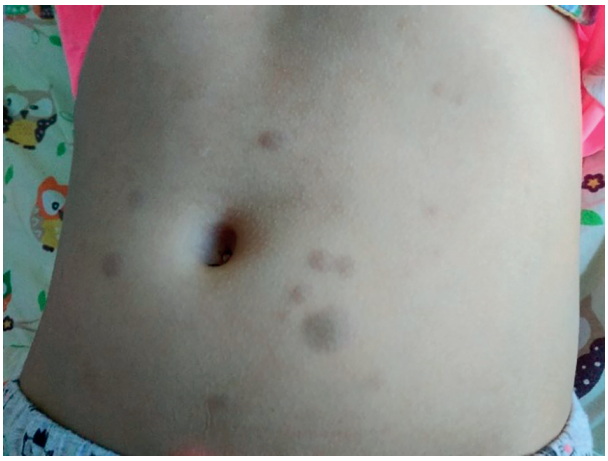

FIGURE 3. Cutaneous infiltrates in the course of acute myeloid leukemia in a 9-year-old girl (own source)

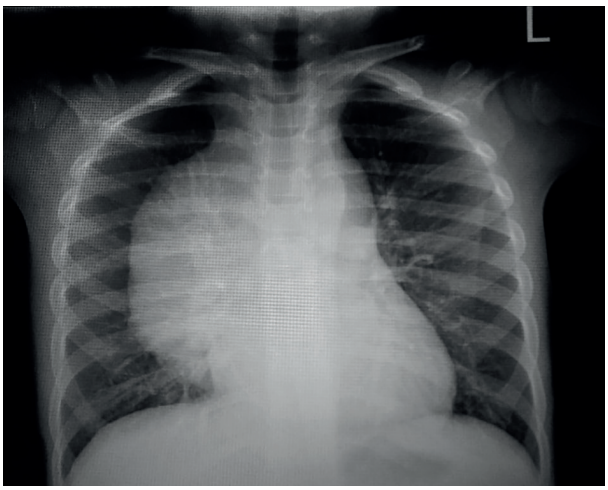

FIGURE 4. Chest X-ray. Mediastinal mass in a 7-year-old boy with T-cell acute lymphoblastic leukemia (own source)

[2, 6]. Moreover, it is necessary to note whether the patient presents with other symptoms such as dyspnea, dilated neck and chest veins, facial and upper body edema, and cyanosis, which are characteristic of superior vena cava syndrome. On physical examination, diminished breath sounds and dullness to percussion over the lung fields can be detected. Superior vena cava syndrome represents a medical emergency, predominantly caused by rapidly progressive non-Hodgkin lymphoma or leukemia, necessitating immediate transfer to pediatric oncology-hematology facilities for urgent cytoreductive therapy [2, 7, 9, 10].

MUSCULOSKELETAL SYSTEM MANIFESTATIONS

Musculoskeletal pain warranting oncological evaluation demonstrates characteristic features: exacerbation with physical activity, progressive throughout the day, escalating intensity, and resistance to analgesic therapy. Attention should be paid to whether they are accompanied by reduced joint mobility and limping [6]. Localized pain accompanied by swelling or anatomical deformation necessitates bilateral radiographic imaging. While osseous pain frequently indicates primary bone malignancy, it may also manifest secondary to leukemic subperiosteal infiltration or metastatic bone involvement from other primary neoplasms.

Pathologic fracture through neoplastically infiltrated or weakened bone may represent the initial manifestation of osteosarcoma or Ewing sarcoma [2, 6]. Osteosarcoma, the most prevalent primary malignant bone neoplasm, characteristically involves the distal femur or proximal tibia; therefore, knee pain in adolescents during periods of rapid growth warrants heightened clinical suspicion. While primary pediatric bone tumors most commonly demonstrate predilection for the periarticular knee region, they may arise in any osseous structure, including the cranial vault, ribs, and vertebrae. This pattern of multifocal skeletal involvement, with characteristic local bone destruction, is particularly typical of Langerhans cell histiocytosis [12].

While systemic inflammatory disorders are frequently considered in the differential diagnosis of osteoarticular pain with pyrexia or subfebrile states, bone marrow evaluation remains essential to exclude hematopoietic malignancies. This is particularly crucial as glucocorticoid therapy, commonly employed in rheumatologic conditions, is also utilized in acute lymphoblastic leukemia induction protocols. Temporary symptomatic improvement with corticosteroids may obscure underlying malignancy and delay definitive diagnosis and appropriate therapeutic intervention [13].

ABDOMINAL AND PELVIC SYMPTOMS

Among pediatric abdominal and pelvic malignancies, neuroblastoma and nephroblastoma (Wilms tumor) predominate in children younger than 5 years, while lymphomas, soft tissue sarcomas, and germ cell neoplasms are more prevalent in older age groups. Notably, lymphoma must be considered in the differential diagnosis of intussusception occurring in children over six years of age [3, 6].

Primary presenting manifestations of intra-abdominal neoplasms include increased abdominal circumference, abdominal pain, nausea, vomiting, and constipation. Comprehensive physical examination, performed at each clinical encounter, should include thorough abdominal assessment evaluating contour abnormalities, assessment of liver and spleen size, and exclusion of pathological masses. Testicular examination in boys and vulvar inspection in girls are essential.

Neuroblastoma demonstrates a high incidence of stage IV disease at initial diagnosis, significantly compromising therapeutic outcomes despite intensive treatment protocols. Notably, advanced-stage disease carries only 30–50% probability of cure [14]. This malignancy exhibits predilection for intra-abdominal primary location in approximately two-thirds of cases [2]. Neuroblastoma is referred to as the "king of general symptoms" [15], due to its diverse, nonspecific symptomatology that may simulate various neoplastic and non-neoplastic conditions [14]. Clinical manifestations encompass abdominal pain, cachexia, altered bowel habits, pyrexia or subfebrile states, fatigue, behavioral alterations, and weight loss [2].

Nephroblastoma (Wilms tumor) frequently demonstrates insidious, asymptomatic progression, ultimately manifesting with hematuria, micturition disturbances, and increased abdominal circumference. On physical examination, in addition to pathological abdominal resistance, hypertension may be present [2]. Detection of any intra-abdominal mass or hepatosplenomegaly, particularly when accompanied by constitutional symptoms such as appetite disorders, pyrexia, or abdominal pain, necessitates ultrasonographic evaluation of the abdomen and retroperitoneal space [2, 5, 6].

NEUROLOGICAL SYMPTOMS

Neurological manifestations are documented across multiple tumor types, with an 88% prevalence in patients presenting with CNS neoplasms [6]. It is the second most frequent pediatric neoplastic disorder. Cephalalgia constitutes the initial presenting symptom in more than one-third of intracranial neoplasms, typically preceding additional neurological manifestations.

Rapid diagnostic evaluation is required for headaches occurring in early morning or night hours, disrupting sleep, particularly when accompanied by morning emesis and apathy [2, 6]. The characteristic pattern demonstrates gradual, progressive symptom intensification. Activities increasing intracranial pressure (coughing, sneezing, abdominal tensing), typically intensify the pain [16]. Headaches may be accompanied by vomiting, which sometimes may be the only symptom of a proliferative process. These occur in morning hours, usually without preceding

nausea, demonstrating projectile character (sudden ejections) with head position changes, independent of meals [16]. Among other alarming symptoms are focal deficits secondary to cerebral involvement, including afebrile focal seizures in previously non-epileptic children, ataxia, visual disturbances, paralysis, and paresis. Sudden learning difficulties, personality changes, and developmental delay also raise significant concern [5, 6, 16].

In leukemia, the most prevalent pediatric malignancy, cephalalgia may result from anemia, vascular complications, cerebral and meningeal involvement, or cranial neuropathies – predominantly affecting cranial nerves VII, III, IV, and VI [2]. Cephalalgia may also manifest secondary to arterial hypertension associated with pheochromocytoma or neuroblastoma [17–19].

OCULAR MANIFESTATIONS

Retinoblastoma represents the predominant intraocular neoplasm, with peak incidence before the second year of life. Clinical manifestations include leukocoria (abnormal white pupillary reflex, frequently detected in flash photography), strabismus of the affected eye, and visual impairment.

Ophthalmologic manifestations including exophthalmos, strabismus, nystagmus, and visual disturbances may indicate intraocular or CNS neoplasms. Neuroblastoma may be presented with Horner syndrome or paraneoplastic opsoclonus-myoclonus syndrome, characterized by the clinical triad of ataxia, myoclonus, and chaotic saccadic eye movements. Advanced neuroblastoma characteristically presents with periorbital ecchymoses ("raccoon eyes") secondary to orbital soft tissue infiltration by malignant cells [2, 5, 6, 20].

CONCLUSIONS

Clinical awareness of neoplastic manifestations and maintenance of high oncological vigilance in pediatric practice facilitates early-stage disease detection, thereby optimizing therapeutic outcomes and survival probability.

DISCLOSURES

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