Spectrum of Syndromic Disorders Associated with Pediatric Tumors

Evolving Role of Practical Imaging Assessment

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KEYWORDS

• Syndromic disorders • Pediatric tumors • Imaging • Assessment

KEY POINTS

- Multi-organ system abnormalities in pediatric patients should alert to syndromic associations and trigger genetic counseling.
- Despite chromosomal localization and gene identification, phenotypic manifestations of these syndromes are highly variable.
- Early and accurate diagnosis of the syndrome allows better appropriation of care and prompt life-saving surveillance. A multidisciplinary team approach is essential.
- Radiologic imaging plays a pivotal role in surveillance, diagnosis, and treatment in these syndromic tumors as lesions may be disparate and spatially broad in span.
- Future advancements in whole-body MR imaging and potentially PET/MR imaging may mitigate ionizing radiation in the imaging evaluation of syndromic tumors in pediatric patients.

INTRODUCTION

Although most pediatric tumors develop sporadically, advancements in genetic testing and improved understanding of familial association with certain type of neoplasms have expanded the range of cancer predisposition syndromes that contribute to specific tumors in the pediatric population. Although these syndromic tumors still represent a minority of incidences of total pediatric tumors, recognition of these syndromes is growing rapidly. Most syndromic disorders associated with pediatric tumors demonstrate a clear genetic mode of transmission, such as autosomal dominant or x-linked transmission. Others show distinctive familial tendencies without identification of a causal gene. In general, many of these syndromes occur because of errors in gene functioning that impact tumor suppressor genes, oncogenes, or DNA stability repair genes.

Recognition of these syndromes is crucial to optimize clinical care and family counseling. Generally, this requires a multidisciplinary team including genetic counselors, pediatric oncologists, radiologists, and surgeons who are able to tailor biochemical and imaging surveillance strategies to the specific needs of pediatric patients. In

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certain situations, prophylactic surgery may be considered to prevent expected cancers. The aim of these strategies should be to aid in early detection and treatment of childhood cancers. Appropriate, early screening is even more critical in pediatric patients given their long-expected life span in which to manifest these tumors.

Although the list of genetic tumor predisposition syndromes is ever increasing with better understanding of genetics and transmission, for the scope of this review, the authors focus on the relatively commonly encountered syndromes with attention to key genetic traits, clinical features, imaging findings, and treatment as well as current management options.

IMAGING TECHNIQUES

Ultrasound

Ultrasound (US) is the primary initial modality for abdominal imaging in children. It provides multiplanar imaging and has 3-dimensional (3D) capabilities.[1] As smaller pediatric patients with minimal visceral fat, children are well suited to US imaging and can usually be imaged with high-frequency transducers (>7 MHz), which provide excellent resolution. US is also well tolerated in children without sedation or anesthesia; real-time imaging provides ample opportunity to optimize a study with uncooperative patients.

Because sonography does not use ionizing radiation, it is an ideal modality for screening examinations whereby repeated imaging could contribute to a substantial radiation dose over a long interval of screening. Additionally, US is relatively inexpensive in comparison with computed tomography (CT) and MR imaging; among pediatric patients who may need repeated imaging examinations, this can represent a substantial cost savings over a long period.

Newer techniques in US, including 3D sonography, elastography, and US contrast, are rapidly gaining acceptance in clinical practice and have the potential of transforming US. Three-dimensional imaging allows more accurate evaluation of anatomy with improved volumetric measurements. Although most frequently used in adult cardiac and renal imaging, there is untapped potential in pediatric oncology, whereby 3D US could delineate spatial relationships for surgical planning and tumor resection. Elastography estimates the difference in stiffness between tissues by assessing the compressibility of the tissue when subjected to transducer pressure. This technique may contribute to the diagnosis of malignancy by identifying the ways in which tumor alters the mechanical properties of tissues.[2,3] Finally US contrast agents use microscopic bubbles of air or perfluorocarbon gas bubbles that create backscatter that can be detected by the transducer. Although intravenous (IV) US contrast is not used in pediatric clinical practice in the United States, early research suggests that this contrast may be beneficial in tumor imaging, specifically to identify tumor vascularity.[3]

Computed Tomography

CT should be used judiciously in children because of their radiosensitivities (higher than that of adults) and longer expected life spans, during which radiation-induced neoplasms may manifest.[4] In pediatric patients with tumor-predisposition syndromes, the risk of eventual neoplasm is much higher than the average population; CT should be used sparingly, especially in patients with DNA repair defects. Certainly, US and MR imaging are the preferred modalities for imaging these children.

In acute, life-threatening scenarios, CT can be essential for emergency imaging. It may also provide important information when MR imaging is contraindicated or in clinical settings where US and MR imaging have suboptimal sensitivities, such as in the detection of small lung nodules. When the benefits of CT exceed potential harm, CT usage should be optimized using the principles of ALARA (as low as reasonably achievable) to permit appropriate diagnosis and treatment.

MR Imaging and Whole-Body MR Imaging

MR imaging provides excellent soft tissue contrast without the use of ionizing radiation, rendering it an essential noninvasive tool in the imaging strategy for pediatric patients with tumor predisposition syndromes. The emergence of whole-body MR imaging (WB MR imaging) technology is especially pertinent in the surveillance of pediatric patients with these syndromes, because many of these syndromes are associated with tumors that may span large (extensive) anatomic regions, which may be imaged in a single session with WB MR imaging. WB MR imaging has been used in patients with lymphoma but is also used as a screening tool in patients with neurofibromatosis type 1 and Li-Fraumeni because these syndromes are associated with a high tumor burden that may be scattered throughout discontinuous anatomic areas.[5]

WB MR imaging can be performed within 45 to 60 minutes on both 1.5- and 3.0-T magnets. Sequences can be obtained with continuous table motion, and ever-improving coil technology allows for even shorter examination times. Theoretic advantages of imaging on a 3.0 T-magnet include