Int J Clin Exp Pathol 2015;8(9):11543-11548
www.ijcep.com /ISSN:1936-2625/IJCEP0012676

Original Article

Pattern of primary tumors and tumor-like lesions of bone in children: retrospective survey of biopsy results

Esra Akyüz Özkan[1], Ceren Canbey Göret[2], Zeynep Tuğba Özdemir[3], Serdar Yanık[4], Meryem Doğan[5], Aylin Gönültaş[6], Ayşe Neslin Akkoca[7]

[1]Department of Pediatrics, Bozok University Medical Faculty, Yozgat, Turkey; [2]Department of Pathology, Haydarpasa Numune Training and Research Hospital, Istanbul; [3]Department of Internal Medicine, Bozok University Medical Faculty, Yozgat, Turkey; [4]Department of Pathology, Iskenderun State Hospital, Hatay, Turkey; [5]Department of Pathology, Atatürk University Medical Faculty, Erzurum, Turkey; [6]Department of Pathology, Tekirdağ State Hospital, Tekirdağ, Turkey; [7]Department of Family Medicine, Iskenderun State Hospital, Hatay, Turkey

Received July 9, 2015; Accepted August 21, 2015; Epub September 1, 2015; Published September 15, 2015

Abstract: Background: Although primary bone tumors are relatively uncommon, they constitute the most important tumors in patients less than 20 years. We aimed to determine the frequencies of primary bone tumors and tumor-like lesions of bone and the anatomical sites of their occurrence. Methods: A retrospective review of histopathology reports of all bone specimens received in a private pathology laboratory in Istanbul between 2009 and 2015. Results: A total of 57 patients (aged 5 to 18 years) with a mean of 13.12 years were studied. Thirty five patients (61.4%) were males and 22 (38.6%) were females. Fifty five (94.4%) of the tumors were benign. Osteochondroma was the commonest tumor accounting for 31 cases (54.3%) followed by osteoid osteoma, 9 cases (15.7%). Chondrosarcoma observed in two patients and Ewing sarcoma in one patient as malignant tumors. Of the 57 bone tumors 13 (22.8%) occurred in the upper extremities, while 44 (77.2%) were in the lower extremities. Proximal humerus was the most commonly involved site in upper extremity tumors, with osteochondromas representing the most frequent type of tumor (4 patients; 7%). In the lower extremities again osteochondromas were the most common type of tumor (8 cases, 14%), with the femur being the most common site of involvement (18 patients, 31.5%). Of the patients with tumor-like lesions; four patients had fibrous dysplasia, 4 patients had non-ossified fibromas, 4 patients had simple bone cysts and 3 had aneurismal bone cyst. Conclusion: This study showed that primary bone tumors were mainly benign, settled predominantly in the lower extremities mostly in the femur with a male preponderance. Osteochondroma was the most common benign bone tumor. We didn't observed osteosarcoma, which is the most frequent malignant bone tumor.

Keywords: Benign, bone tumors, malignant, pediatric

Introduction

Although bone tumors comprise only 0.2% of all tumors, they represent the 3rd leading tumor type in younger populations with important diagnostic and therapeutic implications [1].

Pediatric bone tumors may manifest with a variety of symptoms depending on the localization, size and type of the tumor. Typically the pain is nocturnal or elicited by activity, with progressive increase in intensity in later stages. Clinical examination may reveal a swelling or palpable mass, in addition to limitation in the range of motion, skin changes, neurogenic deficits, vascular defects, or pathological fractures. High fever, malaise, and weight loss generally occur with metastases.

Primary malignant bone tumors occur more commonly in children and adolescents than in adults. Their etiopathogenesis is unclear and they usually exhibit a slow growth pattern. Previous radiotherapy for bone tumors and a history of trauma may also increase the risk. White male children are at increased risk of bone tumors. Hereditary tumors such as retinoblastoma or Li-Fraumeni syndrome (multiple neoplasms, particularly breast cancer, adrenal gland carcinoma, leukemia, and soft tissue sar-

Table 1. Bone tumors according to the tissue of origin

	No.	%
Osteoblastic	9	15.7
Chondroblastic	33	57.8
Fibrous tissue	7	12.2
Cystic lesions	7	12.2

comas) are also associated with an increase in the risk of bone tumors [2, 3]. According to generally accepted ICCC (International Classification of Childhood Cancer), malignant bone tumors in children are divided into osteosarcoma, chondrosarcoma, Ewing tumor and related bone sarcomas, "other specified malignant bone tumor" and "unspecified malignant bone tumor". Osteosarcoma and Ewing's sarcoma commonly occur in children [4].

In patients with bone tumors, radiological examination is complementary to the clinical examination, providing even more information than the clinical examination in many instances. The objectives of the radiological examination include providing information that may assist in differential diagnosis, in determining the nature and extent of the tumor as well as the appropriate biopsy site, and in the monitorization of the effect of treatment [5]. Biopsy represents the last step in the assessment that is essential in the management of all malignant tumors and also for benign lesions in certain circumstances. An accurate diagnosis without biopsy can usually be readily made by X-ray alone in lesions such as simple bone cysts, fibrous cortical defects, and osteochondromas.

Materials and methods

A total of 57 benign or malignant tumors of osseous or cartilaginous tissue origin diagnosed between January 2009 and April 2015 at Istanbul Ekin Private Pathology laboratory comprised the study sample population.

Large biopsy samples were initially cut by a saw for preparation for fixation, and then were fixated using 10% buffered neutral formaldehyde. Following 1 day of fixation, the biopsy samples with osseous tissue were decalcified with 20% formic acid, which is utilized for general decalcification procedures. The diagnosis, age at the time of diagnosis, and gender distribution of the benign and malign tumors were evaluated.

Results

Of the 57 pediatric cases with bone tumors, 35 were male and 22 were female with a mean age of 13.12 years (range: 5-18 y). Fifty five (94.4%) of the tumors were benign.

Nine lesions (15.7%) were osseous in origin, 33 (57.8%) were found to arise from the cartilage tissues, and 15 (26.3%) were tumor-like lesions (**Table 1**). The clinic features of the bone tumors were summarized in the **Table 2**.

There were 9 cases of osteoid osteomas among those children with bone tumors (15.7%), with 8 male and one female patient, with a mean age of 14.88 years old.

Of the tumors of cartilaginous origin, 31 patients (54.3%) had osteochondroma, and of these 21 were male and 10 were female with a mean age of 12.51 years old.

Simple bone cysts, aneurismal bone cysts, fibrous dysplasia, and non-ossifying fibromas were found in 4 (7%), 3 (5.2%), 4 (7%), and 4 (7%) of the patients with tumor-like lesions, respectively.

Of the 57 bone tumors 13 (22.8%) occurred in the upper extremities, while 44 (77.2%) were in the lower extremities. Proximal humerus was the most commonly involved site in upper extremity tumors, with osteochondromas representing the most frequent type of tumor (4 patients; 7%). Of the tumors involving the metacarpal bones, 2 were osteochondromas or one non-ossifying fibroma. Again, of the tumors in the upper extremities, one patient had Ewing's sarcoma in the mandibula, one had osteochondroma in the radial bone, and one patient had aneurysmal bone cyst of the vertebra. One patient had osteoid osteoma in the humerus. There were no cases of osteoblastomas or osteosarcomas in the upper extremities. Of the tumors of cartilaginous origin in the upper extremities, 6 patients (10.5%) had osteochondromas, 4 in the humerus and 2 in the metacarpal bones. No other benign or malignant tumors of cartilaginous origin were detected in the upper extremities. Again, fibroosseous lesions, there was only one case of non-ossifying fibroma in the metacarpal bones. Two patients had humeral simple bone cysts, while another had aneurysmal bone cyst in the humerus and another in the vertebra.

Table 2. Clinic features of the bone tumors in children

Origin	Most frequent site	Mean age (year)	Most common sex	%
Chondroblastic				
Osteochondroma	Femur	12.51	Male	54.3
Chondrosarcoma	Femur, tibia	13	Male-Female	3.5
Osteoblastic				
Osteoid osteoma	Femur	14.88	Male	15.7
Tumor-like lesions				
Fibrous dysplasia	Femur	13.5	Male-Female	7
Non-ossified fibroma	Tibia-femur-metacarpal bone	11.33	Female	7
Simple bone cyst	Femur-humerus	12.75	Female	7
Aneurismal bone cyst	Humerus, fibula, vertebra	11	Female	5.2

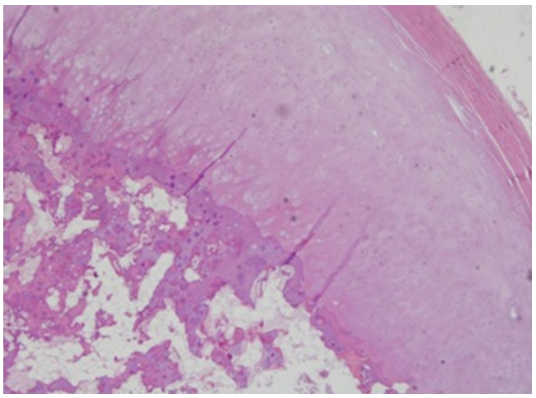

Figure 1. Osteochondroma lesion has a cartilaginous cap within the trabecula of bone underlying fibrous connective tissue (H&E & 40).

In the lower extremities osteochondromas were the most common type of tumor (8 cases, 14%), with the femur being the most common site of involvement (18 patients, 31.5%). Similarly, the most frequent tumor type in this localization, i.e. femur, was osteochondroma (7 patients, 12.2%), followed by osteoid osteoma (4 patients, 7%). Osteochondroma (8 patients, 14%), osteoid osteomas (5 patients, 8.7%), and simple bone cysts (2 patients, 3.5%) most commonly occurred at the proximal femur. Osteochondroma was the most frequent type of tumor in the lower and upper extremities.

Of the tumors of osseous origin in the lower extremity, 8 patients (14%) had osteoid osteoma, with no cases of osteosarcomas. Four patients had the lesion in the diaphysis of the femur, while had the tumor in proximal tibia, and 3 in the toes. Osteochondroma was the most common type of chondroblastic tumors (25 patients, 43.8%), followed by chondrosarcoma occurring in 2 cases (3.5%), one each in tibia and femur. Solitary osteochondromas were located in distal femur in 9, proximal tibia in 8, metatarsal bones in 8, and fibula in one patient.

Of the patients with tumor-like lesions, four patients had fibrous dysplasia and 4 patients had non-ossified fibromas. Of the latter 4 lesions, two were localized in distal tibia, while one was in femur and one localized in metacarpal bone. Of the 4 patients with fibrous dysplasia, two were in femur; one was a lesion in tibia and feet. Four patients were found to have simple bone cysts, two were localized in the femur and two were in humerus. Of the 3 patients with aneurismal bone cysts, one lesion in humerus, fibula, and vertebra, one in each.

Discussion

Bone tumors are classified as benign or malignant according to the tissue of origin, as well as their patterns of growth and behavior [6-8]. The majority of pediatric bone tumors are of benign character with distinctive and specific radiographic and clinical features, obviating the need for biopsy [9]. Common benign bone tumors include osteochondroma, endochondroma, osteoid osteoma, osteoblastoma, chondroblastoma and hemangioma. Also, tumor-like lesions that may occur frequently in children include non-ossified fibroma, simple bone cyst, and fibrous dysplasia [10].

Bones comprise cartilaginous and osteoid elements, giving rise to the classification of bone tumors based on the type of proliferating cells originating from these tissues. Osteosarcomas arise from the osteoid tissue and represent the most common type of childhood bone tumors, followed by Ewing's sarcoma of neural origin [11].

The initial step in the assessment of patients with bone tumors is a good medical history, including age, gender, type and duration of

symptoms, localization of the mass, and presence of a history of trauma. The most common benign bone tumor occurring in children is osteochondromas, representing 10 to 15% of all bone tumors and 20 to 50% of all benign bone tumors [12]. Bone tumors occur more commonly in males. The most common presenting symptom is pain and the most common site of occurrence is the knee and its adjacency. X-ray examination is the initial and fundamental test in the diagnosis of bone tumors. Other examinations that are certainly required for the diagnosis and staging include computed tomography, magnetic resonance imaging, and scintigraphy. Biopsy is the final step in the assessment and staging.

While benign bone tumors exert a pressure effect on normal tissues and cause bone resorption by the osteoclastic cells, malignant bone tumors also result in the destruction of normal tissues as well. The site and appearance of the lesions as well as the patient age give important clues regarding the type of bone tumors. Malignant bone tumors comprise 2 to 4% of all tumors in children under 15 years of age, while this figure rises to 6.5% in those between 15 and 19 years of age [13, 14]. Most benign tumors are confined within the limits of the anatomic structure in which they arise from, leading to the bone growth in that direction. While malignant tumors exhibit a bi-compartmental behavior, outgrowing the cortex into the adjacent soft tissues. Benign tumors may exhibit a slow growth pattern parallel to the normal growth of the individuals and stop growing at later stages, while others may show a progressive enlargement requiring wide excision. Malignant tumors, on the other hand, have two types of behavior, namely the “low” or “high” grade behavior with corresponding growth patterns [11].

Small sized multiple lesions with readily discernible sclerotic margins and without cortical destruction are frequently benign in nature, as compared to potentially malignant lesions causing concerns with blurred margins, cortical destruction and accompanying periosteal reaction, larger dimensions, and soft tissue extensions [15].

Of the 57 cases with pediatric bone tumors, 35 patients were male and 22 were female, with a mean age of 13.12 years old. Of the tumors 22.8% and 77.2% occurred in the upper and lower extremities, respectively. The most common site of involvement in the upper extremity was proximal humerus, and osteochondromas were the most frequent tumors at this site. Again, osteochondromas represented the most frequent type of lower extremity bone tumors, with femur being the most frequent site of involvement. In the literature osteochondromas are most common benign tumors; our results were compatible with the literature. But we couldn’t obtain osteosarcoma which is the most common malignant bone tumors. Of the tumor like-lesions simple bone cysts, fibrous dysplasia, and non-ossifying fibromas observed equal frequency (7%).

Van den Berg et al obtained 1474 children with bone tumors and they reported the incidence of bone tumors was 79.3 per 1,000,000. Osteochondromas were the most prevalent tumors, followed by aneurysmal bone cysts with male preponderance [16]. Senac et al conducted a retrospective review of 268 biopsies of the bone who were less than 10 years of age. Benign tumors were found much more frequently than malignant lesions Osteochondroma and histiocytosis X were the most common lesions [17]. Lasebikan et al studied 68 cases and reported that primary bone tumors were commonest in young males, usually benign and affecting the tibia. A total of 28 (41.1%) were benign, 21 (30.9%) were malignant while 19 (27.9%) were tumor-like conditions. The commonest benign tumor was osteochondroma, accounting for 44.7% of non-malignant lesions, while fibrous dysplasia was the commonest tumor-like condition (23.4%) [18]. Obalum et al reviewed 242 patients aged 7.5 to 62 years old and they found that osteochondroma and osteosarcoma were the most common benign and primary malignant bone tumors [19]. Mohammed et al revealed that again osteochondroma and osteosarcoma were the most common benign and malignant tumors respectively in young adults [20]. A multicenter study showed that primary bone tumors were common amongst males and teenagers among 698 cases and most common was benign again [21]. Abdulkareem et al reported that osteochondroma and giant cell tumors are the commonest benign tumors while osteosarcoma is the most common primary bone tumor among 77 cases all occurring in the first two decades of life [22].

Osteochondroma (exostosis) is a mass lesion developing due to the growth of a group of cartilage cells separated from the normal growth plate toward other directions rather than the long axis of the bone. It is the most common benign tumor of the bone (25-35%), and is more common among males [23]. Most common sites of involvement include the metaphysis of the long bones, and more rarely the metadiaphysis (mostly bones around the knee and proximal humerus). It has a growth pattern that resembles a drifting away from the nearest epiphysis [24]. Lesions have a stalk (most common) or maybe wide based. Although mostly sporadic, osteochondromas may also occur at the site of radiotherapy secondary to radiation [25, 26]. It generally has a growth pattern accompanying the growth during childhood, and its growth should come to a halt when the skeletal development is completed. Mostly it is an asymptomatic condition, while it may sometimes be associated with bone deformity, or symptoms secondary to the pressure effect in adjacent neuro-vascular structures or to fractures. A typical radiographic characteristic is the continuation of the spongy part of osteochondroma with the spongy bone of the main bone [24]. A thickness of cartilage cap exceeding 2.5-3 cm may suggest malignant transformation [23, 24]. Osteochondroma on microscopic examination, underlying trabeculae form by endochondral ossification of cap and cartilaginous cap similar to a physis. The cartilage consists of chondrocytes without binuclear pleomorphism and hyperchromatism in liner position (**Figure 1**).

In current study Ewing sarcoma and chondrosarcoma observed as malignant tumors. Ewing sarcoma seen in a girl who was 16 years old localized at the mandibula. Ewing's sarcoma is the second most common malignant pediatric bone tumor following osteosarcomas, with a peak occurrence between 10 and 15 years of age [27]. A more differentiated form includes the primitive neuro-ectodermal tumor (PNET). It is more common in Caucasians, with an equal sex distribution. Patients generally present with local pain and mass. Generally the lesion can be palpated with erythema on the skin covering the lesion [28]. Erythrocyte sedimentation rate may be increased along with leukocytosis. The symptoms may mimic those of osteomyelitis. Most common sites of involvement include the pelvis, followed by the metaphysis of the long bones (femur > tibia > humerus > ribs) [27]. Tumors of the diaphysis typically have central or eccentric metaphyseal localization [29]. Extension into the epiphysis is rare. The aggressive periosteal reaction may take the form of spiculations or onion skin reaction. Under microscopic examination, Ewing's sarcoma consists of densely packed uniform small cells. The cells have a scant cytoplasm with a PAS positive stain and a round blue nucleus without prominent nucleoli.

In this study, other malignant tumor was chondrosarcoma. It was seen in a girl who was 12 years old, localized at the tibia and other one was 14 year-old male localized at the femur. Chondrosarcomas are uncommon during childhood (5%) and generally are secondary lesions rather than being primary chondrosarcomas [30]. In most instances, it involves large bones such as pelvis and shoulder bones, metaphysis of long bones, ribs, or vertebrae. They are generally large, expansive, destructive, lytic lesions. Under microscopic examination, chondrosarcoma included increased numbers of cartilage cells with atipic nuclear pleomorphism and hyperchromatism as well as binucleated chondroblasts within the blue-white cartilage matrix. Myxomatous degeration is seen.

Conclusion

Consistent with the literature data, osteochondroma was the most common type of tumor, occurring more commonly in male children. The peak incidence was in the second decade and commonest site was the lower extremity, particularly in the femur. However, there were no cases of osteosarcoma, which is the most commonly reported malignant tumor.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Esra Akyüz Özkan, Department of Pediatrics, Bozok University Medical Faculty, Yozgat, Turkey. Tel: 05067026694; Fax: 03542140612; E-mail: uzdresra@gmail.com

References

[1] Lawrence W Jr. Soft tissue sarcomas in adults and children: a comparison. CA Cancer J Clin 1994; 44: 197-199.

[2] Arndt CAS. Neoplasms of bone. Nathan and Oski's Hematology of Infancy and Childhood. In: Nathan DG, Orkin SH, Ginsburg D, Look TA, editors. Philadelphia, WB: Saunders Company; 2007. pp. 2146-2151.
[3] Heare T, Hensley MA, Dell'Orfano S. Bone tumors: osteosarcoma and Ewing's sarcoma. Curr Opin Pediatr 2009; 21: 365-372.
[4] Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International Classification of Childhood Cancer, Third Edition. Cancer 2005; 103: 1457-1467.
[5] Güngör Ş, Karakoç Y, Arıkan M, Metin E, Gürler D. Demographic Features of Childhood Benign Bone Tumors and Evaluation of Clinical Approach. Acta Oncologica Turcica 2008; 41: 7-13.
[6] Enneking WF. Musculoskeletal tumor surgery. 1st edition. New York, NY: Churchill Livingstone; 1983.
[7] Pettersson H, Springfield DS, Enneking WF. Radiologic management of musculoskeletal tumors. Philadelphia: Springer publishers; 1999.
[8] Enneking WF, Spanier SS, Goodman MA. A system for the surgical staging of musculoskeletal sarcoma. Clin Orthop 1980; 153: 106.
[9] Aboulafia AJ, Kennon RE, Jelinek JS. Benign bone tumors of childhood. J Am Acad Orthop Surg 1999; 7: 377-388.
[10] Gurney J, Swensen A, Bulterys M. Malignant bone tumors. Cancer Incidence and Survival among Children and Adolescents: United States SEER Program 1975-1995. In: Ries L, Smith MA, Gurney JG, Linet M, Tamra T, Young JL, editors. Bunin GR National Cancer Institute: SEER Program; 1999. pp. 99-110.
[11] Kısmet E, Köseoğlu V. Bone tumors in childhood. Turkiye Klinikleri J Pediatr-Special Topics 2004; 2: 899-903.
[12] Karakurt L, Yilmaz E, Varol T, Ozdemir H, Serin E. Solitary osteochondroma of the elbow causing ulnar nerve compression: a case report. Acta Orthop Traumatol Turc 2004; 38: 291-294.
[13] Smith MA, Ries LAG. Chidhood cancer: Incıdence, survival, and mortality in Principles and Practice of Pediatric Oncology. 4th edition. In: Pizzo PA and Poplack DG, editors. Philadelphia: Lippincott Williams and Wilkins; 2002. pp. 1-12.
[14] Caudill JS, Arndt CA. Diagnosis and management of bone malignancy in adolescence. Adolesc Med State Art Rev 2007; 18: 62-78.
[15] Yıldız C, Erler K, Atesalp AS, Basbozkurt M. Benign bone tumors in children. Curr Opin Pediatr 2003; 15: 58-67.
[16] Van den Berg H, Kroon HM, Slaar A, Hogendoorn P. Incidence of biopsy-proven bone tumors in children: a report based on the Dutch pathology registration "PALGA". J Pediatr Orthop 2008; 28: 29-35.
[17] Senac MO Jr, Isaacs H, Gwinn JL. Primary lesions of bone in the 1st decade of life: retrospective survey of biopsy results. Radiology 1986; 160: 491-495.
[18] Lasebikan OA, Nwadinigwe CU, Onyegbule EC. Pattern of bone tumours seen in a regional orthopaedic hospital in Nigeria. Niger J Med 2014; 23: 46-50.
[19] Obalum DC, Giwa SO, Banjo AF, Akinsulire AT. Primary bone tumours in a tertiary hospital in Nigeria: 25 year review. Niger J Clin Pract 2009; 12: 169-172.
[20] Mohammed A, Isa HA. Pattern of primary tumours and tumour-like lesions of bone in Zaria, northern Nigeria: a review of 127 cases. West Afr J Med 2007; 26: 37-41.
[21] Obalum DC, Eyesan SU, Ogo CN, Enweluzo GO. Multicentre study of bone tumours. Niger Postgrad Med J 2010; 17: 23-26.
[22] Abdulkareem FB, Eyesan SU, Akinde OR, Ezembakwe ME, Nnodu OE. Pathological study of bone tumours at the National Orthopaedic Hospital, Lagos, Nigeria. West Afr J Med 2007; 26: 306-311.
[23] Stacy GS, Heck RK, Peabody TD, Dixon LB. Neoplastic and tumorlike lesions detected on MR imaging of the knee in patients with suspected internal derangement: Part I, intraosseous entities. AJR Am J Roentgenol 2002; 178: 589-594.
[24] Alyas F, James SL, Davies AM, Saifuddin A. The role of MR imaging in the diagnostic characterisation of appendicular bone tumours and tumour-like conditions. Eur Radiol 2007; 17: 2675-2686.
[25] Vlychou M, Athanasou N. Radiological and pathological diagnosis of paediatric bone tumours and tumour-like lesions. Pathology 2008; 40: 196-216.
[26] Libshitz HI, Cohen MA. Radiation-induced osteochondromas. Radiology 1982; 142: 643-647.
[27] Peersman B, Vanhoenacker FM, Heyman S, Van Herendael B, Stam M, Brys P, Verstraete KL, Samson I, Sybers J, Van Dyck P, Parizel PM, De Schepper AM. Ewing's sarcoma: imaging features. JBR-BTR 2007; 90: 368-376.
[28] Yaw KM. Pediatric bone tumors. Semin Surg Oncol 1999; 16: 173-183.
[29] Laor T, Jaramillo D, Oestrich A. Skeletal system. Practical Pediatric Imaging: Diagnostic Radiology of Infants and Children. In: Kirks DR, Griscom NT, editors. 3rd edition. Philadelphia: Lippincott-Raven; 1998. pp. 327-510.
[30] Adler CP, Kozlowski K. Primary Bone Tumors and Tumorous Conditions in Children. London: Springer-Verlag; 1993.