Ectomesenchymoma: case report and review of the literature

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Ectomesenchymoma (EMCH) is a rare tumor that may arise in the brain or soft tissue. This tumor type is defined as a form including ectodermal components represented by neuroblasts or ganglion cells and differentiated mesenchymal structures of various types. The mesenchymal component is most often a rhabdomyosarcoma, but liposarcoma, malignant fibrous histiocytoma, leiomyosarcoma, chondrosarcoma, malignant schwannoma, and osseous elements have also been recorded. We report a case of an abdominal malignant ectomesenchymoma, containing three components, schwannoma, embryonal rhabdomyosarcoma, and ganglion cells, in a four-month-old infant. We also review 43 previously reported cases.

Key words: ectomesenchymoma, rhabdomyosarcoma, ganglion cells, malignant schwannoma.

Ectomesenchyme refers to the mesenchymal cells that are derived from the neural crest. Ectomesenchymomas (EMCH) are malignant tumors believed to arise from this tissue. They are characterized by both neuroectodermal and mesenchymal components[1]. These tumors are traditionally composed of well-differentiated neuroblastic cells (neuroblastoma, ganglio-neuroblastoma, ganglioneuroma), peripheral primitive neuroectodermal tumors (PNET) and one or more malignant mesenchymal elements, usually rhabdomyosarcoma. It stands as a distinct clinicopathologic entity[2]. This rare tumor has been described in the central nervous system and in various soft-tissue sties. In this report we describe a four-month-old infant who had an intra-abdominal ectomesenchymoma, and we review the literature.

Case Report

A four-month-old boy was admitted to our hospital because of a one-week history of progressive distention of the abdomen. There was no history of vomiting. On physical examination, the child appeared moderately ill and anemic. He had a rectal temperature of 36.6°C, and a heart rate of 152 per min. His weight and length were 6 kg and 64 cm, respectively. He had a moderately distended abdomen with active bowel sounds, and a large, nontender, smooth, palpable mass extending from the umbilicus to the inguinal region in the right lower quadrant. Prerectal mass was detected by rectal examination.

Laboratory examination revealed a blood hemoglobin of 7.0 g/dl, hematocrit 19.8% white cell count (13,800) per cubic millimeter, and a platelet count of 556,000 per cubic millimeter. CA-125 and 15-3 levels were higher than normal values (72.8, 22.9 respectively). Other biochemical and urinary analysis results were unremarkable and other tumor markers not detectable.

Abdominal radiography revealed a few dilated loops of small intestine, with gas and stool in the rectum. A computed tomographic (CT) scan of the abdomen, obtained after oral administration of contrast material, showed a solid mass, 8.7x5.5 cm, that displaced the bladder anteriorly and superiorly.

The tumor was surgically removed. The tumoral specimen from the intraabdominal surgery measured 9x8.5x6 cm and weighed 250 g. This mass appeared to be well circumscribed but non-encapsulated. Cut surface of the lesion showed fibrillar appearance of a firm mass, predominantly gray-white in color. Areas of necrosis and hemorrhage were present.

Microscopically, the tumor was densely cellular and composed predominantly of small, round and spindle-shaped cells with high nuclear-to-

cytoplasmic ratio and a high mitotic rate. The tumor had three components, schwannoma, embryonal rhabdomyosarcoma, and ganglion cells. The rhabdomyosarcomatous component had poorly differentiated areas composed of small, polygonal cells having round, hyperchromatic nuclei, and scant cytoplasm. This component displayed some recognizable round, oval, or spindle rhabdomyoblasts. Some rhabdomyoblasts were idendtified by variably abundant eosinophilic cytoplasm that was commonly granular or fibrillar (Fig. 1). The schwannomatous component had typical spindle-shaped nerve sheath cells with hyperchromatic nuclei and a considerable number of cells with mitosis (Fig. 2). Ganglion cells displaying various degrees of maturity were mixed with spindle-shaped cells (Fig. 3).

Immunohistochemical stains were performed for desmin, myoglobin, neuron-specific enolase (NSE), and S-100 on formalin-fixed tissue. The rhabdomyosarcomatous component displayed strong cytoplasmic staining for desmin and myoglobin. The schwannomatous component was negative for desmin and myoglobin, and positive for S-100. The ganglion cells were positive for NSE.

With the characteristic properties described above, the tumor was diagnosed as an ectomesenchymoma.

Postoperative follow-up was uneventful. He was discharged on the 5th postoperative day, and referred to the pediatric oncology clinic for chemotherapy.

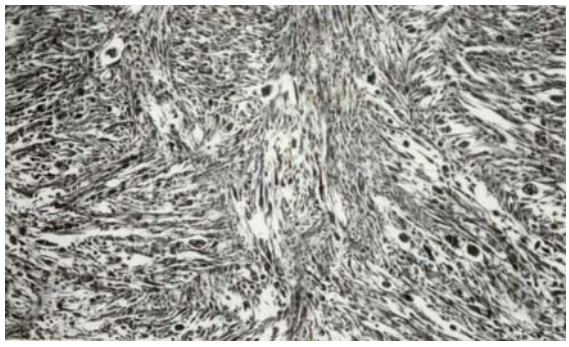

Fig. 1. Rhabdomyoblastic differentiation in the tumor mass. Some rhabdomyoblasts are identifying with abundant eosinophilic cytoplasms (H-E X 125).

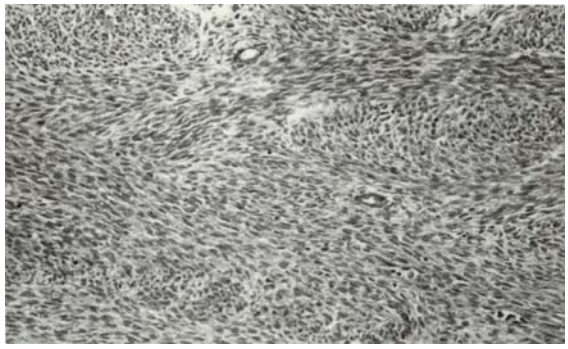

Fig. 2. The schwannomatous component composed of typical spindle-shaped nerve sheath cells with hyperchromatic nuclei and considerable mitotic figures (H-E X 125).

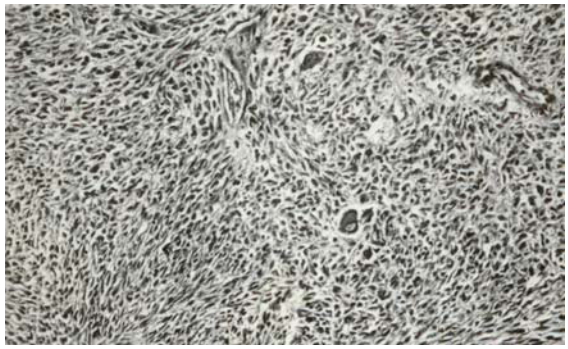

Fig. 3. The ganglion cells mixed with spindle-shaped cells (H-E X 125).

Discussion

Malignant ectomesenchymomas are rare tumors composed of neuroblast and/or ganglion cells and malignant mesenchymal tissue(s) of various types, usually rhabdomyosarcoma[3,4].

The most widely accepted theory suggests that this tumor arises from the remnants of migratory neural crest cells and thus from the mesenchyme[2-10].

In the late nineteenth century, Platt[11] discovered that the dorsal ectoderm of the head contributed to the mesenchymal cells forming the cartilage of the visceral arches and dentine. She coined the term "mesectoderm", but the term ectomesenchyme is now popularly used to designate mesenchymal cells of neural crest origin. Holimon and Rosenblum[4] proposed the

term "gangliorhabdomyosarcoma" for a tumor in the cerebellopontine angle containing ganglioneuroma and rhabdomyosarcomatous elements. Later, Naka et al.[8] proposed the term EMCH after finding a variety of malignant mesenchymal elements in a retroperitoneal tumor mixed with ganglioneuroblastoma.

The clinical, histological, and cytochemical data for all 44 reviewed cases of ectomesenchymoma (including the case we report) are summarized in Table I. This tumor affects predominantly young children: 81.6% (39.5% infants and 42.1% 1-13 years old) were children under 13 years old and 18.4% are adults. The male-to-female ratio

Table I. Review of Cases in the Literature

No.	Reference	No. of cases	Age	Presentation	Gross appearance	Histology	Treatment	Follow-up
1	Ingraham (7)	1	10 yrs	Cerebellar	NA	Atypical GC, RMS	Incomplete res	Died 12 mo.
2	Holimon (4)	1	2.5 yrs	Ear and nasopharynx	Polypoid, firm, gray-white, necrotic mass	GN, RMS	CT, RT	Died 6 mo., met.
3	Naka et al. (8)	1	2 yrs	Abdominal	Fragile, gray, necrotic zones	NB, GN, RMS, UM, LS, chondroid areas	P. Res, RT, CT	Died 6 mo., met.
4	Karcıoğlu et al. (9)	1	6 mo.	Facial	Gray-white, lobulated, friable mass	GN, RMS, Sch, melanocytes	P. Res, CT, RT	No. Rec. 7 mo.
5	Shuangshoti (16)	1	20 yrs	Neck	Encapsulated firm, gray-white, cystic and necrotic areas	GN, RMS, malignant Sch., meningioma, osseous component	Res., local rec. 3 mo., RT	NA
6	Schmidt et al. (22)	1	New-born	Cheek	Circumscribed, Lobulated tan-gray	NB, RMS	CT, res. At 6 mo, rec., res. and CT	Adriamycin Toxicity; died 18 mo.
7	Cozzutto et al. (6)	1	3 yrs	5 Cord	Encapsulated	GC, RMS, MFH,LM	Res. and CT	No. rec. after 3 yrs
8	Cozzutto et al. (6)	1	NA	NA	NA	GC, IE	NA	NA
9	Shuangshoti et al. (14)	1	49 yrs	Thigh	Firm, lobulated, chondroid, necrotic areas	NB, glial tumors, chondrosarcoma	Res, RT, CT	Died 11 mo., met.
10	Sirikulchayannota (17)	1	25 yrs	Wrist	Circumscribed, Yellow-white mass	NB, malignant Sch.	Mulitple excision and amputations	Lost to follow-up After amputation
11	Kodet et al. (18)	1	7 mo.	Paratesticular	NA	GN, RMS	Res., RT CT	No rec 12 yrs
12	Kodet et al. (18)	1	8 mo.	Perineal	NA	GN,RMS	RT, CT	Died at age 4 yrs
13	Kodet et al. (18)	1	4 mo.	Pelvic	NA	GN, RMS	CT, res.	No rec. 9 mo
14	Kawamoto et al. (3)	1	10 mo.	Retroperiton	Encapsulated, fibrous myxoid, necrotic tissue	GN, RMS	Rs. and CT	No rec. 3 yrs
15	Kawamoto et al. (3)	1	4 mo.	Abdomen	Encapsulated, soft, lobulated	NB, RMS	Res. and CT	No rec. 16 mo.
16	Kasantikul et al. (19)	1	5.5 yrs	NA	NA	Neuroglia, SM, CD	NA	Rec. 2 mo.
17	Kasantikul et al. (19)	1	1 yr	Retroperiton	NA	GN, RMS	NA	Died 1 mo., met.
18	Kasantikul et al. (19)	1	20 yrs	Scrotum	NA	GN, RMS	NA	NA
19	Kasantikul et al. (19)	1	36 yrs	Parapharynx	NA	Neuroglia, MFH	Excision, RT	No rec. 6 mo.
20	Strother et al. (10)	1	NA	NA	NA	NA	NA	NA
21	Paulus et al. (20)	1	1.5 yrs	Meningeal	NA	NA	NA	NA
22	Fellinger et al. (21-22)	1	NA	NA	NA	NA	NA	NA
23	Dias et al. (23)	1	NA	NA	NA	NA	NA	NA
24	Matsko et al. (15)	1	5.5 yrs	Orbita	NA	NE, RMS	P. Res, CT, RT	No rec. 18 mo.
25	McCune et al. (24)	3	4-20 yrs	Thigh, arm and abdominal cavity	NA	Case 1: PNET, RMS Case 2: PNET, RMS Case 3: NB, RMS	NA	NA
26								
27								
28	Pellin et al. (25)	1	NA	NA	NA	PSTS, SM, NE	NA	NA
29	Kogner et al. (26)	2	4 yrs	NA	NA	NA	NA	NA
30			6 yrs					

Table I. Review of Cases in the Literature (Continue)

No.	Reference	No. of cases	Age	Presentation	Gross appearance	Histology	Treatment	Follow-up
31	Kilpatrick et al. (27)	1	9.5 mo	Scrotal	NA	Mature GC, RMS	NA	Alive 9.5 yrs
32	Apostolides et al. (28)	1	35 yrs	VIIth nerve	NA	GC, AT, Sch, SM	Total res	NA
33	Mouton et al. (29)	1	7 mo.	Scrotum	Well-C.	GC, RMS, LDCCP	Surgery CT	No rec. 7 mo.
34	Mouton et al. (29)	1	8 mo.	Pelvic	Well-C., yellow-graft	GC, RMS	CT, res. of tumor	No rec.
35	Mouton et al. (29)	1	6 mo.	Inguinal	Firm, white nodular	GC, RMS, LDCCP	Res., CT	No rec. 18 mo.
36	Mouton et al. (29)	1	4.4 yrs	Forearm	NA	NE, RMS, LDCCP	Surgery, CT, res.	No rec. 14 mo.
37	Mouton et al. (29)	1	2 mo.	Scrotal	Circumscribed	NE, LDCCP	Biopsy, CT, res.	No rec. 32 mo.
38	Hajivassilou et al. (13)	1	5 mo.	Pelvic	NA	GN, RMS	CT, total res.	No. rec. 18 mo.
39	Goldsby et al. (30)	1	16 mo.	Abdominal	NA	GC, SC, CD	Res., RT, CT	NA
40	Freitas et al. (31)	1	3.8 yrs	Intracranial	Irregular boundaries, Whitish and rubbery	GC, RMS	Res, rc. 4 mo. Later, RT, CT	Died 14 mo. after res.
41	Govender et al. (1)	1	5 mo.	Prostate	Lobulated tumor with a Rubbery consistency	GN, RMS	Biopsy, surgery, CT, res., CT	Died 8 mo. after res.
42	Tse et al. (32)	1	13 yrs	Retroperiton	Well-C, firm	Mature GC, RMS	NA	NA
43	Papos et al. (33)	1	10 yrs	Cerebral	NA	NA	NA	NA
44	Current case	1	4 mo.	Intraabdominal	Well-C., firm and gray-White cut section	RMS, malignant Sch., GC	Res., CT	No more follow-up

AT : Adipose tissue, CD: Cartilaginous differentiation, CT: Chemotherapy, GC: Ganglion cells, GN: Ganglioneuroma, IE: Indefinite elements, LDCCP: Less differentiated cells and cellular processes, LM: Leiomyoma, LS: Liposarcoma, met: Metastases, MFH: Malignant fibrous histiocytoma, mo: Monts, NA: Data not available, NB: Neuroblastoma, NE: Neural elements, PNET: Peripheral primitive neuroectodermal tumors, P. Res: Partial resection, PSTS: Primitive soft tissue sarcoma, Rec: Recurrence, Retroperiton: retroperitoneal, RMS: Rhabdomyosarcoma, Res: Resection, RT: Radiotherapy, Sch: Schwannoma, SM: Smooth muscle, SC: Spindle cells, S cord: Spermatic cord, UM: Undifferentiated mesenchyme, Well-C: Well-circumscribed.

was 20: 14 (58.8% and 41.2%) and anatomical sites were reported in 36 of these 44 cases as follows: the head and neck (11 cases 30.5%). (6 cases 16.7%), the scrotum (6 cases 16.7%), the abdomen (5 cases 13.9%), the retroperitonael space (4 cases 11.1%), the pelvis (2 cases 5.6%), the perineum (1 case 2.8%), and the prostate (1 case 2.8%)[1,3,4,6-10,12-33]. In the present case the patient was four months old and male. The tumor had intraabdominal location.

Clinically significant symptoms are uncommon and have usually been related to local pressure from the tumor. Laboratory examinations generally cannot help except in cases where

neuroblastomatous components are present, with laboratory data showing elevated vanillylmandelic acid in urine[31]. In our case, laboratory results were nonspecific.

On examination by the naked eye, these cases are well circumscribed gray or tan, and composed of firm tissue. Some cases were described as being lobulated and having focal necrotic areas (Table I).

Histological data were available for 37 tumors: ganglioneuroma was found in 12 tumors (32%), ganglion cells in 11 (30%), and neuroblastoma in 6 tumors (16%), and other neural elements were described in 8 (22%) of these lesions. Rhabdomyosarcoma was present in 31 (84%), and other mesenchymal elements were found in 9 (24%) cases.

In our case, the tumor was well circumscribed but not encapsulated. It was a firm mass and predominantly white in color. Cut surface of the tumor was fibrillar in appearance. Areas of necrosis and hemorrhage were present.

Microscopically, the tumor was composed of ganglion cells, schwannoma and embryonal rhabdomyosarcoma areas.

Ectomesenchymomas are frequently confused with rhabdomyosarcomas due to the fact that their neural components are easily overlooked. However, high concentration of the plasma neuropeptide-Y-like immunoreactivity (P-NPY-LI) in ectomesenchymoma can distinguish this tumor from rhabdomyosarcoma, which presents normal concentrations of the P-NPY-LI[26].

The differential diagnosis of ectomesenchymoma includes mainly teratoma, Wilms' tumor, benign and malignant triton tumors, and other collision tumors[2,6,9,13,17].

The therapeutic management data were mentioned in 27 of 44 cases, including the current case (Table I). Resection together with pre- or post-surgery chemotherapy was the treatment that presented the best results, with only two deaths in 13.

Due to the fact that we could not follow-up this patient, we have no information about the prognosis of the case.

We believe that in the differential diagnosis of tumors in childhood and infancy, the ecto-mesenchymoma should always be remembered.

REFERENCES

1. Govender D, Hadley GP. Ectomesenchymoma of the prostate: histological diagnostic criteria. Pediatr Surg Int 1999; 15: 68-70.
2. Tsokos M. Peripheral primitive neuroectodermal tumors. Diagnosis, classification, and prognosis. Perspect Pediatr Pathol 1992; 16: 27-98.
3. Kawamoto EH, Weidner N, Agostini RM Jr, Jaffe R. Malignant ectomesenchymoma of soft tissue. Report of two cases and review of the literature. Cancer 1987; 59: 1791-1802.
4. Holimon JL, Rosenblum WI. "Gangliorhabdomyosarcoma": a tumor of ectomesenchyme. J Neurosurg 1971; 34: 417-422.
5. Bittinger A, Rossberg A, Rodehuser M. Primary malignant ectomesenchymoma of the orbit. Gen Diagn Pathol 1997; 221-225.
6. Cozzutto C, Cormeli A, Bandelloni R. Ecto-mesenchymoma. Report of two cases. Virschows Arch A Pathol Anat Histopathol 1982; 398: 185-195.
7. Ingraham FD, Bailey OT. Cystic treatomas and teratoid tumors of the central nervous system in infancy and childhood. J Neurosurg 1946; 3: 511-532.
8. Naka A, Matsumoto S, Shirai T, Itoh T. Ganglioneuroblastoma associated with malignant mesenchymoma. Cancer 1975; 36: 1050-1056.
9. Karcıoğlu Z, Someren A, Mathes SJ. Ectomesenchymoma. A malignant tumor of migratory neural crest (ectomesenchyme) remnants showing ganglionic, schwannian, melanocytic and rhabdomyoblastic differentiation. Cancer 1977; 39. 2486-2496.
10. Strother Dr, Parham DM, Houghton PJ. Expression of the 5.1 H11 antigen, a fetal muscle surface antigen, in normal and neoplastic tissue. Arc Pathol Lab Med 1990; 114: 593-596.
11. Platt JS. Ectodermic origin of the cartilage of the head. Anat Anz 1893; 8: 506-509.
12. Schmidt D, Mackay B, Osborne BM, Jaffe N. Recurring congenital lesion of the cheek. Ultrastruct Pathol 1982; 3: 85-90.
13. Majivassilou CA, Carachi R, Simpson E, Patrick WJ, Young DG. Ectomesenchymoma: one or two tumors? Case report and review of the literature. J Pediatr Surg 1997; 32: 1351-1355.
14. Shuangshoti S, Kasantikul V, Suwangool P, Chittmittrapap S. Malignant neoplasm of mixed mesenchymal and neuroepithelial origin (ectomesenchymoma) of thigh. J Surg Oncol 1984; 27: 208-213.
15. Matsko TH, Schmidt RA, Milam AH, Orcutt JC. Primary malignant ectomesenchymoma of the orbit. Br J Ophthalmol 1992; 76: 438-441.
16. Shuangshoti S, Chutchavaree A. Parapharyngeal neoplasm of mixed mesenchymal and neuroepithelial origin. Arch Otolaryngol 1980; 106: 361-364.
17. Sirikulchayanonta V, Wongwaisayawan S. Malignant ectomesenchymoma (neoplasm of mixed mesenchymal and neuroepithelial origin) of wrist joint. J Med Assoc Thai 1984; 67: 356-361.
18. Kodet R, Kashuri N, Marsden HB, Road NA, Raafat F. Gangliorhabdomyosarcoma: a histopathological and immunohistochemical study of three cases. Histopathology 1986; 10: 181-193.

19. Kasantikul V, Shuangshoti S, Cutchavaree A, Bunyaphiphat P. Parapharyngeal malignant ecto-mesenchymoma: combined malignant fibrous histiocytoma and primitive neuroectodermal tumour with neuroglial differentiation. J Laryngol Otol 1987; 101: 508-515.

20. Paulus W, Slowik F, Jellinger K. Primary intracranial sarcomas: histopathological features of 19 cases. Histopathology 1991; 18: 395-402.

21. Fellinger EJ, Garin-Chesa P. Triche TJ, Huvos AG, Rettig WJ. Immunohistochemical analysis of Ewing's sarcoma cel surface antigen p30/32MIC2. Am J Pathol 1991; 139: 317-325.

22. Garin-Chesa P, Fellinger EJ, Huvos AG, et al. Immunohistochemical analysis of neural cell adhesion molecules. Differential expression in small round cell tumors of childhood and adolescence. Am J Pathol 1991; 139: 275-286.

23. Dias P, Parham DM, Shapiro DN, Tapscott SJ, Houghton PJ. Monoclonal antibodies to the myogenic regulatory protein MyoD1: epitope mapping and diagnostic utility. Cancer Res 1992; 52: 6431-6439.

24. McCune BK, Patterson K, Chandra RS, Kapur S, Sporn MB, Tsokos M. Expression of transforming growth factor-beta isoforms in small round cell tumors of childhood. An immunohistochemical study. Am J Pathol 1993; 142: 49-58.

25. Pellin A, Boix J, Blesa JR, Noguera R, Carda C, Llombart-Bosch A. EWS/FLI-1 rearrangement in small round cell sarcomas of bone and soft tissue detected by reverse transcriptase polymerase chain reaction amplification. Eur J Cancer 1994; 30: 827-831.

26. Kogner P, Bjork O, Theodorsson E. Plasma neuropeptide Y in healthy children: influence of age, anaesthesia and the establishment of an age-adjusted reference interval. Acta Paediatr 1994; 83: 423-427.

27. Kilpatrick SE, Teot LA, Geisinger KR, et al. Relationship of DNA ploidy to histology and prognosis in rhabdomyosarcoma. Comparison of flow cytometry and image analysis. Cancer 1994; 74: 3227-3233.

28. Apostolides PJ, Spetzler RF, Johnson PC. Ectomesenchymal hamartoma (benign "ecto-mesenchymoma") of the VIIIth nerve: case report. Neurosurgery 1995; 37: 1204-1207.

29. Mouton SC, Rosenberg HS, Cohen MC, Drut R, Emms M, Kaschula RO. Malignant ectomesenchymoma in childhood. Pediatr Pathol Lab Med 1996; 16: 607-624.

30. Goldsby RE, Bruggers CS, Brothman AR, Sorensen PH, Beckwith JB, Pysher TJ. Spindle cell sarcoma of the kidney with ganglionic elements (malignant ectomesenchymoma) associated with chromosomal abnormalities and a review of the literature. J Pediatr Hematol Oncol 1998; 20: 160-164.

31. Freitas AB, Aguiar PH, Miura FK, et al. Malignant ectomesenchymoma. Case report and review of the literature. Pediatr Neurosurg 1999; 30: 320-330.

32. Tse VE, Doucet J, Pearl R, Phillips MJ. Rhabdomyosarcoma metastasizing as a malignant ectomesenchymoma. Ultrastruct Pathol 1999; 23: 267-273.

33. Papos M, Pekrun A, Herms JW, et al. Somatostatin receptor scintigraphy in the management of cerebral malignant ectomesenchymoma: a case report. Pediatr Radiol 2001; 31: 169-172.