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Case Report

Primitive myxoid mesenchymal tumor of the infancy in abdominal cavity: report of a rare case

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Abstract: Primitive myxoid mesenchymal tumor of the infancy (PMMTI) is an extremely rare soft tissue tumor. We report a case of 2-year-old girl presenting with omentum and intestinal wall involvement in abdominal cavity with prominent refractory ascites. Histologically, the tumor consisted of primitive spindle or polygonal cells dispersing in a myxoid background with delicate blood vessels. Immunohistochemically, tumor cells expressed vimentin and NSE but were negative for AE1/AE3, CK5/6, TTF1, desmin, SMA, MyoD1, myogenin, ALK, CD34, calretinin, WT1, HBME-1, D2-40, S-100 protein, CD56, synaptophysin, CD99, CD20, CD3, CD30. Fluorescence in situ hybridization (FISH) showed absences of chromosome translocation involving *DDIT3, EWSR1* and *ETV6*. The patients undergone a palliative surgery and succumbed after 2 months. To our knowledge, this is the first case of PMMTI affecting abdominal cavity and demonstrating a more unfavorable prognosis.

Keywords: Primitive myxoid mesenchymal tumor of the infancy, abdominal cavity, soft tissue, clinicopathology

Introduction

Pediatric malignant soft tissue neoplasms are less frequent compared to the adults, and rhabdomyosarcoma ranks as the most common entity [1]. However, there are also a collection of benign fibroblstic- or myofibroblastic-derived tumors principally arising in the children [2]. But the fibroblastic tumors of childhood with intermediate biologic behavior mainly include inflammatory myofibroblastic tumor, infantile fibrosarcoma, and Primitive myxoid mesenchymal tumor of the infancy (PMMTI). The latter is a newly rare and limited-recognized soft tissue neoplasm [3]. It predominantly presents in pediatric group and has a propensity to occur in peripheries with locally aggressive behavior and a potential of metastasis. Some cases were described as a case report, however, most of which mainly developed in the trunk, extremities or head and neck [3]. Herein, we report a 2-year-old girl of PMMTI with extensively involvement of abdominal cavity with a sinister outcome using a cytological, histological and molecular study to further discuss the distinct clincopathologic features, differential diagnosis and prognosis of PMMTI.

Case presentation

A 2-year-old girl was admitted for increasing abdominal distension with an irregular fever as high as 38.5°C. The patient was admitted to our hospital due to lacking marked remission after multiple anti-infective therapies. X-ray plain film showed obviously abdominal distention and mildly intestinal pneumatosis with n significantly dense region, suggestive of the possibility of severe ascites (**Figure 1**), which was further verified by the computer tomography scan (CT). Abdominal ultrasound revealed that diffuse and inhomogeneous thickening affecting omentummajus with the thickest lesion measuring 20 mm in diameter; blood flow signals could be focally appreciated in color doppler flow imaging (CDFI) (**Figure 2**). Laboratory tests manifested red blood cell (RBC) 4.99×10^{12}, white blood cell (WBC) 12.5×10^{9}, hemogolobin 92.0 g/L, platelets 543×10^{9}, total protein (TP) 51.2 g/L, albumin 32.7 g/L, globulin 18.5 g/L, C-reactive protein 3.8 mg/L, erythrocyte sedimentation (ESR) 8.1 mm/h, adenosine deaminase (ADA) 0.3 U/L; IgG and IgM against antigens of cysticercuscellulosae, paragonimus, toxoplasma gondii and

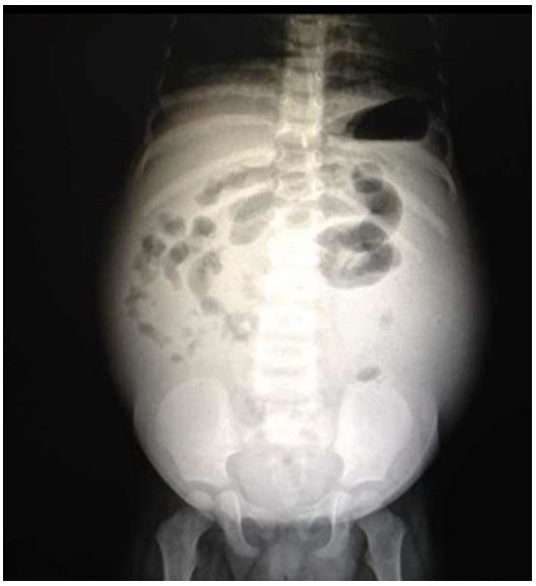

Figure 1. X-ray plain film showed obviously abdominal distention and mildly intestinal pneumatosis with an extensively dense region, suggestive of the possibility of severe ascites.

trichina were negative. Bone-marrow smear illustrated iron deficiency anemia characteristic of increasing polychromatophilic or orthochromatic normoblasts. A positively experimental treatment of anti-mycobacterium tuberculosis was performed, though deficient in a positive result by tuberculin purified protein derivative (PPT) test and T-SPOT.TB test. However, the condition was still in the doldrums except for temporary recovery to normal level of body temperature. A collection of symptomatic treatments including nutritional support, anti-infection, albumin supplementation, appropriate diuresis were performed. Nevertheless, the patient did not show an evident improvement and ruled out continuing therapy and eventually succumbed after 2 months.

Materials and methods

The specimen was fixed by 4% formalin, and then embedded routinely in paraffin and stained with hematoxylin and erosin. Immunohistochemical studies were performed using commercial antibodies in the VentanaBenchMark XT instrument (Ventana System, Tucson AZ). The antibodies included AE1/AE3, CK5/6, vimentin, TTF1, desmin, SMA, MyoD1, myogenin, ALK, CD34, calretinin, WT1, HBME-1, D2-40, S-100 protein, CD56, synaptophysin, NSE, CD99, CD20, CD3, CD30, Ki-67 (all above from Ventana, prediluted).

Fluorescence in situ hybridization (FISH) evaluation for *ETV6, EWSR1* and *DDIT3* rearrangement and *MDM2* amplification were performed on 4 μm-thick paraffin section with LSI ETV6 (Abbott, Chicago, IL), EWSR1 (Abbott, Downers Grove, IL), DDIT3 (Abbott, Chicago, IL) dual color break-apart probe and MDM2/CEP 12 probe (Abbott, North Chicago, IL), respectively, based on the manufacturer's instruction.

Results

Cytologically, tumor cells in Thinprep cytologic test (TCT) manifested as scatters or groups of round or oval cells with pale cytoplasm and open chromatin and several small nucleoli; some nuclei were eccentric, suggestive of cells rich in mucus (**Figure 3**). In paraffin embedded deposited slicing, some significant proliferated mesothelial cells expressing WT1 and calretinin tended to obscure the scattered mucin-contained cells.

Some fragmented omental adipose tissues were obtained through a biopsy, which measured 5 cm×5 cm×1 cm showing gray-white in color with superimposed mucous and granular appearance in the cut surface. Microscopically, the tumor presented with an irregularly nodular growth pattern involving the mesenteric adipose tissue (**Figure 4**), which consisted of monotonously primitive cells dispersing in the prominent myxoid matrix with a viable proliferation of delicate vascular network and small mucous pools or microcysts (**Figure 5**). In periphery of nodules or blood vessels was slightly high cellularity (**Figure 6**). Tumor cells revealed short spindle, round or polygonal figuration with tapering ends and fine nuclei with inconspicuous nucleoli and scant mitoses (<1/10 HP); few pale eosinophilic or amphiphilic cytoplasm, occasionally with small vacuoles, could be seen (**Figure 7**).

Immunohistochemically, the tumor cells were totally negative for AE1/AE3, CK5/6, TTF1, desmin, SMA, MyoD1, myogenin, ALK, CD34, calretinin, WT1, HBME-1, D2-40, S-100 protein, CD56, synaptophysin, CD99, CD20, CD3, CD30 other than vimentin (**Figure 8**) and NSE (**Figure 9**). The proliferative index Ki-67 was 10%. FISH analysis failed to detect the arrangement of

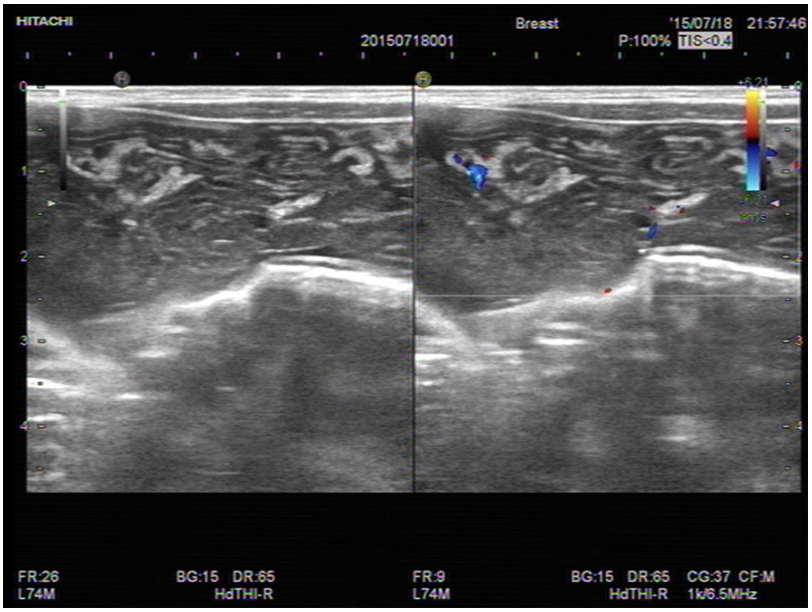

Figure 2. Abdominal ultrasound revealed that diffuse and inhomogeneous thickening affected omentummajus (Left) and focal of blood flow signals could be appreciated in CDFI (Right).

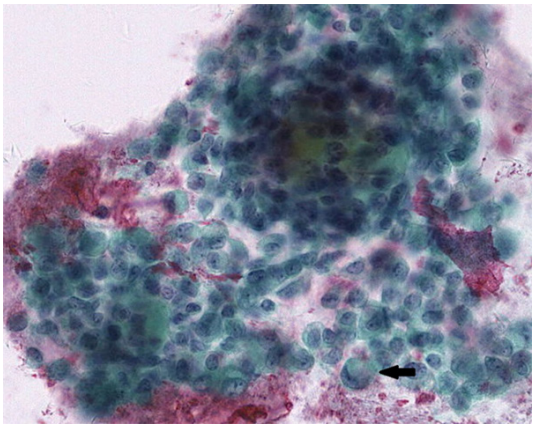

Figure 3. Thinprep cytologic test (TCT) revealed round or oval cells with pale cytoplasm and open chromatin and several small nucleoli; Note that some nuclei were eccentric (Papanicolaou staining, magnification, 400×).

ETV6, *DDIT3*, *EWSR1* and amplification of *MDM2*.

Discussion

First elucidated by Alaggio R et al. in 2006, PMMTI is an extraordinarily rare soft tissue with clinicopathological overlap with infantile fibrosarcoma (IFS) or infantile fibromatosis [3]. No more than 30 cases have been reported in the literature [3-13] (**Table 1**). Clinically, PMMTI develops in newborns or infants less than 1 year other than 3 cases affecting a child aging 15 months, 3 years and 4 years respectively [4, 5, 12]. The hitherto involved anatomic locations include trunk, extremities, head and neck [3-12]. On gross examination, the tumor principally presents as an unencapsulated and multinodular mass with focal infiltration measuring from 2 to 15 cm [3, 9]. The cut surface usually shows gray-white fleshy, myxoid, or gelatinous appearance in central areas but more firm peripherally [3, 7]. However, this is the first report that omenta involvement imparting a significant thickened appearance with superimposed numerous granular nodules followed by refractory ascites resulting in prominent compression of the intestinal tract. One possible reason why our case discriminately showed widespread lesions likely lies in relatively unlimited anatomic space. Scattered or clustered round cells with abundant intracytoplasmic mucus in the daily ascites smear observation of pediatrics is uncommon. Additionally, in the paraffin embedded deposited slicing, ubiquitously proliferated mesothelial cells arranged in papillary architecture expressing mesothelium-related markers may contribute to the diagnosis of mesothelioma, a diagnostic scapegoat, to obscure the true process. However, mesothelioma usually affects middle aged or elderly population and rarely displays a large amount of mucous cytoplasm, which needs a further consideration for the final diagnosis.

Histologically, diffuse sheets of small primitive tumor cells embedded in the myxoid stroma with a vaguely nodular architecture [3]. Many mucus pools and haphazardly delicate blood vessels can be easily appreciated. Focal condensed areas of tumor cells form short bundles and fascicles, especially around the capillaries, with or without increased collagen [3, 6]. The

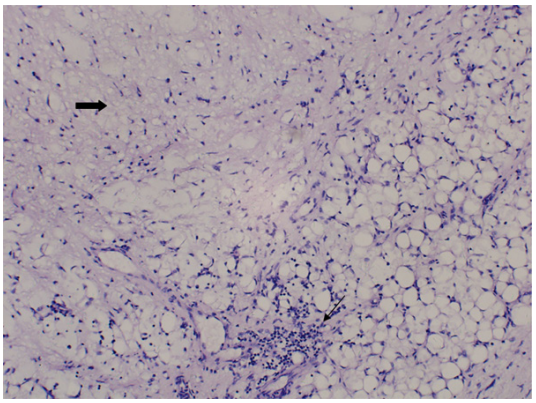

Figure 4. The spindle tumor cells (coarse arrow) involved the mesenteric adipose tissues with inflammatory infiltration (thin arrow) (biopsy, HE, magnification, 200×).

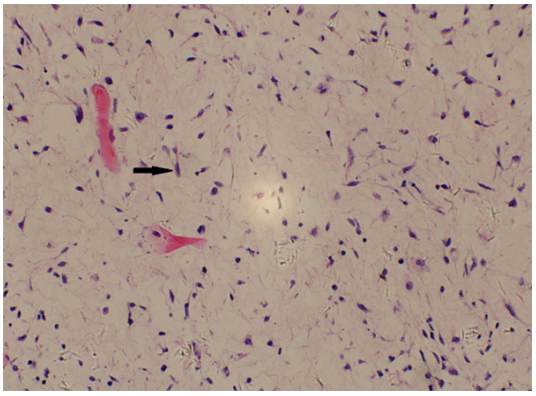

Figure 7. Spindle, round or polygonal tumor cells (arrow) with inconspicuous nucleoli and pale eosinophilic or amphiphilic cytoplasm, occasionally with small vacuoles (biopsy; HE; magnification, 200×).

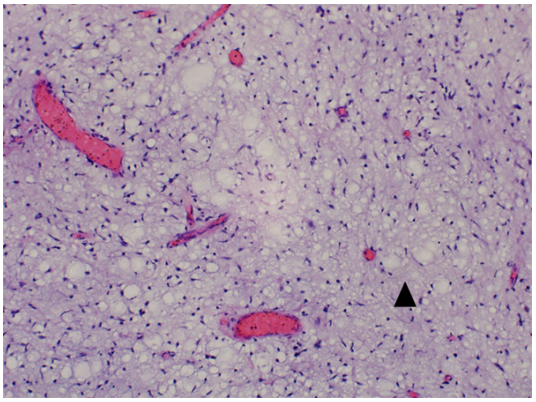

Figure 5. Primitive tumor cells in myxoid matrix (triangle) with a delicate vascular proliferation and small mucoumicrocysts (biopsy; HE; magnification, 200×).

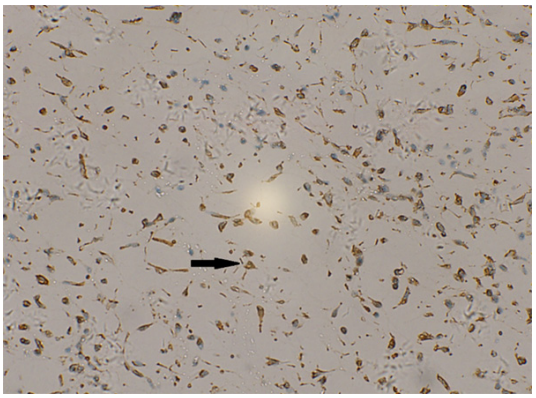

Figure 8. Tumor cells show expression of vimentin (arrow) (biopsy; immunohistochemisry; magnification, 200×).

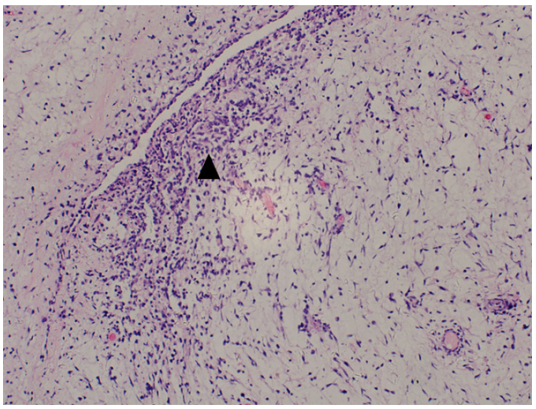

Figure 6. Some dense areas of tumor cells (triangle) in periphery of nodules or blood vessels (biopsy; HE; magnification, 100×).

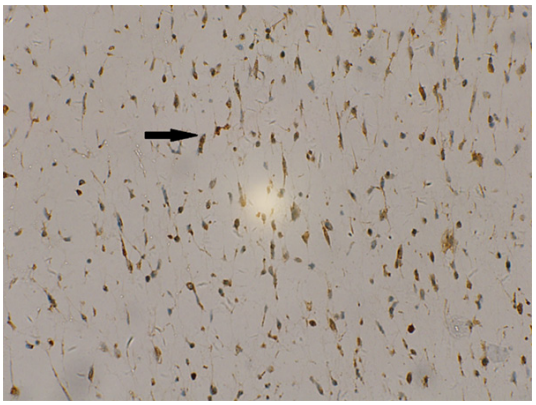

Figure 9. NSE is immunoreactive in this case (arrow) (biopsy; immunohistochemistry; magnification, 100×).

immunohistochemical profile of PMMTI is nonspecific, with reactivity for vimentin and no expression for cytokeratin, EMA, SMA, MSA, bcl-2, desmin, MyoD1, myogenin, S-100 pro-

Table 1. Summary of PMMI studies with complete clinicopathology

Reference (Year)	Gender/Age	Location	presentation	Immunohistochemistry	Cytogenetic features	Treatment	Follow-up
Alaggio R et al. Case 1 (2006)	Male/5 mo.	Larynx, neck	Mass, respiratory fatigue	Vimentin+/desmin/myogenin-/S100-/MSA-/SMA-/Cytokeratin-/bcl-2-	46, X der (Y)t(Y;9)(q12;p11) der (9) t(3;Y;9) (p13;q12;p11) or t(3;9) (p12;p11), der (18)t(1;18)(q12;q23); ETV6-NTK3-	Chemotherapy; Resection	4 yrs. AWD;
Alaggio R et al. Case 2 (2006)	Male/1 mo.	Right Thigh	Large mass	Vimentin+/desmin/myogenin-/S100-/MSA-/SMA-/Cytokeratin-/bcl-2-	46, XY; ETV6-NTK3-	Chemotherapy; Resection	4 yrs. NED
Alaggio R et al. Case 3 (2006)	Male/2 wk.	Left forearm	Large mass	Vimentin+/desmin/myogenin-/S100-/MSA-/SMA-/Cytokeratin-/bcl-2-	ETV6-NTK3-	Resection	1 yr. NED
Alaggio R et al. Case 4 (2006)	Male/2 mo.	Left Paraspinal soft tissue	Mass	Vimentin+/desmin/myogenin-/S100-/MSA-/SMA-/Cytokeratin-/bcl-2-	Unknown	Unknown	NA
Alaggio R et al. Case 5 (2006)	Female/3 wk.	Cervical and superaclavicular soft tissue	Mass	Vimentin+/desmin/myogenin-/S100-/MSA-/SMA-/Cytokeratin-/bcl-2-	NA	Resection	6 mo. AWD
Alaggio R et al. Case 6 (2006)	Female/newborn	Back, neck, chest, abdomen, spinal canal	Mass	Vimentin+/desmin/myogenin-/S100-/MSA-/SMA-/Cytokeratin-/bcl-2-	ETV6-NTK3-	Resection	6 wk. DWD (sepsis)
Lam J et al. (2010)	Male/2 d.	Right midback	Papule	Vimentin+/CD68+ (weak)/CD34+ (focal)/CD1a-/S100-/MART-1-/tyrosinase-/langerin-/MAC387-/SMA-/actin-/myogenin-/myoglobin-/desmin-/CD34-/CD31-/CD45-/CKpan-/mast cell tryptase-	ETV6-NTK3-	Resection	38 mo. NED
Mulligan L et al. (2011)	Female/8 mo.	Thenareminence	Firm and painless mass	Vimentin+/desmin-/MyoD1-/myogenin-/CLA-/S100-/EMA-/AE1/AE3-/CD31-/CD34-/INI1+/β-catenin-	ETV6-NTK3-	Resection	5 yrs. NED
Gong Q et al. Case 1 (2012)	Male/5 mo.	Beside trachea and thyroid gland	Wheezy phlegm and respiratory unease; nodule	CD99+/CD117 (weak)/nestin+ (weak)/S100-/CD34-/CD31-/desmin-/myogenin-/SMA-/cytokeratin-/Syn-/CD56-/CD30-/HMB45-/P53-/CD1a-/CD68-/bcl-2-	ETV6-NTK3-	Resection	5 mo. AWD
Gong Q et al. Case 2 (2012)	Female/3 d.	Dorsal lumbar	Mass	CD99+/CD117 (weak)/nestin+ (weak)/S100-/CD34-/CD31-/desmin-/myogenin-/SMA-/cytokeratin-/Syn-/CD56-/CD30-/HMB45-/P53-/CD1a-/CD68-/bcl-2-	ETV6-NTK3-	Resection	NA
Saito A et al. (2013)	Female/5 mo.	Sacrococcygeal region	Mass	Vimentin+/Glut1-/Syn/desmin-/myogenin-/MSA-/AE1/AE3-/S100-/EMA-/CD34-	46XX; ETV6-NTK3-	Resection	24 mo. NED
Su TC et al. (2013)	Male/3 mo.	Scalp	Mass	Vimentin+/CD99+ (weak)/SMA-/desmin-/S100-/NSE-/P63-/CD34-	ETV6-NTK3-	Resection	18 mo. NED
Cuthbertson DW et al. (2014)	Female/3 mo.	Hard plate	Slowly enlarge mass	SMA+ (focal)/S100+ (focal)/desmin-/myogenin-/MSA-/β-catenin-	ETV6-NTK3-	Chemotherapy; Resection	6 mo. AWD
Cipriani NA et al. (2014)	Female/15 mo.	Left ankle	Growing lesion	Vimentin+/CD34+ (patchy)/CKpan-/desmin-/actin-/SMA-/Syn-/CgA-/MUC4-	51XX; +10, +11, +17, +18, +19	Resection	1 mo. NED
Wang H et al. Case 1 (2014)	Male/4 yr.	Neck	Large mass	Vimentin+/SMA-/MSA-/desmin-/actin-/S100-/CD34-/EMA-/AE1/AE3-/CAM5.2-	NA	Resection	2 yrs. DOD
Wang H et al. Case 2 (2014)	Male/2 dy.	Neck	Mass	Vimentin+/SMA-/MSA-/desmin-/actin-/S100-/CD34-/EMA-/AE1/AE3-/CAM5.2-	NA	Resection	NED

Wang H et al. Case 3 (2014)	Famle/3 mo.	Waist	Mass	Vimentin+/SMA-/MSA-/desmin-/actin-/S100-/CD34-/EMA-/AE1/AE3-/CAM5.2-	NA	Resection	NED
Guilbert MC et al.	Female/7 mo.	Left neck	Increasing mass	Vimentin+/NF/Syn/desmin-/myogenin-/SMA-/MDM2-/WT1/S100-	No EWSR arrangement	Resection; Chemotherapy	Transformation; 70 mo. AWD
Forster JH et al. (2016)	Female/3 mo.	Left upper chest wall	Increasing mass	Vimentin+/β-catenin-/desmin-/myogenin-/SMA-/EMA-/S100-	46XX; ETV6-NTK3-	Resection	3 mo. NED

NA, not available; NED, no evidence of disease; DOD, dead of disease; AWD, alive with disease.

tein, CD34, CD31, CD45, Syn, or NSE [6, 8, 12]. So was our case except for immunoreactivity for NSE, however, the latter without specificity. CD99 in our case is negative, which is different from that reported by Gong Q et al. [6]. However, as we know, CD99, positive in numerous entities, is a not specific in pathologic diagnosis practice, and therefore could not as mandatory diagnostic marker for PMMTI. Little information is available about the cytogenetic or molecular genetic features of PMMTI. The ETV6-NTRK6 gene fusion of infantile fibrosarcoma is absent [11]. Recently, Kao YC et al. found *BCOR* exon 16 internal tandem duplications is a frequent scenario in PMMTI (6/7) compared with infantile sarcoma (15/29) and infantile undifferentiated round cell sarcoma (9/22) [13].

The commonly differential diagnosis include IFS, infantile fibromatosis, myofibrosarcoma/low-grade myofibroblastic sarcoma, low-grade fibromyxoid sarcoma, lipoblastoma, and myxoidliposarcoma. Combination of morphological, immunohistochemical and molecular features can tell them apart. IFS shows poorly formed fascicular growth pattern with focal herringbone figuration and has more dense cellular appearance and increasing atypia with frequently mitotic activity which are rare encountered in PMMTI, though IFS can focally exhibits makedlymyxoid background as a mimicker. Detection of ETV6-NTRK3 by FISH aids distinguishing them [14]. Different from PMMTI, diffusely fascicular and infiltrative growth pattern and expression of myofibroblast-related immunostains, such as SMA, are characteristic manifestation of myofibrosarcoma/low-grade myofibroblastic sarcoma, and infantile fibromatosis, the latter also positive for β-catenin. Lipoblastoma predominantly occurs in infancy and childhood before 3 years and has a predilection of involvement of trunk and extremities instead of abdominal cavity. Notwithstanding focal presentation of myxoid area containing bland primitive spindle cells and delicate branching vasculature reminiscent of myxoidliposarcoma, both of the two entities rare develop in enterocoelia and presence of PLAG1 (lipoblastoma) and DDIT3 (myxoidliposarcoma) gene arrangement has diagnostic values.

The tumor seems not to be responsive to chemotherapy; radical resection is, at present, the mainstay of treatment [11]. Local recurrence and metastasis have been documented, and in addition, a case of transformation to undifferentiated sarcoma was reported [3, 7, 9]. Accordingly, PMMTI may fall within the soft tissue neoplasms with intermediate or low-malignant biological potential. However, the child of our case eventually succumbed to the disease, mainly because abdominal cavity implicated were likely to show a sinister process with refractory ascites followed by serious dyspepsia, under-nourishment and fluid and electrolyte disturbance, which were most possible reasons of death. A clear understanding with regard to biologic and prognostic characters needs increasing accumulation of information about this entity, but the fact of at least intermediate nature has been widely accepted [3, 7, 9, 11].

In conclusion, PMMTI is a rare soft tissue tumor with distinct chinicopathological characteristics and usually arise in infancy and childhood. Omentum in the enterocelia also can be involved other than most commonly anatomic location, which seems to have an unfavorable prognosis. Combination of clinic, histologic and relevant molecular studies are beneficial for establishing the correct diagnosis.

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Disclosure of conflict of interest

None.

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