Original Article

Clinical features, treatment strategies, and prognosis of epithelioid inflammatory myofibroblastic sarcoma in children: a multicenter experience

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Background: Inflammatory myofibroblastic tumors (IMTs) are a spectrum of tumors that range in morphology and biological behavior from benign, intermediate, to apparently malignant and epithelioid inflammatory myofibroblastic sarcoma (EIMS) is one of the malignant subtypes. This study tried to provide experience and new ideas for treating this rare disease.

Methods: This study retrospectively analyzed and followed up 12 children with EIMS admitted to Beijing Children's Hospital, Baoding Children's Hospital, and Children's Hospital of Chongqing Medical University from August 2016 to May 2022.

Results: Of the 12 children, 7 were male and 5 were female, with a median age of 74.50 [interquartile range (IQR), 61.50–90.00] months. Of these patients, eight had a single lesion and four had multiple lesions. The maximum diameter of the single tumor foci was 19.30 cm, the full meridian of the multiple tumor foci target lesions was 32.67 cm, and the median maximum tumor size was 11.99 (IQR, 7.80–15.70) cm. The site of disease was the abdominopelvic cavity in eight cases, the thoracic cavity in two cases, the maxillofacial region in one case, and the larynx in one case. The clinical manifestations were predominantly elevated body temperature (n=8). There was one case of *ROS1* fusion mutation and nine cases of *ALK* fusion mutation. Of the 12 children, 6 were biopsied at the initial diagnosis and 6 were surgically treated. Follow-up treatment included preoperative neoadjuvant chemotherapy (n=4), peritoneal thermal perfusion therapy (n=2), targeted therapy (n=3), postoperative chemotherapy (n=5), and radiotherapy (n=3). The follow-up time was 14.50 (IQR, 10.50–31.50) months, with eight cases of tumor-free survival, two cases of death, and two cases of loss of follow-up.

Conclusions: EIMS in children is extremely rare and clinically aggressive. The clinical presentation is nonspecific, and the initial diagnosis of the tumor is often large. Mutations in the *ALK* gene are common in EIMS. Surgery is the mainstay of EIMS treatment, and patients benefit from a multidisciplinary combination

that includes targeted therapies, with long-term prognosis remaining subject to ongoing follow-up.

Keywords: Epithelioid inflammatory myofibroblast sarcoma (EIMS); children; clinical features; precise treatment; prognosis

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Introduction

Inflammatory myofibroblastic tumors (IMTs) are a spectrum of tumors that range in morphology and biological behavior from benign, intermediate, to apparently malignant (1). Epithelioid inflammatory myofibroblastic sarcoma (EIMS) is one of the malignant subtypes and is highly aggressive with a poor prognosis (2,3). First described by Mariño-Enríquez *et al.* in 2011 (4), EIMS is rare in clinical practice, and its clinical diagnosis is difficult, with histological patterns and immunohistochemical features being needed for a definitive diagnosis. Meanwhile, treatment is limited and mainly surgical (5). Precision medicine involves the application of modern genetic technology, molecular imaging technology, and bio-information technology combined with the patient's living environment and clinical data to achieve precise treatment and diagnosis and to develop a personalized disease prevention and treatment plan (6). In this study, the clinical features, treatment strategies, and prognoses of 12 pediatric cases with EIMS were summarized with the aim of describing the clinical experience, providing new ideas for managing this rare disease, and exploring the treatment of EIMS in the context of precision medicine. We present this article in accordance with the STROBE and AME Case Series reporting checklists (available at https://tp.amegroups.com/article/view/10.21037/tp-23-590/rc).

Highlight box

Key findings

- Epithelioid inflammatory myofibroblastic sarcoma (EIMS) in children is rare in clinical practice. Fever is the most common clinical manifestation. A variety of treatment methods are beneficial to his survival, especially targeted therapy.

What is known and what is new?

- EIMS is rare in the pediatric population.
- We found that combination therapy, including targeted therapy, appears to benefit children with EIMS.

What is the implication, and what should change now?

- This study, which included the largest pediatric EIMS cohort to date, suggests that it is important to better understand EIMS to avoid missed or misdiagnosed cases and implement multidisciplinary combination of treatments for these children.

Methods

Study design

In this retrospective descriptive study, information on clinical features, laboratory test results, treatment protocols, and imaging examinations was summarized. Tumor staging was performed according to the AJCC Cancer Staging Manual (7), and histopathology scores were determined according to the Fédération Nationale des Centres de Lutte Contre le Cancer (FNCLCC) guidelines (8,9). The presence of genetic mutations in children was determined by fluorescence in situ hybridization (FISH) or next-generation sequencing (NGS). The effectiveness of nonsurgical treatment was evaluated using the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 (10).

Participants and setting

The data of 12 children with EIMS confirmed by pathology admitted to Beijing Children's Hospital, Baoding Children's Hospital, and Children's Hospital of Chongqing Medical University from August 2016 to May 2022 were retrospective analyzed. The specific criteria used was from the World Health Organization (WHO) classification of tumors soft tissue and bone tumors (fifth edition), which indicates EIMS as "*plump epithelioid or histiocytoid tumor cells with vesicular chromatin*, *prominent nucleoli*, *and amphophilic or eosinophilic cytoplasm*, *often admixed with neutrophils in an abundant myxoid stroma*" (11).

All children in this study were followed up by outpatient

review and telephone. This retrospective study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Medical Ethics Committee of Beijing Children's Hospital (No. 2023-3-087-R), and the requirement for informed consent was waived for this retrospective descriptive study due to its non-invasive nature, lack of additional medical procedures or costs for participants, and absence of privacy or commercial interests involvement. Baoding Children's Hospital and Children's Hospital of Chongqing Medical University were informed and agreed with this study.

Variables and data sources

Disease outcomes included survival, disease progression, and death. We defined disease progression if tumor size increases by at least 20% from the nadir of the summed measurements, new distant metastases, and recurrence after treatment. The size of the tumor was derived from enhanced computed tomography (CT) examination, which is used to assess the maximum diameter of the tumor, and this method is more feasible in clinical practice. Tumor efficacy evaluation for nonsurgical treatments was performed according RECIST 1.1, which is considered valid and feasible in the evaluation of treatment efficacy in solid tumors (10).

Bias

Because the pathologists at the three children's medical centers had different levels of knowledge of the disease, each included patient was reviewed by a senior pathologist at all three centers to unanimously confirm that the patient had EIMS in order to minimize possible misdiagnosis. In addition to the pathology data, the children's case management, laboratory test results, and imaging studies were reviewed by a senior clinician, radiologist, and laboratory technologist to minimize data errors.

Study size

Due to the extreme rarity of the disease, only 12 cases of EIMS were included through a joint multicenter study.

Statistical methods

SPSS 26.0 (IBM Corp.) was used for statistical processing. The variables were tested for normality: normally distributed measurement data are expressed as the mean ± standard deviation and nonnormally distributed measurement data are expressed as the median with interquartile range.

Results

Participants

A total of 12 cases of EIMS were included in this study: 5 were from Beijing Children's Hospital, 4 from Children's Hospital of Chongqing Medical University, and 3 from Baoding Children's Hospital. All of the included children were reviewed and confirmed as EIMS by three senior pathologists.

Descriptive data

General clinical features

There were seven males and five females with a median age of 74.50 [interquartile range (IQR), 61.50–90.00] months and a minimum age of 6 months. Eight cases had a single lesion, and four had multiple lesions. The maximum diameter of the single tumor foci was 19.3 cm, the full meridian of the multiple tumor foci target lesions was 32.67 cm, and the median maximum tumor meridian was 11.99 (IQR, 7.80–15.70) cm. The site of onset was the abdominopelvic cavity in eight cases, the thoracic cavity in two cases, the maxillofacial region in one case, and the larynx in one case. The clinical presentation was dominated by elevated body temperature (n=8), abdominal pain (n=3), abdominal distention (n=2), palpable swelling (n=2), hoarseness with dyspnea (n=1), and weakness (n=3) (*Table 1*). All 12 children had no family history of tumor-related genetic diseases or other tumors.

Laboratory findings and imaging characteristics

All 12 children admitted in this study had abnormal laboratory findings, of which elevated C-reactive protein (CRP) (n=9) was predominant, followed by elevated platelet (PLT) count (n=7), elevated white blood cell count (n=6), and varying degrees of decreased hemoglobin (n=6); in biochemical blood tests, increased prealbumin (n=7) and decreased albumin (n=8) were common, as was an abnormal albumin-globulin ratio (n=9; Table S1). EIMS has no typical clinical or imaging features and can be found in various body parts, leading it to be easily misdiagnosed preoperatively. Because the interstitial tumor is often edematous or mucinous, a CT scan with enhancement

Table 1 Clinical characteristics, treatment pattern, and prognosis of 12 children with EIMS

Case	Age (m)	Sex	Primary site	Clinical presentation	With or without fever	No. of foci	Initial tumor size (cm)	Treatment modalities	Stage	Prognosis	Follow-up time (m)
1	91	Female	Pelvic and abdominal	Abdominal pain	No	Multiple	32.67	Lumpectomy biopsy + neoadjuvant chemotherapy + targeted therapy + tumor progression + surgery and peritoneal thermal perfusion	$T_4N_0M_0$	Dead	12
2	6	Male	Pelvic and abdominal	Abdominal distention, palpable swelling	Yes	Single	13.40	Surgery	$T_4N_0M_0$	Alive	17
3	60	Male	Pelvic and abdominal	Fever	Yes	Single	10.60	Surgery + tumor recurrence + chemotherapy + surgery and thermal perfusion of the abdominal cavity + chemotherapy + radiotherapy	$T_3N_0M_0$	Alive	21
4	68	Female	Pelvic and abdominal	Abdominal distention	No	Single	19.30	Surgery + chemotherapy + targeted therapy	$T_4N_0M_0$	Alive	9
5	75	Male	Maxillofacial	Facial swelling	Yes	Multiple	10.80	Excisional biopsy + neoadjuvant chemotherapy + radiotherapy	$T_4N_0M_0$	Dead	9
6	91	Female	Chest	Abdominal pain	Yes	Multiple	5.90	Lumpectomy biopsy	$T_1N_0M_0$	Lost to follow-up	–
7	66	Female	Throat	Hoarse voice, breath-holding	No	Single	0.65	Surgery + chemotherapy + radiotherapy	$T_1N_0M_0$	Alive	30
8	55	Male	Pelvic and abdominal	Abdominal pain	Yes	Multiple	16.10	Puncture biopsy + targeted therapy	$T_4N_0M_0$	Alive	11
9	74	Female	Pelvic and abdominal	Fever	Yes	Single	7.72	Surgery	$T_1N_0M_0$	Lost to follow-up	–
10	97	Male	Chest	Weakness	No	Single	8.04	Luminal biopsy + neoadjuvant chemotherapy + surgery + chemotherapy	$T_2N_0M_0$	Alive	78
11	84	Male	Pelvic and abdominal	Wasting and weakness	Yes	Single	13.18	Surgery	$T_1N_0M_0$	Alive	12
12	87	Male	Pelvic and abdominal	Wasting and weakness	Yes	Single	14.52	Luminal biopsy + neoadjuvant chemotherapy + surgery	$T_1N_0M_0$	Alive	36

EIMS, epithelioid inflammatory myofibroblast sarcoma; m, months; T, extent and size of the primary tumor; N, lymph node dissemination; M, presence or absence of metastasis.

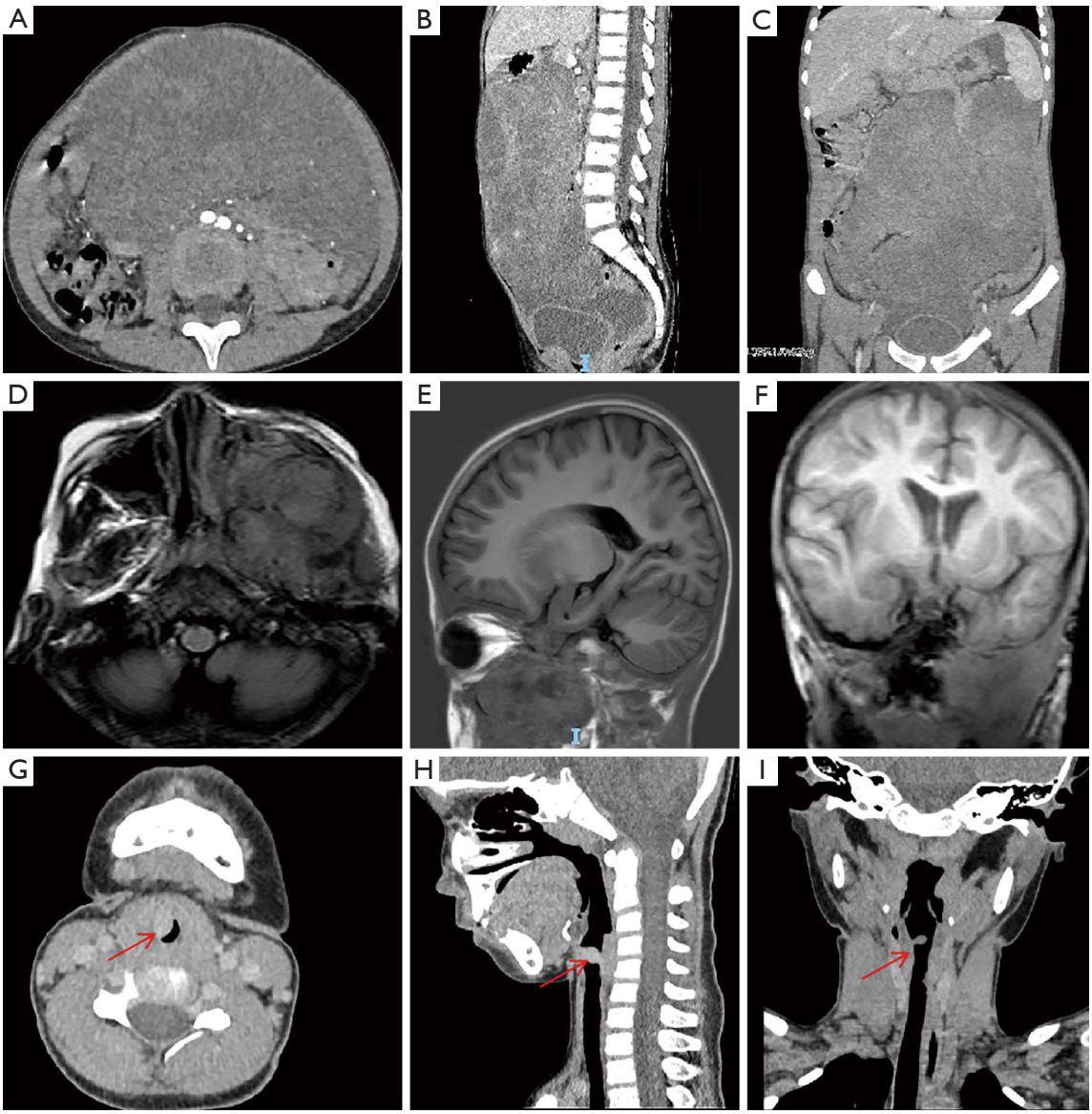

Figure 1 Imaging data of EIMS in children. (A-C) A female, 68-month-old child (case 4) in whom pelvic and abdominal cavity enhancement CT suggested a giant pelvic and abdominal occupancy with inhomogeneous enhancement, with a maximum diameter of 19.30 cm. (D-F) A male, 75-month-old child (case 5) in whom maxillofacial MR suggested a giant left maxillofacial occupancy with a maximum meridian of 10.80 cm. (G-I) A female, 66-month-old child (case 7) in whom enhanced CT suggested a laryngeal occupancy with a maximum meridian of 0.65 cm (arrows). EIMS, epithelioid inflammatory myofibroblast sarcoma; CT, computed tomography; MR, magnetic resonance.

appears hypointense, whereas enhanced scans of dense areas rich in tumor cells are markedly enhanced (*Figure 1*).

Pathological histology and molecular type characteristics

Three senior pathologists reviewed the pathology in this study, and a definitive diagnosis of EIMS was made. Pathological features included full-bodied epithelioid or histiocytic tumor cells with vesicular chromatin, prominent nucleoli, and amphipathic or eosinophilic cytoplasm, often mixed with neutrophils in an abundant mucus-like stroma. In terms of immunohistochemistry (IHC), *ALK* positivity was most common (n=9), followed by desmin positivity (n=8), smooth muscle actin (SMA) positivity (n=7) and

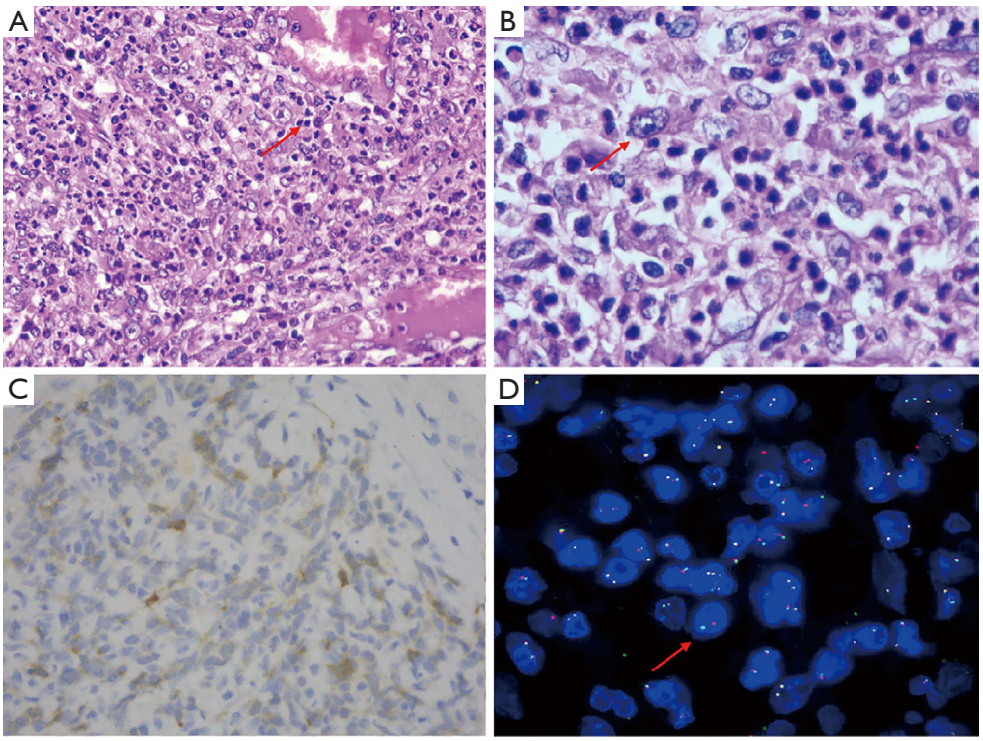

Figure 2 Pathological image of a child with EIMS. A male, 87-month-old child (case 12) in whom HE staining with high magnification revealed a large degree of neutrophil infiltration (A, arrow, ×200) with obvious nuclei (B, arrow, ×400), immunohistochemistry indicated *ALK* perinuclear positivity (C, ×200), and FISH detection showed ALK gene breakage of 23% (D, arrow, ×400). EIMS, epithelioid inflammatory myofibroblast sarcoma; HE, hematoxylin and eosin; FISH, fluorescence in situ hybridization.

CD30 positivity (n=7). In terms of histological grade, six cases were grade I and five cases were grade II. At the molecular level, the presence of fusion mutations in the *ALK* gene was confirmed by FISH in 8 of the 12 children included in this study, while the partner gene was unknown. The presence of fusion mutations was confirmed in two cases by next-NGS. One case had the *BANBP2-ALK* fusion mutation with an *SHQ1* missense mutation (c.1096C>T p.H366Y); in the other case, initial NGS suggested a *TFG-ROS1* fusion mutation (c.1450_1451 del p.Y484HfsTer19). After tumor progression during targeted therapy, repeat NGS suggested *ROS1* [G2032R exon38 single nucleotide variants (SNV)] and a new *C2CT* (R377H exon6 SNV) *KMT2C* [c.13895-1G>T (splice site change) SNV] mutation (*Figure 2* and *Table 2*).

Outcome data

Of the 12 children in this study, 6 were biopsied and 6 were treated surgically at the time of initial diagnosis. Of the six children who underwent biopsy, one was lost to follow-up after abandoning treatment, one achieved complete response (CR) after receiving targeted therapy (*ALK* inhibitors) (case 8), and the remaining four received neoadjuvant chemotherapy. Of the four children who received neoadjuvant chemotherapy, two were indicated for surgery and treated accordingly, and all are currently alive. One case had no significant change in tumor size after neoadjuvant chemotherapy, was followed up with targeted therapy (*ROS1* inhibitors), obtaining partial response (PR) that lasted only 3 months because of drug resistance, the tumor progressed and was treated with surgery and peritoneal thermal perfusion. After surgery, the child was retargeted with targeted drugs based on the NGS results. However, the child still died from disease progression (case 1). One case received radiotherapy and died from tumor progression (case 5). Of the six children initially treated with surgery, one was lost to follow-up because the patient withdrew from the trial and there was no outpatient record or telephone contact. Three children were followed up without other treatment after surgery, and two of them

Table 2 Pathological, histological, and molecular characteristics of the 12 children with EIMS

Case	Number of mitoses (10/HPF)	Percentage of microscopic necrosis (%)	Histological grade	IHC					Type of gene mutation
				ALK	Desmin	SMA	CD30	Ki-67 (%)	
1	2	75	II	–	+	+	+	10	*TFG-ROS1* fusion
2	2	25	II	+NM	+	+	+	20	*ALK*
3	0	99	II	+NM	–	+	+	25	*ALK*
4	1	5	II	+NM	+	+	–	8	*BANBP2-ALK* fusion
5	5	0	I	+NM	–	–	+	20	NA
6	2	0	I	+NM, +PN	+	+	+	40	NA
7	1	0	I	+PN	+	–	+	20	*ALK*
8	NA	NA	NA	+NM	+	–	+	7–10	*ALK*
9	10–15	5	II	+PN	+	–	–	10–15	*ALK*
10	5–10	0	I	+PN	–	+	–	20	*ALK*
11	7–10	0	I	+NM	–	–	–	30	*ALK*
12	5–10	0	I	+NM	+	+	–	30	*ALK*

+, positive cells; –, negative cells. EIMS, epithelioid inflammatory myofibroblast sarcoma; HPF, high-power field; IHC, immunohistochemistry; SMA, smooth muscle actin; +NM, nuclear membrane staining; +PN, cytoplasmic staining with perinuclear accentuation; NA, data not available.

remain event free to date; meanwhile, one case experienced tumor recurrence after surgery and was treated again with surgery and thermal perfusion of the peritoneal cavity followed by chemotherapy and radiotherapy and is now tumor free (case 3). Two children received postoperative chemotherapy: one received targeted therapy (*ALK* inhibitors) sequentially after postoperative chemotherapy due to a large preoperative tumor (case 4), and the other was treated with local radiotherapy due to poor tolerance of postoperative chemotherapy (case 7). Regarding efficacy evaluation, four children received neoadjuvant chemotherapy, with one achieving PR and three stable diseases. Three children received targeted therapy, with one achieving CR, one PR, and one being evaluated with no tumor foci postoperatively. Regarding prognosis, the median follow-up time was 14.50 (IQR, 10.50–31.50) months: eight children survived, two died, and two were lost to follow-up (*Figure 3*).

Discussion

EIMS, a subtype of IMT, is an extremely rare soft tissue tumor, which is particularly rare in pediatric children but aggressive and harmful to the child if misdiagnosed or missed. The understanding of this disease is limited and remains to be thoroughly investigated. Therefore, in this study, the cases from three children's medical centers were combined to form the largest pediatric EIMS cohort to date. The aim of this study was to provide a summary of experience and new ideas for managing this rare disease and to explore the treatment of EIMS in the context of precision medicine.

In terms of clinical characteristics, EIMS has a predilection for the abdominopelvic cavity but has also been observed in other areas of the body (12), including the pleura, pericardium, and intracranial space (13-16), For the first time, this study reports a case of a child with primary laryngeal EIMS, who had hoarseness with dyspnea and a solitary tumor of only 0.65 cm in size (*Figure 1G-1I*). Apart from this case, the children had large tumors at first diagnosis, with eight cases having tumors >10 cm in their largest transits. The remaining clinical data were nonspecific and were mainly related to the location and size of the tumor, with pelvic and abdominal tumors often presenting with abdominal distention or discomfort (n=5). Elevated inflammatory markers (n=9) were common in the children with EIMS, in addition to varying degrees of anemia and reduced albumin, suggesting a poor nutritional status, possibly related to the high nutritional consumption of the tumor. At the same

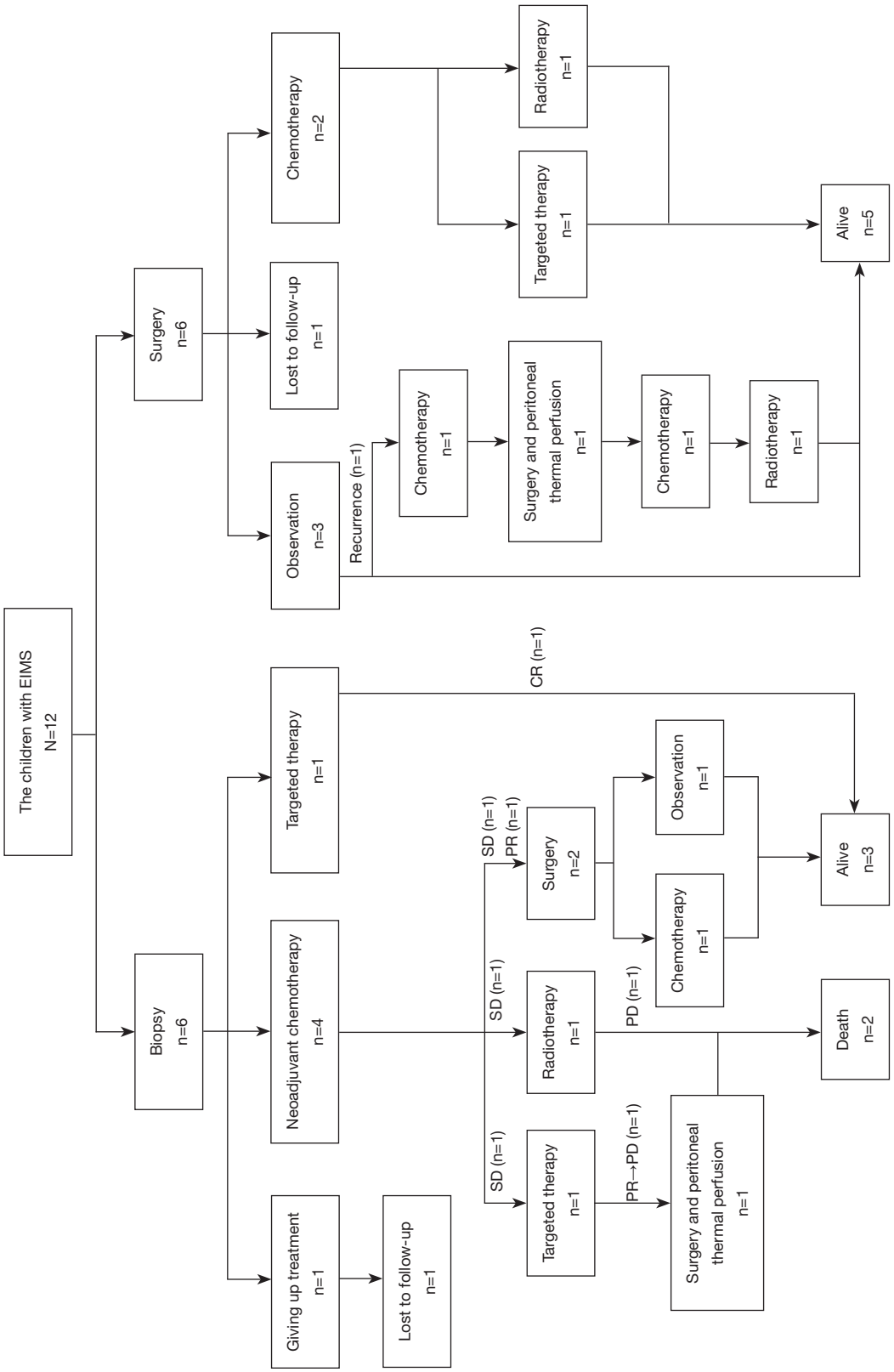

Figure 3 Flowchart of the treatment strategy for the 12 children with EIMS. EIMS, epithelioid inflammatory myofibroblast sarcoma; SD, stable disease; PR, partial response; CR, complete response; PD, progressive disease.

time, when the above laboratory parameters are abnormal, we should be inclined to consider EIMS as a rare tumor in the clinical diagnosis process.

The histomorphology of the EIMS pathology was characterized by round or epithelioid tumor cells, with ganglion-like and Reed Sternberg-like cells and an abundant mucus-like stroma, in which a predominantly neutrophilic inflammatory cell infiltrate was visible (17,18) (*Figure 2*). According to IHC, EIMS shows diffuse, perinuclear or nuclear membrane expression of *ALK*. Previous studies have reported that fusion mutations in the *ALK* gene are extremely common in those with EIMS (4,19), and the presence of fusion mutations in *ALK* was confirmed by FISH or NGS in 9 of the 12 children in this study, which is consistent with previous reports in the literature. Genomics has been applied to pediatric malignancies, especially sarcomas (20,21). The genomic background of tumors can be more effectively and accurately detected using molecular testing techniques to achieve precision treatment (22).

In terms of treatment, surgery has been the mainstay therapy applied in previous studies. Surgical resection can lead to a cure for children assessed to have complete tumor resection. In addition, surgery can provide postoperative pathology to help clarify the diagnosis and guide subsequent treatment. However, there is a lack of effective treatment options for children evaluated for inoperable disease; targeted therapy has been previously reported to be effective in IMTs (19,23,24), so genetic testing-based precision targeted therapy and combination therapy may have considerable potential in the treatment of EIMS. In four cases in this study, neoadjuvant chemotherapy was used, with one case showing tumor shrinkage (PR) and three showing no significant change, suggesting neoadjuvant chemotherapy is a potentially effective treatment option for inoperable children. Most cases of EIMS possess fusion mutations in the *AKL* gene, and *ALK* inhibitors are a potential treatment option (3,4,25). The literature reports the significant efficacy of the *ALK* inhibitor crizotinib in patients with unresectable or metastatic IMTs, including EIMS (26-28), with remission being achieved with the replacement of second-generation *ALK* inhibitors or third-generation *ALK* inhibitors after crizotinib resistance (29,30). Of the two children in this study who were treated with crizotinib, one achieved CR at 12 months on crizotinib and the other had no evaluable tumor foci postoperatively. Both are currently tumor free, and thus clarifying the presence or absence of *ALK* mutations in children with EIMS may be essential to identifying those children who may benefit from targeted therapy with *ALK*. In addition to *ALK* fusion mutations, some children with EIMS have fusion mutations in the *ROS1* gene (31). Previous cases have reported that children with *ROS1* fusion mutations respond well to targeted therapy with ROS1 inhibitors (23,32,33). In our study, case 1 had a *TFG-ROS1* fusion mutation with a germline *FANCE* shift mutation, and the *ROS1* mutation promoted cell growth and division, leading to tumor formation. Subsequently, the child was treated with targeted drugs according to the NGS results and achieved a 3-month PR of disease remission, as evidenced by the shrinkage of the tumor foci and improvement in the general status of the child. However, the tumor progressed again after 3 months, as manifest by its larger size, and thus surgery with intraperitoneal thermal perfusion therapy was administered; however, 1 month after surgery, the tumor progressed again in the abdominal cavity, manifesting as a new nodule of ovarian tumor. A repeat NGS suggested *ROS1* and new *C2CT* and *KMT2C* mutations. Mutation of the *CTCF* gene leads to increased genomic instability and decreased DNA damage repair ability, thus promoting tumorigenesis and progression (34). Meanwhile, the *KMT2C* gene encodes a histone methyltransferase, which is involved in the regulation of gene expression and cell cycle regulation. Studies have reported that mutations in the *KMT2C* gene lead to increased genomic instability and decreased DNA damage repair capacity, which is associated with the development of a variety of tumors, including esophageal cancer (35), gastric cancer (36), and colorectal cancer (37). However, as the treatment progresses, treatment-sensitive tumor cells are eliminated, while treatment-insensitive tumor cells dominate, and the degree of tumor heterogeneity changes. This can further help explain why applying targeted drugs in children at the early stage appears to be effective and why tumor progression occurs in the later stage despite targeted therapy or surgery being applied. Perhaps if tumor progression is detected during targeted therapy, NGS can be rechecked to clarify whether there are new mutations and help adjust the treatment plan to achieve precise treatment.

Due to its malignant oncological behavior, EIMS is best treated by complete surgical resection. Even if the tumor site is surgically resected, there is still a possibility of recurrence (38). In this study, one child experienced tumor recurrence four months after the initial surgery, but no recurrence was observed during the tumor follow-up after reoperation. This suggests that children with recurrence can still benefit from reoperation for complete tumor resection.

Children who cannot undergo complete surgical resection may receive benefit from preoperative neoadjuvant chemotherapy with targeted therapy. In related studies, the local recurrence and distant metastasis rates in the early stages of EIMS recognition exceeded 80% and 25%, respectively, and invasiveness and recurrence rates of EIMS were higher than those of IMTs (2,4). No distant metastases occurred in any of the 12 cases of EIMS in this study. Moreover, the use of more advanced treatment options in addition to surgery, including preoperative neoadjuvant chemotherapy (n=4), intraperitoneal thermal perfusion therapy (n=2), targeted therapy (n=3), postoperative chemotherapy (n=5), and radiotherapy (n=3), contributed to providing better outcomes in these cases. Therefore, aggressive multimodality combination therapy for children with EIMS maybe improves their prognosis.

A few limitations to this study should be addressed. As EIMS is rare in clinic and even rarer in the pediatric field, the sample included in this study—despite it being the largest cohort of its kind reported thus far—was small. Furthermore, we employed a retrospective design, and clinical information was missing or lost. In addition, EIMS was only identified in the last decade and therefore only a relatively short follow-up period could be observed.

Conclusions

EIMS in children is extremely rare and clinically aggressive. The clinical presentation is nonspecific, and at initial diagnosis, the tumor is often large. Mutations in the *ALK* gene are common in EIMS. Surgery is the mainstay of EIMS treatment, and patients can benefit from a multidisciplinary combination, including targeted therapies. The long-term prognosis remains subject to ongoing follow-up.

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Footnote

Reporting Checklist: The authors have completed the STROBE and AME Case Series reporting checklists. Available at https://tp.amegroups.com/article/view/10.21037/tp-23-590/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tp.amegroups.com/article/view/10.21037/tp-23-590/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This retrospective study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Medical Ethics Committee of the Beijing Children's Hospital (No. 2023-3-087-R), and the requirement of informed consent was waived for this retrospective descriptive study due to its non-invasive nature, lack of additional medical procedures or costs for participants, and absence of privacy or commercial interests involvement. Baoding Children's Hospital and Children's Hospital of Chongqing Medical University were informed and agreed with this study.

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