CASE REPORT

Undifferentiated (Embryonal) Sarcoma of the Liver. Case Report and Review of Literature

Mohammed S. Saeed*, Thukaa T. Yahya,Osama E. Hudder***, Issraa A. Hussein******

ABSTRACT:

Undifferentiated (embryonal) sarcoma of the liver was first defined as a separate clinicopathological entity in 1978. it is uncommon hepatic tumor of mesenchymal origin, usually observed in children and teenage, but also infrequently encounter in adult. It represent about 9-15% of all hepatic tumor in children. We report a case of undifferentiated embryonal sarcoma of the liver in a 6 year old girl who presented with non specific right hypochondrial pain and mass with fever. Laboratory studies of the liver function were normal and the other tests were non specific. Ultrasonography and CT scan showed a large heterogeneous mass ranging from cystic tissue with multiple septa to more predominant solid component in the right lobe of the liver. Exploratory laparotomy was performed and revealed a large mass in the right lobe and part of the left lobe of the liver. Tumor resection was performed and about 70% of the total liver was resected. Macroscopically, tumor was large solitary globular firm predominant solid mass weighing 1100gm and measuring 18 x 12 x 8 cm, with variegated cut surface of solid, cystic, necrotic and hemorrhagic areas. Microscopically, the tumor has a variable but distinctive sarcomatous appearance, composed of spindle, oval and stellate-shaped sarcomatous cells, with marked nuclear pleomorphism, closely packed in whorls or scattered loosely in a myxoid ground substance. Numerous bizarre multinucleated giant cells, containing large intracytoplasmic hyaline globules with ample mitosis many of which are atypical. Tumor cells entrapped hyperplastic bile ducts. Accordingly the diagnosis of undifferentiated embryonal sarcoma of the liver was performed. Conclusion: Prompt detection of this aggressive tumor with complete surgical resection is the key to a successful outcome. Prognosis recently improved following postoperative chemotherapy.

KEY WORDS: undifferentiated embryonal sarcoma of the liver, mesenchymal origin, sarcomatous appearance.

INTRODUCTION:

Primary hepatic tumors are rare, but unfortunately two-thirds of them are malignant which account for about 2% of total solid pediatric malignancy. Primary hepatic tumors representing the third most common abdominal cancer encountered in pediatric practice, after Wilms' tumor and neuroblastoma[1,2]. Undifferentiated (embryonal) sarcoma of the liver, also known as undifferentiated liver sarcoma, is a rare malignant hepatic tumor affecting predominantly older children aged 6-10 years [1]. Undifferentiated (embryonal) sarcoma of the liver is the fourth most common malignant hepatic tumors following hepatoblastoma, infantile haemangioendothelioma and hepatocellular carcinoma [3]. It represent about 9-15% of all hepatic tumors in children[4]. We report a case of a 6 year old girl with undifferentiated (embryonal) liver sarcoma. The clinical, radiological & pathological characteristics of this tumor were studied.

CASE REPORT:

A 6 year old girl presented to the pediatric surgery center at Al-Khansa'a Maternity Teaching Hospital with history of non-specific right hypochondriac pain, right hypochondriac mass and fever (Fig. 1). There was no history of jaundice, nausea or loss of weight. she had no significant past or family history, and no history of drug intake or allergies. Her general physical examination was unremarkable. Yellowish discoloration of skin or sclera, spider naevi and palmer erythema all were absent. Systemic examination revealed massive hepatomegaly. His blood count and liver function tests were normal. Alpha fetoprotein was upper

*Pathology Department, College of Medicine, University of Mosul.
**Pathology Lab, Al-Khansa'a Maternity Teaching Hospital, Mosul.
*** Department of Surgery, Nineveh College of Medicine, University of Mosul.
****Department of Pathology, College of Medicine, Baghdad University, Iraq.

normal. Ultrasonography revealed a large mass in the right lobe of the liver. Contrast enhanced CT Scan revealed a large, hypodense mass in the right lobe of the liver. Exploratory laparotomy was performed and revealed a large mass in the right lobe of the liver. Tumor resection was performed and about 70% of the total liver was resected (Fig. 2). Pathologic review of the specimen revealed a large right hepatic mass extended and involved part of the left hepatic lobe, measuring 18 × 12 × 8 cm. The histological examination showed malignant sarcomatous tissue with giant neoplastic cells and residual hepatocytes suggestive of Undifferentiated Liver Sarcoma.. Sarcomatous tissue with severe atypia of the neoplastic cells and focal presence of giant cells, was also present. The patient postoperative course was uneventful and was discharged home 2 weeks after the operation. Patient was referred for adjuvant chemotherapy.

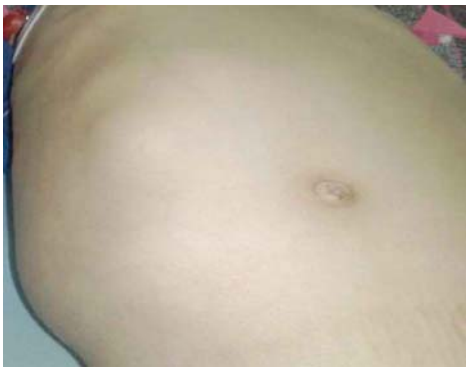


Figure 1: Large right hypochondrial mass in a 6 year old girl

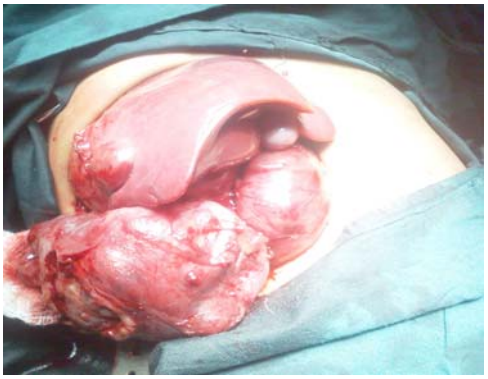


Figure 2: Tumor involve the right lobe and part of left lobe of the liver

DISCUSSION:

Undifferentiated (embryonal) sarcoma of the liver is a rare tumor, first described as a separate clinicopathologic entity in 1978 on the basis of an Armed Forces Institute of Pathology series by Stocker et al who represented a series of 31 cases which showed typical histologic features of. undifferentiated embryonal sarcoma of the liver. Before that, different nomenclature was used include malignant mesenchymoma, fibromyxosarcoma, primary sarcoma of the liver and mesenchymoma. [1,5].

Undifferentiated (embryonal) sarcoma of the liver is typically diagnosed in childhood between 6 years and 10 years, and about 88% of cases occurring among patients younger than 15 years, but also infrequently encountered in adult [6,7]. Till date, about 150 pediatric cases of undifferentiated embryonal sarcoma of the liver have been reported in the literature [5,8]. While only 70 cases of undifferentiated (embryonal) sarcoma of the liver were reported in adult worldwide since this clinicopathological entity was defined [9,10,11]. There does not seem to be sex predominance in this type of tumor in contrast to other hepatic cancers of childhood [12]. In this current presented case the

patient age was 6 year old girl, which is the typical age for this type of tumor.

Embryonal sarcoma of the liver is a rapidly growing malignant tumor [12]. It usually presents with abdominal mass and/or abdominal pain. Other complaints include fever, weight loss, anorexia, malaise, lethargy, and nausea and vomiting [13,14].

Hemorrhage into or rupture of the tumor occurs occasionally [12,15]. Dyspnea from tumor extending into the right atrium via the inferior vena cava has occurred [16]. Jaundice is usually absent and there is usually no abnormality in the liver function with a normal or alpha fetoprotein. The other laboratory studies are usually non-specific [5,9]**.** Our case presented with right hypochondrial pain and mass associated with fever. There was normal liver enzymes and function tests, with normal alpha fetoprotein level. Other tests were non specific.

Imaging studies (sonography and CT) demonstrate somewhat heterogeneous appearances, ranging from cystic tissue with multiple septa to more predominant solid component in the right lobe of the liver as this tumor most often affecting the right hepatic lobe [17,18]. Occasionally, the lesion can be predominantly cystic on ultrasonography and may be mistaken for a hydatid cyst [19]. The image studies including ultrasonography and CT scan of our reported case show a large heterogeneous mass ranging from cystic tissue with multiple septa to more predominant solid component in the right lobe of the liver. There was no other intraabdominal mass.

Macroscopically tumor was large solitary, globular, firm, predominant solid, weighing 1100 gm and measuring 18 x 12 x 8 cm Cut sections show variegated surface with solid, cystic, necrotic and hemorrhagic areas (Fig. 3).

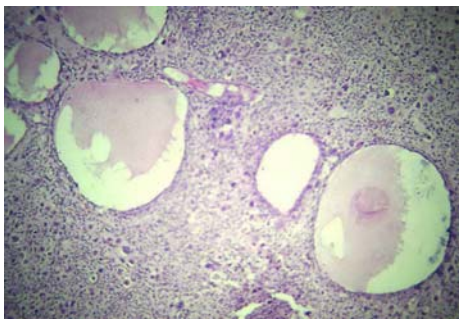
(A)

(B)

Figure 3: A-Large solitary globular tumor. B-Cut sections show variegated sections of predominant solid, cystic, hemorrhagic and necrotic areas.

Microscopically the tumor has a variable but distinctive sarcomatous appearance. It is composed of spindle, oval and stellate-shaped sarcomatous cells, with marked nuclear pleomorphism, closely packed in whorls or scattered loosely in a myxoid ground substance. Numerous bizarre multinucleated giant cells, containing large intracytoplasmic hyaline globules with ample mitosis many of which are atypical. Tumor cells entrapped hyperplastic bile ducts. Tumor shows foci of necrosis and hemorrhage (Fig. 4).

Tumor cells are constantly positive for vimentin, CD68, alpha 1-antitrypsin and alpha 1-antichymotrypsin particularly the large multinucleated cells [20]. However, other immunohistochemical studies show widely divergent differentiation into mesenchymal and epithelial phenotypes and so has no specific or diagnostic relevance, therefore, the diagnosis should be based mainly on morphological features [21,22,23]. The intracytoplasmic hyaline globules are diastase resistant periodic acid-Schiff positive [6,11,22]. Unfortunately there were no specific immunohistochemical markers of this tumor in our locality.



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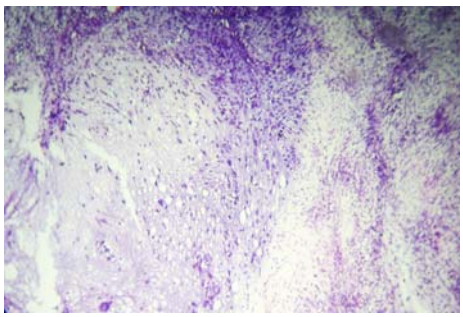

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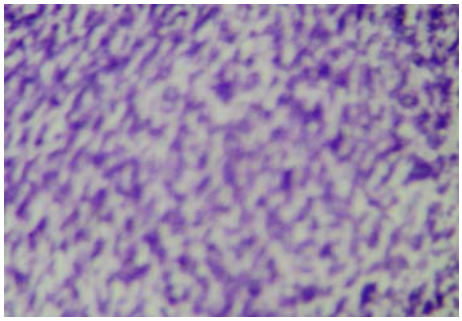

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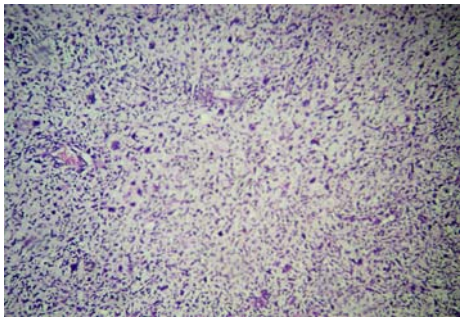

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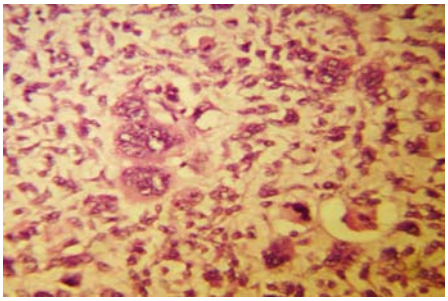

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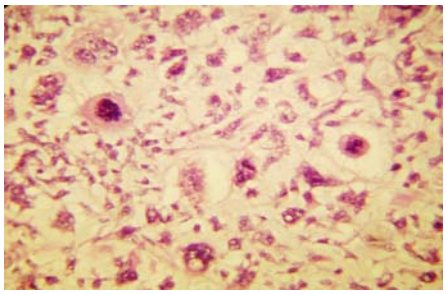

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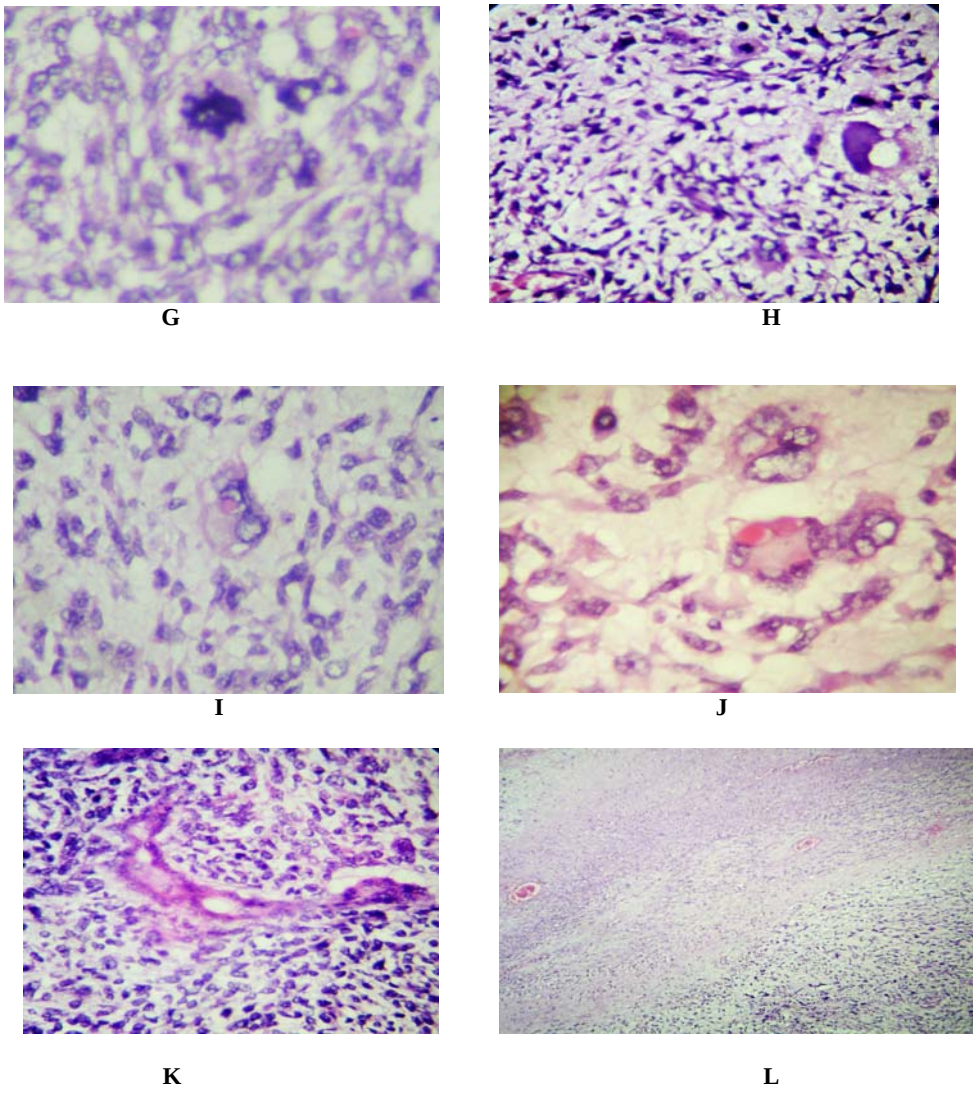

Figure 4: A- Primitive mesenchymal cells with cystic areas filled with serosanguineous secretion. B- Areas of myxoid background. C, D, E, F, G and H- Stellate and spindle mesenchymal cells some arrange in fascicles with numerous global distribution of multinucleated giant cells showing atypical mitosis. I and J- Intracytoplasmic large hyaline globules. K- Tumor cells entrapped hyperplastic bile ducts. L- Foci of necrosis

Morphologically , the distinction between undifferentiated embryonal sarcoma of liver and biliary tract rhabdomyosarcoma can be uncertain because of some pathologic similarity. Study done by Nicol et al shows that in cases of undifferentiated embryonal sarcoma of the liver, the male: female ratio was 1:1 and the median age was 10.5 years and histologically, hyaline globules and diffuse anaplasia were consistently present. Whereas the cases of biliary tract rhabdomyosarcoma had a male: female ratio of 1.8:1 with a median age of 3.4 years and routinely lacked diffuse anaplasia and hyaline globules. Immunohistochemical myogenin and MyoD1 were uniformly negative in undifferentiated embryonal sarcoma of the liver and routinely positive in the majority of biliary tract rhabdomyosarcoma [24].

The exact histogenesis of undifferentiated embryonal sarcoma of the liver remains unresolved,. However, immunohistochemical and ultrastructural studies show fibroblastic, histiocytic and fibrohistiocytic and primitive mesenchymal features, thus resembling pleomorphic malignant fibrous histiocytoma [11,12,25]. In the presented

study, the tumor was morphologically composed of primitive mesenchymal cells with a divergent histological differentiation toward fibroblastic & histiocytic lines.

Although there is no standard treatment mentioned in the literature for undifferentiated embryonal sarcoma of the liver, surgery with neo-adjuvant or adjuvant chemotherapy is the optimal treatment of choice[26]. Other researchers have shown that neo-adjuvant or adjuvant chemotherapy, and/or radiotherapy when necessary, can remarkably improve a patient's survival. [27,28,29]. As local recurrence and distant metastases are common, especially to peritoneum, pleura and lung, and rarely to the inferior vena cava, it is worth recommending that adjuvant chemotherapy be considered in patients presenting with this rare tumor [27,28]. As there are no serum markers to evaluate the response or predict local recurrence, regular abdominal ultrasound or CT scan should be considered for evaluation and to look for any possible recurrence or metastasis. Once there is an evidence of recurrence, resection of the tumor whenever feasible should be performed [6].

The prognosis of undifferentiated embryonal sarcoma of the liver is generally poor. Stocker et al who first defined this entity showed these tumors as having a poor prognosis with median survival of less than 1 year (1). However, since 1990, long term survivors after multiagent chemotherapy have been reported and their outcome appears to have improved substantially over the last decades [29,30]. One study of pediatric patients showing 71% survival at 20 years [28].

CONCLUSION:

Undifferentiated embryonal sarcoma of the liver is a rare, highly malignant primitive mesenchymal hepatic tumor affecting predominantly pediatric patient. Prognosis recently improved after a complete surgical resection of the tumor followed by postoperative chemotherapy.

REFERENCES:

1. Stocker JT, Ishak KG. Undifferentiated (embryonal) sarcoma of the liver: Report of 31 cases. Cancer. 1987;42:336-48.
2. Reynolds M. Pediatric liver tumors. Surg Oncol. 1999;16:159.
3. Yoon W, Kim JK, Kang HK. Hepatic Undifferentiated Embryonal Sarcoma: MR Findings. JCAT 1997;21:100-2.
4. Dev U, Digumarthy SR, Peri N, Reddy JM, Bheerappa, Sundaram C.: Embryonal Sarcoma Of The Liver: A Case Report. Inter J Pathol [serial on the internet]. 2003 [cited 2010 Jul 4]; 2 (2): [about 4 p]. Available from: http://www.ISPUB.com/embryonal sarcoma of the liver.
5. Iqbal K, Xian Z.M, and Yuan C. Undifferentiated liver sarcoma- rare entity: a case report and review of literature. J Med Case Reports. 2008;2:20. doi:10.1186/1752-1947-2-20. PubMed Central PMCID: PMC2253550.
6. Dai CL, Xu F, Shu H, Xu YQ, Huang Y. Undifferentiated (embryonal) sarcoma of liver in adult: a case report. World J Gastroenterol. 2005;11:926-9.
7. Tokunaga Y, Ryo J, Hoppou T, Kitaoka A, Tokuka A, Osumi K, Tanaka T: Hepatic undifferentiated (embryonal) sarcoma in an adult: a case report and review of the literature. Eur J Gastroenterol Hepatol. 2000;12:1247-51.
8. Sodhi KS, Bekhitt E, Rickert C. Paradoxical hepatic tumor: Undifferentiated embryonal sarcoma of the liver. Indian J Radiol Imaging. 2010;20:69-71.
9. Sakellaridis T, Panagiotou I, Georgantas T, Micros G, Rontogianni D, and Antiochos C. Undifferentiated embryonal sarcoma of the liver mimicking acute appendicitis. Case report and review of the literature. Word J Surg Oncol [serial on the internet]. 2006 [cited 2010 Jul 14];4:9. Available from: http://www.wjso.com/content/4/1/9.
10. Jimenez Fuertes M, Lopez Andujar R, de Juan Burgueno M, Moya Herraiz A, Sanjuan Rodriquez F, Montalva Oron E. Hepatic undifferentiated (embryonal) sarcoma in an adult: a case report and review of the literature. Gastroenterol Hepatol. 2008;31:12-7.
11. Nishio J, Iwasaki H, Sakashita N, Haraoka S, Isayama T, Naito M, Miyayama H, Yamashita Y, Kikushi M. Undifferentiated (embryonal) sarcoma of the liver in middle aged adults: smooth muscle differentiation determined by immunohistochemistry and electron microscopy. Hum Pathol. 2003;34:246-52.
12. Aghajanzadeh M, Riazi H, Kohsari MR, Jafroodi M, Hoda S, Ashtiani MN. Undifferentiated (embryonal) sarcoma of the liver: Case report and review of the literature. Saudi J Gastroenterol. 2003;9:139-41.

13. Ming-Hsien Wu, Cheng-Chung Wu, Po-Cheung K. Undifferentiated sarcoma of the liver in an adult: A case report. Formosan J Surg. 2001;34:138-42.

14. Padilla-Rodriguez A, Hermandez-Gonzalez M, Alcantara-Uazquez A. Undifferentiated sarcoma of the liver: Report of a case in an adult. Rev Med Hosp Gen Mex. 2002;65:168-72.

15. Yedibela S, Reck T, Ott R, Muller V, Papadopoulos T, Hohenberger W. Undifferentiated, embryonal sarcoma as a rare case cause of spontaneous liver rupture in adults. Chirurg. 2000;71:101–5.

16. Lack EE, Schloo BL, Azumi N, Travis WD, Grier HE, Kozakewich HP. Undifferentiated (embryonal) sarcoma of the liver. Clinical and pathologic study of 16 cases with emphasis on immunohistochemical feature. Am J Surg Pathology. 1991;15:1-16.

17. Buetow PC, Buck JL, Brown LP, Marshall WH, Ros PR, Levine MS, Goodman ZD: Undifferentiated (Embryonal) Sarcoma of the Liver: Pathologic Basis of Imaging Findings in 28 cases. Radiology. 1997,203:779-83.

18. Kim M, Tireno B, Slanetz PJ. Undifferentiated Embryonal Sarcoma of the Liver. AJR. 2008;190:261-62.

19. Joshi SW, Merchant NH, Jambhekar NA: Primary multilocular cystic undifferentiated (embryonal) sarcoma of the liver in childhood resembling Hydatid cyst of the liver. Br J Radiol. 1997;70:314-16.

20. Ma L, Liu YP, Geng CZ, Tian ZH, Wu GX, Wang XL. Undifferentiated embryonal sarcoma of the liver in an old female: case report and review of the literature. World J Gasstroenterol. 2008;14:7267-70.

21. Kiani B, Ferrell LD, Qualman S, Frankel WL Immunohistochemical analysis of embryonal sarcoma of the liver. Appl Immunohistochem Mol Morphol. 2006;14:193-7.

22. Zheng JM, Tao X, Xu AM, Chen XF, Wu MC, Zhang SH. Primary and recurrent embryonal sarcoma of the liver: clinicopathological and immunohistochemical analysis. Histopathology. 2007;51:195-203.

23. Wei ZG, Tang LF, Chen ZM, Tang HF, Li MJ. Childhood undifferentiated embryonal liver sarcoma: clinical features and immunohistochemistry analysis. J Pediatr Surg. 2008;43:1912-19.

24. Nicol K, Savell V, Moore J, Teot L, Spunt SL, Qualman S. Distinguishing undifferentiated embryonal sarcoma of the liver from biliary tract rhabdomyosarcoma: a Children's Oncology Group study. Pediatr Dev Pathol. 2007;10:89-97.

25. Aoyama C, Hachitanda Y, Sato JK, Said JW, Shimada H. Undifferentiated (embryonal) sarcoma of the liver. A tumor of uncertain histogenesis showing divergent differentiation. Am J Surg Pathol. 1991;15:615-24.

26. Almogy G, Lieberman S, Gips M, Pappo O, Edden Y, Jurim O, Simon Slasky B, Uzieli B, Eid A: Surgical outcomes of surgical resections for primary liver sarcomas in adults: results from a single center. Eur J Surg Oncol. 2004,30:421-7.

27. Kim DY, Kim KH, Jung SE, Lee SC, Park KW, Kim WK: Undifferentiated (embryonal) sarcoma of the liver: combination treatment by surgery and chemotherapy. J Pediatr Surg. 2002;37:1419-23.

28. Bisogno G, Pilz T, Perilongo G, Ferrari A, Harms D, Ninfo V, Treuner J, Carli M: Undifferentiated sarcoma of the liver in childhood: a curable disease. Cancer. 2002;94:252-57.

29. O'Sullivan MJ, Swanson PE, Knoll J, Taboada EM, Dehner LP. Undifferentiated embryonal sarcoma with unusual features arising within mesenchymal hamartoma of the liver: report of a case and review of the literature. Pediatr Dev Pathol. 2001;4:482–89.

30. Walker NI, Horn MJ, Strong RW, Lynch SV, Cohen J, Ong TH, Harris OD. Undifferentiated (embryonal) sarcoma of the liver. Pathologic findings and long-term survival after complete surgical resection. Cancer. 1992;69:52–59.

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