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横纹肌肉瘤临床病理分析

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[摘　要]　**目的：**探讨横纹肌肉瘤(rhabdomyosarcoma，RMS)临床特点、病理形态及免疫表型。**方法：**回顾性分析39例RMS的临床资料、组织学形态、免疫组织化学。**结果：**39例RMS中，胚胎性RMS 24例，腺泡状RMS 11例，多形性RMS 3例，梭形/硬化性RMS 1例，多见于青少年，好发于头颈部。31例Desmin(+)，32例MyoD1(+)，15例Myogenin(+)，3例因形态典型，未行免疫组织化学检查。**结论：**RMS是一种好发于青少年的高度恶性肿瘤。组织学形态上表现为原始的小圆细胞及不同比例的横纹肌母细胞，免疫组织化学表达Desmin，MyoD1和myogenin。

[关键词]　横纹肌肉瘤；组织学分型；免疫表型

Clinicopathological analysis of rhabdomyosarcoma

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Abstract　**Objective:** To explore clinical features, pathological morphology, immunohistochemistry of rhabdomyosarcoma (RMS). **Methods:** The clinical characteristics, histological morphology and immune phenotype of 39 cases of RMS were retrospectively analyzed. **Results:** The 39 cases of RMS involved 24 cases of embryonal RMS (ERMS), 11 cases of alveolar RMS (ARMS), 3 cases of pleomorphic RMS (PRMS), and 1 case of spindle/sclerosing RMS (SRMS). The diseased region was in head and neck and more likely in teenagers. Immunohistochemical methods showed positive staining for Desmin in 31 cases, positive staining for MyoD1 in 32 cases, and also positive staining for Myogenin in 15 cases. Three of these cases did not performed immunohistochemistry due to the typical morphology. **Conclusion:** RMS is a kind of high malignant tumor which frequently arose in teenagers. The histomorphology shows the original small round cells and different proportions of rhabdomyoblasts, while immunohistochemistry shows that Desmin, MyoD1 and myogenin are expressed.

Keywords　rhabdomyosarcoma; histologic classification; immune phenotype

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横纹肌肉瘤(rhabdomyosarcoma，RMS)是一种显示骨骼肌分化的原始间叶性高度恶性肿瘤，好发于青少年，头颈部多见。2013版WHO将其分为胚胎性(包括葡萄簇样和间变性)、腺泡状(包括实体型和间变性)、多形性及梭形细胞/硬化性4种主要类型[1]。结合临床病理与免疫组织化学，可提高诊断的准确性。本研究重点讨论RMS的临床特征、组织学形态、免疫表型，以提高对RMS的认识。

1 对象与方法

1.1 对象

收集福建省肿瘤医院2007年1月1日至2017年12月30日经病理证实的39例RMS病例(包括外院会诊的19例)，分析其年龄、性别构成、发病部位等。本研究经福建医科大学附属福建省肿瘤医院医学伦理委员会批准，所有患者知情同意。

1.2 方法

所有标本经4%中性甲醛固定，常规脱水，石蜡包埋，切片厚4 μm，二甲苯脱蜡，乙醇彻底冲洗，HE染色，显微镜观察。免疫组织化学染色，采用MaxVision二步法，Ventana自动免疫组织化学染色仪操作。结蛋白(Desmin)、肌调节蛋白(MyoD1)、肌浆蛋白(Myogenin)等抗体均购自福州迈新生物技术开发有限公司。免疫染色阳性定义：MyoD1，Myogenin均为核着色，Desmin胞质着色。

2 结果

2.1 临床病理分型资料

在39例RMS中，胚胎性最多，其次为腺泡性(表1)。在胚胎性RMS中，男11例，女13例，年龄2~45(平均20.5，中位20)岁，高峰年龄为10~<20岁和20~<30岁，性别间差异无统计学意义(P>0.05，图1)。胚胎性RMS好发于头颈部[44%，鼻腔占72.7%(8/11)]，其次为泌尿生殖系统[20%，其中宫颈占40%(2/5)]，四肢和躯干各占16%，腹腔占4%(图2)。在腺泡状RMS中，男4例，女7例，年龄5~54(平均31.9，中位34)岁(图3)。腺泡状RMS好发于头颈部(73%)，其余部位例如四肢、躯干、腹股沟也可发生(图4)。而多形性RMS仅3例，患者年龄分别为27，34，56岁，发生部位分别是纵膈、大腿、精索。梭形/硬化性RMS仅1例，女性，38岁，肺部转移灶。

表 1 39 例 RMS 各分型病例数及所占比例

Table 1 Number and proportion of each subtype in 39 cases of RMS

组织学分型	例数	构成比/%
胚胎性	24	61.54
腺泡状	11	28.20
多形性	3	7.70
梭形/硬化性	1	2.56
总例数	39	100.00

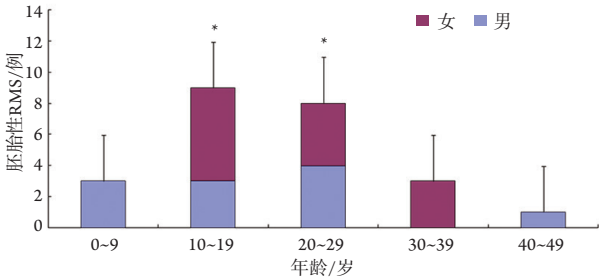

图1 24例胚胎性RMS患者年龄和性别分布图

Figure 1 Distribution of age and gender of 24 patients with embryonal RMS

*：高峰年龄，性别差异无统计学意义(P>0.05)。

*: peak ages, with no significant different in gender (P>0.05).

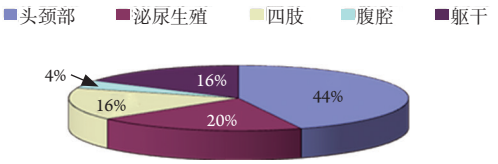

图2 24例胚胎性RMS发病部位分布图

Figure 2 Distribution of location of 24 patients with embryonal RMS

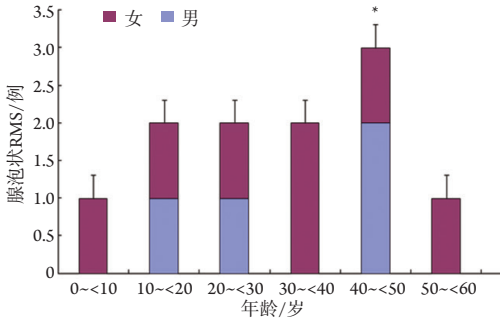

图3 11例腺泡状RMS年龄和性别分布

Figure 3 Distribution of age and gender of 11 patients with alveolar RMS

*：高峰年龄，略大于胚胎性RMS

*: peak ages, which was slightly older than that of embryonal RMS

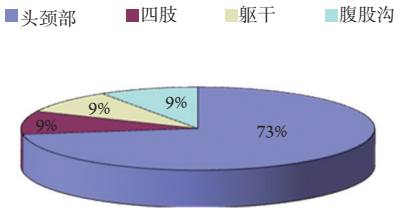

图4 11例腺泡状RMS发病部位分布图

Figure 4 Distribution of location of 11 patients with alveolar RMS

2.2 组织学形态

胚胎性RMS主要由原始的小圆形间叶细胞、不同比例的横纹肌母细胞构成，其中原始间叶细胞一般胞质稀少，核圆形或卵圆形，核染色质深，核分裂象易见。腺泡状RMS肿瘤细胞形成腺泡状结构，部分细胞显示骨骼肌分化特征。多形性RMS一般由大圆形、多边形或梭形等异型性明显的细胞构成，并可见骨骼肌分化细胞。梭形细胞RMS主要由束状排列的梭形细胞构成，类似肌纤维母细胞或平滑肌细胞，偶见横纹肌母细胞(图5)。

2.3 免疫表型

RMS免疫组织化学通常表达Desmin，MyoD1，Myogenin，且MyoD1，myogenin(图6)为核染色对于RMS诊断有辅助作用。本研究中3例因形态典型，未行免疫组织化学，Desmin阳性表达率为86.11%(31/36)，MyoD1阳性表达率88.89%(32/36)。19例未行Myogenin检测，Myogenin阳性表达率75%(15/20)。

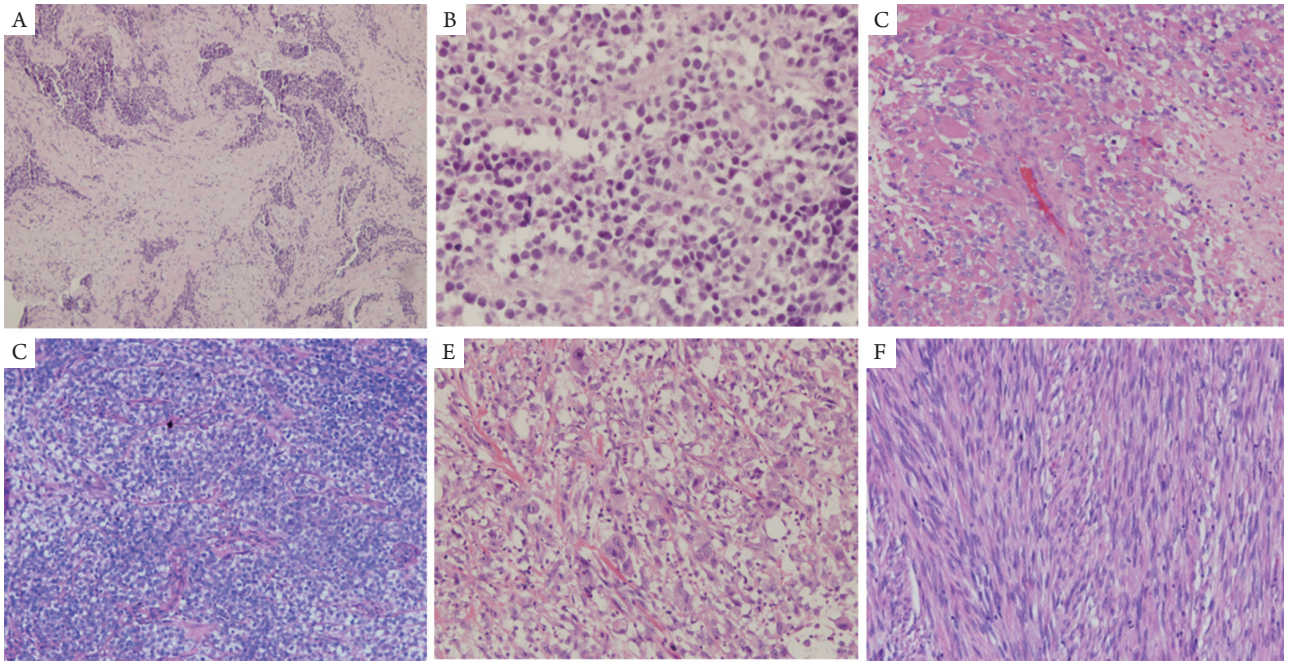

图5 RMS的病理特征

Figure 5 Pathological feature of RMS

(A)原始间充质样细胞呈挤压性分布(HE，×100)；(B)原始小圆细胞体积小、胞质稀少(HE，×200)；(C)局部可见不同比例的横纹肌母细胞(HE，×200)；(D)肿瘤细胞排列成腺泡状(HE，×200)；(E)大圆形、多边形的肿瘤细胞，异型性明显(HE，×200)；(F)肿瘤细胞呈梭形、束状排列(HE，×200)。

(A) Primitive mesenchymal cells were compressively distributed (HE, ×100); (B) Primitive mesenchymal cells with small size and few cytoplasm (HE, ×200); (C) Different proportions of rhabdomyocytes were found locally (HE, ×200); (D) Tumor cells were arranged in acinar shape (HE, ×200); (E) Large circular, polygonal rhabdomyoblast with obvious heterogeneity (HE, ×200); (F) Tumor cells are fusiform and bunchy (HE, ×200).

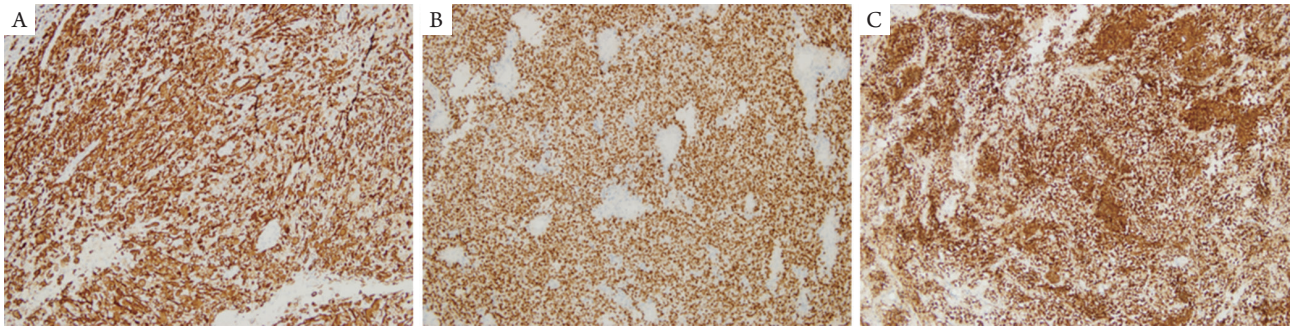

图6 RMS的免疫表型(×200)

Figure 6 Immunophenotype of RMS (×200)

(A)Desmin弥漫细胞质阳性；(B)Myogenin弥漫细胞核阳性；(C)MyoD1弥漫细胞核阳性。

(A) Neoplastic cells are positive for Desmin; (B) Neoplastic cells are positive for Myogenin; (C) Neoplastic cells are positive for MyoD1.

3 讨论

1854年，Weber[2]首次描述RMS；1894年，由Berard[3]首次报道胚胎性RMS；1946年，Stout[4]报道多形性PRMS；1956年，有学者[5]首次报道腺泡状ARMS；1958年，Horn和Enterline[6]提出将RMS分为胚胎性、葡萄簇状样、腺泡状和多形性RMS。肉瘤是极其复杂且具异质性的恶性肿瘤，对特定患者行个体化治疗前，精确病理分类必不可少。

胚胎性RMS最常见，发病年龄通常<10岁，平均7岁，5岁以下占36%，青少年约占18%[7]，较少发生于成年人，好发部位头颈部(尤其眼眶、鼻腔、鼻旁窦等)、泌尿生殖道、盆腔腹膜后等部位[8]。腺泡状RMS较常见，仅次于胚胎性，主要发生于10~25岁的青少年，好发四肢深部软组织，其次是头颈部、躯干等[9-10]。多形性RMS较少见，多发生在45岁以上的成年人[11]，好发下肢，尤其是大腿。梭形细胞RMS少见，好发于儿童和青少年，成年亦可[12]，最常见发病部位是睾丸旁[13]。

RMS免疫组织化学通常表达Desmin，MyoD1，Myogenin[14-17]等，对诊断有一定的特异性，部分胚胎性RMS可表达WT-1[18]，有一定的鉴别意义。在本研究中Desmin(86.11%)，MyoD1(88.89%)，Myogenin(75%)均有较高表达率。近年关于Ras介导的RMS发生发展通路的研究[19]发现YAP蛋白在其中起重要作用，并认为YAP蛋白染色对于腺泡状RMS的诊断可能具有辅助作用。

大多数胚胎性RMS的发病机制为染色体11p15.5丢失导致其上的胰岛素生长因子2(insulin growth factor，IGF2)过度表达[20]。部分腺泡状RMS患者存在TP53，CDKN2A/CDKN2B[21]失活性突变，以及FGFR4[22]激活性突变等。

胚胎性RMS应与神经母细胞瘤、骨外尤文肉瘤/外周原始神经外胚层瘤、嗅神经母细胞瘤、促结缔组织增生性小圆细胞肿瘤、恶性黑色素瘤、恶性淋巴瘤等鉴别。腺泡状RMS应与腺泡状软组织肉瘤、透明细胞肉瘤、透明细胞癌等鉴别。多形性RMS应与未分化多形性肉瘤以及伴有横纹肌母细胞分化的恶性肿瘤等鉴别。免疫组织化学有辅助作用，必要时可进行分子检测鉴别。部分腺泡状RMS从形态上很难与胚胎性RMS相鉴别，有研究[23]指出：70%~80%的腺泡状RMS中可检测到特异性染色体易位t(2;13)(q35;q14)和t(1;13)(p36;q14)，两种易位分别形成相应的融合基因PAX3-FKHR和PAX7-FKHR，而在胚胎性RMS中未见这两种染色体易位，可利用探针FKHR，PAX3进行FISH检测，但目前检测还不普遍。

RMS是一组高度恶性的肿瘤，治疗强调手术、化疗、放疗多学科的综合治疗。预后取决于临床分期、组织学类型、年龄和部位[24]，其中预后最好的是葡萄簇状RMS，腺泡状较胚胎性差，而多形性早期即可发生远处转移。

综上所述，RMS主要发生于婴幼儿或青少年头颈部，组织学形态上表现为原始的小圆细胞及不同比例的横纹肌母细胞，免疫组织化学表达Desmin，MyoD1和Myogenin。由于患病人群年龄较小，早期认识该疾病显得尤为重要。通过临床与病理相结合确诊该疾病，以提高患者生存率。目前，对该肿瘤患者应进行多学科综合治疗，至于RMS的遗传分子机制尚待进一步研究。

参考文献

1. Fletcher CD, Bridge JA, Hogendooyn CW, et al. World Health Organization classification of tumours soft tissue and bone[M]. Lyon: IARC Press, 2013: 127-135.
2. Weber CO. Anatomische untersuchung einer hypertrophieschen zunge nebst bemekugen uber die nubidung querquestreifter muskelfsem[J]. Virhow Arch Pathol Anat, 1854, 7: 115.
3. Berard M. Tumeur embryonnaire dumuscle striae[J]. Lyon Med, 1894, 77: 52.
4. Stout AP. Rhabdomyosarcoma of skeletal muscles[J]. Ann Surg, 1946, 123(3): 447-472.
5. Riopelle JL, Theriault JP. An unknown type of soft part sarcoma: alveolar rhabdomyosarcoma[J]. Ann Anat Pathol (Paris), 1956, 1(1): 88-111.
6. Horn RC Jr, Enterline HT. Rhabdomyosarcoma: A clinicopathological study and classification of 39 cases[J]. Cancer, 1958, 11(1): 181-99.
7. Ognjanovic S, Linabery AM, Charbonneau B, et al. Trends in childhood rhabdomyosarcoma incidence and survival in the United States, 1975-2005[J]. Cancer, 2009, 115(18): 4218-4226.
8. Newton WA Jr, Soule EH, Hamoudi AB, et al. Histopathology of childhood sarcomas, Intergroup Rhabdomyosarcoma Studies I and II: clinicopathologic correlation[J]. J Clin Oncol, 1988, 6(1): 67-75.
9. Enzinger FM, Shiraki M. Alveolar rhabdomyosarcoma. An analysis of 110 cases[J]. Cancer, 1969, 24(1): 18-31.
10. Harms D. Alveolar rhabdomyosarcoma: a prognostically unfavorable rhabdomyosarcoma type and its necessary distinction from embryonal rhabdomyosarcoma[J]. Curr Top Pathol, 1995, 89(89): 273-296.
11. Hollowood K, Fletcher CD. Rhabdomyosarcoma in adults[J]. Semin Diagn Pathol, 1994, 11(1): 47.
12. Cavazzana AO, Schmidt D, Ninfo V, et al. Spindle cell rhabdomyosarcoma. A prognostically favorable variant of rhabdomyosarcoma[J]. Am J Surg Pathol, 1992, 16(3): 229-235.
13. Leuschner I, Newton WA Jr, Schmidt D, et al. Spindle cell variants of embryonal rhabdomyosarcoma in the paratesticular region. A report of the Intergroup Rhabdomyosarcoma Study[J]. Am J Surg Pathol, 1993, 17(3): 221-230.
14. Parham DM, Webber B, Holt H, et al. Immunohistochemical study of childhood rhabdomyosarcomas and related neoplasms. Results of an Intergroup Rhabdomyosarcoma study project[J]. Cancer, 1991, 67(12): 3072-3080.
15. 赖日权, 田野, 安建成, 等. 横纹肌肉瘤与胚胎横纹肌的形态学和免疫组织化学对比观察[J]. 中华病理学杂志, 1993, 22(5): 265-268.
    LAI Riquan, TIAN Ye, AN Jiancheng, et al. The morphological and immunohistochemical comparison of rhabdomyosarcoma and embryonic striated muscle[J]. Chinese Journal of Pathology, 1993, 22(5): 265-268.
16. Kumar S, Perlman E, Harris CA, et al. Myogenin is a specific marker for rhabdomyosarcoma: an immunohistochemical study in paraffin-embedded tissues[J]. Mod Pathol, 2000, 13(9): 988-993.
17. Cessna MH, Zhou H, Perkins SL, et al. Are myogenin and myoD1 expression specific for rhabdomyosarcoma? A study of 150 cases, with emphasis on spindle cell mimics[J]. Am J Surg Pathol, 2001, 25(9): 1150-1157.
18. Carpentieri DF, Nichols K, Chou PM, et al. The expression of WT1 in the differentiation of rhabdomyosarcoma from other pediatric small round blue cell tumors[J]. Mod Pathol, 2002, 15(10): 1080-1086.
19. Ahmed AA, Habeebu SS, Sherman AK, et al. Potential value of YAP staining in rhabdomyosarcoma[J]. J Histochem Cytochem, 2018 [Epub ahead of print].
20. Tombolan L, Orso F, Guzzardo V, et al. High IGFBP2 expression correlates with tumor severity in pediatric rhabdomyosarcoma[J]. Am J Pathol, 2011, 179(5): 2611-2624.
21. Iolascon A, Faienza MF, Coppola B, et al. Analysis of cyclin-dependent kinase inhibitor genes (CDKN2A, CDKN2B, and CDKN2C) in childhood rhabdomyosarcoma[J]. Genes Chromosomes Cancer, 1996, 15(4): 217-222.
22. Li SQ, Cheuk AT, Shern JF, et al.Targeting wild-type and mutationally activated FGFR4 in rhabdomyosarcoma with the inhibitor ponatinib (AP24534)[J]. PLoS One, 2013, 8(10): 108-110.
23. Sorensen PH, Lynch JC, Qualman SJ, et al. PAX3-FKHR and PAX7-FKHR gene fusions are prognostic indicators in alveolar rhabdomyosarcoma: a report from the children's oncology group[J]. J Clin Oncol, 2002, 20(11): 2672-2679.
24. Raney RB, Anderson JR, Barr FG, et al. Rhabdomyosarcoma and undifferentiated sarcoma in the first two decades of life: a selective review of intergroup rhabdomyosarcoma study group experience and rationale for Intergroup Rhabdomyosarcoma Study V[J]. J Pediatr Hematol Oncol, 2001, 23(4): 215-220.

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