Perianal and Perineal Rhabdomyosarcomas - A Retrospective Multicenter Study of 35 Cases

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Abstract

Background

Perianal/perineal rhabdomyosarcoma (PRMS) is rare, easy to be misdiagnosed and has poor prognosis. This study was designed to analyze the clinical, diagnostic, pathological and prognostic features of PRMS, and to explore its therapeutic modality.

Methods

Clinical data of PRMS patients in the Sixth Affiliated Hospital and the Cancer Center of Sun Yat-sen University and related Chinese literatures published between 1987 and 2018 were described and analyzed. Chi-square test was used to test the differences between groups. The Kaplan-Meier methods were used to estimate and compare survival rates.

Results

35 patients, 20 identified in the Chinese literatures and 15 of our center from 1997 to 2019, were included in this study. 34 cases presented as perianal mass and one presented as inguinal mass. 20 patients complained about pain and 16 cases were misdiagnosed as perianal abscess, in which pain was found related to misdiagnosis (p<0.05). The average time from symptoms to pathological diagnosis was 3.1 months. 13 cases were categorized into IRS group III/IV and 20 cases into stages 3/4. 14 Cases were diagnosed as embryonal rhabdomyosarcoma pathologically and 9 as alveolar rhabdomyosarcoma. Five patients survived for more than two years, three of them survived for more than five years. The overall survival rates of two years and five years were 32% and 24% respectively, in which misdiagnosis contributes to poor prognosis (p<0.05). MRI showed that PRMS was closely related to external anal sphincter in 10 cases.

Conclusion

PRMS is easy to be misdiagnosed, which could lead to worse outcome. Patients with painful perianal mass should be evaluated to exclude PRMS. MRI shows PRMS is closely related to external anal sphincter. Comprehensive therapy including radical operation and chemotherapy is recommended.

Background

Rhabdomyosarcoma (RMS) is a common soft tissue malignancy, but primary perianal and perineal rhabdomyosarcoma (PRMS) is extremely rare, accounting for only 2% of all RMS[1]. PRMS is easy to be misdiagnosed and mistreated and the mortality rate is relatively high. In this study, 35 Chinese patients were reviewed to clarify the clinical manifestations, imaging, pathology and prognostic features of PRMS and to explore the optimal therapeutic regimen of this disease.

Patient eligibility

15 PRMS patients treated and followed up at the Sixth Affiliated Hospital (n=6) and the Cancer Center (n=9) of Sun Yat-sen University were reviewed in this study. The perianal region is consist of the area posterior or lateral to the anus and the perineal region is defined as the area between anus and the scrotum or labia magna. Patients with gluteal or deep pelvic primaries involving the perineum or of urogental origin were excluded[2]. Information including patients’ sex, age at first diagnosis, symptoms, preoperative tumor size, pathological type, lymph node involvement, metastasis and treatments were collected and analyzed. The staging and grouping after operation were in accordance with IRS (Intergroup Rhabdomyosarcoma Study) standard[3]. A database of medical journals published in Chinese between 1987 and September 2018 was examined and 20 patients were identified[4-19]. Adding together, 35 patients were included in this study. The Ethics Committee at the Six Affiliated Hospital approved the study.

Statistical analysis

Spss26.0 software package was used for statistical analysis. Chi square test was used to test the differences between groups. The Kaplan-Meier method was used to assess Overall Survival, which was calculated as the time from pathological diagnosis to the point of death or the last follow-up. Survival curves among different patient subgroups were compared with the Mantel log-rank test. P<0.05 was considered significant.

Results

Patient characteristics

Table1 summarizes the data of the patients treated in our center and clinical characteristics of all 35 patients were listed in table2. The study group comprised 10 males and 25 females ranging in age form 1 to 56 years. The most common presenting symptom was perianal/perineal mass, only one patient complained about inguinal mass. Other symptoms including pain, bloody stool, difficult defecation and fecal incontinence (3%) were noted. 15 patients had regional lymphatic metastasis and 5 patients had distant metastasis at the time of diagnosis. The IRS group was I in 1, II in 11, III in 8 and IV in 5 cases. The pre-treatment staging were stage-2 in 6, stage-3 in 15 and stage-4 in 5 cases.

Imaging

15 patients treated in our center received imaging evaluation. 4 patients were examined by color Doppler ultrasound and showed hypoechoic or mix-echoic mass with unclear boundary and irregular shape. Spot blood flow signals were detected by CDFI in 3 cases and 1 has abundant blood flow signals around the mass. These patients were then subjected to ultrasound-guided biopsy and pathology showed RMS. All the 15 patients received CT/MRI scan, which showed
the average maximum diameter of tumor was 6.8cm (1.8-12.2cm). Tumor compression of internal anal sphincter and rectal mucosa was observed in 5 cases and 3 had urogenital involvement was identified in 3 cases. MRI was conducted in 10 patients and showed equal signal on T1WI (n=10) and high (n=5) or mixed (n=5) signal on T2WI in tumors. Furthermore, external anal sphincter (EAS) involvement was observed in all the 15 cases (Figure 1), including 3 having puborectalis involvement and 3 having levator ani involvement (Figure 2). Regional lymph node metastasis was found in 12 patients. 5 patients had distant metastases at the sites including bone, lung, pancreas, breast and pelvic cavity. Clinical stages were determined based on imaging evaluation: 5 cases in stage 2, 6 in stage 3 and 4 in stage 4.

Pathological findings

6 of 15 cases in our 2 centers were histologically confirmed as alveolar RMS (Figure 3) and 9 were embryonal (Figure 4). Myogenin was expressed in all cases. Desmin and vimentin were positive in 5 of 5 cases. MyoD1 was positive in 3 of 4 cases. Of all the 35 patients, 14 were embryonic RMS, 9 were alveolar and 1 was pleomorphic. 11 cases have no histological reports. Desmin (+) (20/20), vimentin (+) (14/14), myogenin (+) (15/15), MyoD1 (+) (9/10) and myoglobin (+) (9/9) are reported in 20 immunohistochemistry available cases.

Treatments and outcomes

10 patients received surgical treatment in our center, primary surgery was performed in 3 (R0=3, Rx=1) and secondary surgery after chemotherapy was performed in 6 (R0=3, R1: n=1; Rx: n=2). Among these patients, 4 received abdominopereineal resection (APR) and 5 received local radical tumor resection (LRR). 1 patient undergone inguinal lymphadenectomy only. 15 patients were in our center received chemotherapy, including MAID (mesna, Adriamycin, Isosulfanamide, dacarbazine), CYVADIC (cyclophosphamide, vincristine, Adriamycin, dacarbazine), CEVAIE (Carboplatin, epirubicin, vincristine, dactinomycin, ifosfamide, etoposide), FOLFIRINOX (fluorouracil, oxaliplatin, calcium folinate) and TP (cisplatin, paclitaxel) regimens. 2 patients received radiotherapy postoperatively and one preoperatively. The median survival time was 14 months (9-120 months). 9 patients died of disease progression after diagnosis (8-25 months).

Taking into account the literatures retrieved from the Chinese database, 18 of 35 received surgical treatment (APR: n=7; LRR: n=11) and 9 of them received radiotherapy or chemoradiotherapy alone. Treatment process was unknown in 8 cases. 15 patients were misdiagnosed as perianal abscess, 14 of them underwent abscessotomy and 1 was treated with intravenous antibiotics only. 1 was misdiagnosed as anal fistula with subsequent fistula resection. Pain is found to be related with misdiagnosis (p=0.010) (Table 3). The average time interval from symptom onset to pathological diagnosis is 3.1 months (3 days to 10 months). 26 months for patients with misdiagnosis history (10 days to 3 months) and 3.4 months (3 days to 10 months) for those without misdiagnosis history. Median survival time was 12 months (Table 2). The 2-year and 5-year overall survival rates were 33% and 25% respectively. Kaplan Meier survival analysis showed misdiagnosis was associated with poor prognosis (P=0.038) (Figure 5).

Discussion

RMS is a malignant mesenchymal neoplasm that exhibits striated muscle differentiation, accounting for 5-10% of all solid tumors and 55-60% of soft tissue sarcomas in pediatric age group[20] but relatively rare in adults[21]. In this retrospective study, however, patients aged ≥20 years accounted for 51%. The most common primary sites for RMS were head/neck, extremities and genitourinary tract[22], perianal and perineal area are rare and considered unfavorable RMS sites[1, 3, 23]. RMS in adults is more likely to occur in unfavorable sites than in adolescents[24], which may explains the majority of adults in this study. In addition, female predominance is noticed in Chinese literatures (71%), similar feature was reported in a Japanese study[25], indicating regional and ethnic differences in the occurrence of this disease.

The prognosis of primary RMS in perianal and perineal area is extremely poor, prognostic factors including age, pathological type, clinical group and staging[26]. In this study, patients older than 20 years comprised 51% of all patients, 38% were classified as alveolar RMS and 52% were categorized into IRS group III-IV, which may contributed to the poor outcome. In addition, misdiagnose rate was 45.7% in this group, which was significantly related to poor prognosis (P=0.038).

PRMS is easy to be misdiagnosed as perianal abscess and may lead to poor prognosis, careful evaluation and differential diagnosis for suspected patients are crucial. Perianal mass is the most common manifestation of both PRMS and perianal abscess. 97% patients presented as perianal mass in this study. Perianal abscess is almost always accompanied by pain[27]. In this study, pain is found to be related with misdiagnosis (P = 0.010). When combined with infection, local redness, swelling and fever can be observed, which resembles perianal abscess and thus leads to high misdiagnosis rate[2]. It is difficult to distinguish PRMS from perianal abscess by symptoms. For firstly-diagnosed patients with painful perianal mass, paying attention to the delay of seeking health care, predisposing factors for abscess formation (immune deficiency, HIV infection, diabetic ketoacidosis and Crohn's disease) and the increasing level of lactate dehydrogenase would be helpful for differential diagnosis[2]. In addition, epidemiological characteristics can provide clues, that perianal abscesses mainly affect adults and male infants younger than 1 year[28-30], which is different from the population features of PRMS reported in literatures[25, 31, 32]. Therefore, solid or even malignant tumor, instead of perianal abscess, should be considered when the patient is a girl presented with perianal mass. Theoretically, misdiagnosis would delay the correct assessment of this disease[2]. However, correlation between misdiagnosis and the average time interval from symptom onset to pathological diagnosis was found insignificant in this study (P = 0.712). On the contrary, the average diagnosis time of misdiagnosed cases is shorter than that of cases without misdiagnosis (2.6 months vs. 3.4 months). The possible reason is that patients' complaints about pain prompted clinicians to carry out emergency abscess incision/resection, rendering an earlier acquisition of postoperative pathological results than those without pain.

Doppler ultrasound is a noninvasive, accessible and radiation-free method for preliminary examination of patients with perianal painful masses suspected as PRMS. It has unique advantages in distinguishing solid, cystic or lacunar masses, providing high specificity and sensitivity of the diagnosis of perianal abscess. Endoanal ultrasound can clarify tumor involvement of the anal canal, and thus provide clues for accurate diagnosis and following treatment[33]. 5
cases of PRMS treated in our center showed solid masses with uneven echo and rich intratumoral blood flow signal with or without clear boundary, which was consistent with the relevant reports[34-36]. 1 case was indicated perianal abscess by Doppler ultrasound, but pathological result following concomitant ultrasound-guided biopsy corrected the diagnosis, suggesting a method to further lower the risk of misdiagnosis. Endoscopic ultrasound-guided fine needle aspiration is recommend for its accuracy and minimal invasion when conducting biopsy[37].

The sonographic features of RMS is variable and nonspecific[38] and it has certain limitation on the assessment of deep-tissue lymph nodes and distant metastasis, hence the necessity of using CT or MRI for further evaluation. MRI has clearer soft tissue imaging compared with CT and can better reveal the invasion of RMS to the adjacent pelvic organs. It has become the first choice for pelvic RMS[39-41] but few reports are available for MRI description of PRMS. By observing the sagittal, coronal, and axial T2 weighted high-resolution images of the pelvis, we found a significant feature of PRMS that the hyposignal of the external anal sphincter (EAS) is replaced by the hypersignal of the tumor, causing a discontinuity of the anal sphincter complex. In some cases, the muscle signal of EAS can be observed cutting into the tumor; a pseudocapsule like structure was formed by the compressed EAS surrounding the tumor (Figure 1).

According to these features, we suggest that PRMS probably originates from EAS. Compression rather than direct invasion of rectal wall and anal canal is observed (n=4), which is different from the characteristics of anal canal cancer[42, 43] and thus valuable for differential diagnosis.

Among the 15 patients treated in our center, 5 underwent abscess incision or drainage previously in other hospitals and 4 of them had poor prognosis. For the 2 patients survived for more than 5 years, one was initially diagnosed as perianal abscess but only treated with antibiotics without surgery; both of them received radical operation (R0) in our center and no evidence of recurrence was found after 5 years' follow up. Wrong surgical treatment can destroy the integrity of tumor and leads to poor prognosis. If PRMS is diagnosed on time and distant metastasis is excluded, surgical treatment should be carried out as soon as possible. Taking into account the tumor is likely to be originated from EAS, ELAPE (extra-levator abdominalperineal excision) could be the choice for most patients to achieve R0 excision. If the tumor was relatively confined and only a small portion of EAS was involved, LRR with reserved anus can be performed. In fact, 5 patients received LRR in our center and 3 of them survived for more than 5 years; 1 recurred due to failure to achieve R0 resection and is undergoing further treatment until now; 1 has no evidence of recurrence after 2 years of follow-up but course of disease was prolonged due to recovaginal fistula caused by surgical damage of perineum. LRR can achieve long-term survival without compromising anal function, but R0 resection must be guaranteed and perineum shall be protected during the operation to avoid rectovaginal/rectourethral fistula.

Optimal treatment of PRMS is controversial. Comprehensive therapy is recommended by relative literatures but most of them are single-center retrospective analysis of few cases. Recently, a multicenter study showed a 64-86% 5-year survival rate of patients receiving chemotherapy combined with surgery or radiotherapy reached[32]. Among the 15 patients treated in our center, 9 received radical operation and chemotherapy and the 5-year OS of them is 57%; the other 6 patients received chemotherapy alone and had poor prognosis. 4 patients received chemoradiotherapy without or without surgery in our center have survived up to now with no evidence of recurrence, but long-term efficacy of radiotherapy remains to be evaluated. Inguinal lymph node metastasis is one of the main factor of poor outcome. In this group, 11 patients were complicated with lymph node metastasis. 5-year survival rate was only 26% for the 9 patients with preoperative inguinal lymph nodes involvement. One patient had ilium lymph node metastasis in 5 months and died in 11 months postoperatively.

Concerning the high incidence of regional lymph node metastasis in PRMS, it is suggested that inguinal lymph nodes resection or irradiation should be performed prophylactically[26], but such aggressive approach may be avoided with the application of PET-CT which can effectively improve the detection rate of lymph node metastasis[44, 45]. Breast metastasis was found in 2 cases in this study, which was also reported in a Japanese literature[25], providing a clue for the specific metastatic pathway and histological characteristic of PRMS.

Conclusion

In summary, primary PRMS is a rare disease. It is easy to be misdiagnosed, which could lead to worse outcome. Patients presented as painful perianal mass should be carefully evaluated to exclude this malignancy. PRMS is found to be closely related to external anal sphincter, MRI should be conducted to determine EAS invasion. Comprehensive therapy including radical operation and chemotherapy is recommended. It is necessary to achieve further improvements in the clinical outcome of PRMS patients by developing new therapeutic modalities.

Abbreviations

RMS:Rhabdomyosarcoma; PRMS:Perianal/perineal rhabdomyosarcoma; CT: Computed tomography; MRI: Magnetic resonance imaging; IRS: Intergroup Rhabdomyosarcoma Study; CDFI: color Doppler flow imaging; EAS: external anal sphincter; APR: abdominoperineal resection; LRR: local radical tumor resection; MAID: mesna+adriamycin+isocyclic amide+dacarbazine; CYVADIC: cyclophosphamide+vincristine+adriamycin+dacarbazine; CEVAIE: carboplatin+epirubicin+ vincristine+dactinomycin+ifosfamide+etoposide; FOLFOX: fluorouracil+oxaliplatin+calcium folinate; TP: cisplatin+paclitaxel

Declarations

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committee of the Sixth Affiliated Hospital, Sun Yat-sen University.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.
Competing Interests
The authors declare that they have no competing interests

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Authors' contributions
YYG and BH contributed to the research design; YYG, DDH, XHW and DLR contributed to the data collection, data analysis, and manuscript writing. JL, DZ, XYL and GC contributed to the data collection and manuscript writing. All authors contributed to the writing review and editing. All authors read and approved the final manuscript.

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References
1. Raney RB, Donaldson MH, Sutow WW, Lindberg RD, Tefft M. Special considerations related to primary site in rhabdomyosarcoma: experience of the Intergroup Rhabdomyosarcoma Study, 1972–76. National Cancer Institute Monograph 1981, 56:69-74.
2. Hill DA, Dehner LP, Gow KW, Pappo AS, Crawford D, Pfauemer SM, Furman WL, Hayes-Jordan AA, McDermott MB: Perianal rhabdomyosarcoma presenting as a perirectal abscess: A report of 11 cases. J Pediatr Surg 2002, 37:576-581.
3. Raney RB, Maurer HM, Anderson JR, Andrassy RJ, Donaldson SS, Qualman SJ, Wharam MD, Wiener ES, Crist WM: The Intergroup Rhabdomyosarcoma Study Group (IRSG): Major Lessons From the IRS-I Through IRS-IV Studies As Background for the Current IRS-V Treatment Protocols. Sarcoma 2001, 59-15.
4. Liu H, He HB, Wu J, Yang CM: A case of adult perianal rhabdomyosarcoma with abscess (Titled in Chinese). Med J West Chin 2011, 023:2431.
5. Liu ZS, Yang FJ, Li D: Perianal rhabdomyosarcoma misdiagnosed as perianal abscess: analysis of two cases (Titled in Chinese). Contemporary Med 2009, 0115.
6. Li LQ, Liu YJ: A Case of Perianal Rhabdomyosarcoma (Titled in Chinese). Railway Med 1993.
7. Mo B, Xu B: A Case Report of Perianal Rhabdomyosarcoma (Titled in Chinese). J Colorectal & Anal Surg 2015, 021:387.
8. Wang JH, Yu L, Yan WX, Jia XJ: A Case of Perianal Rhabdomyosarcoma Treated by synchronous radical Chemoradiotherapy (Titled in Chinese). Chin J Lab Diagn 2018, 022:1590-1591.
9. Chen YQ, Qian HH, Huang JC, Li GN: Perianal rhabdomyosarcoma: report of 3 cases and clinical analysis (Titled in Chinese). Chin J Crit Care Med (Electronic Version) 2008, 1:39-40.
10. He LZ, Wang ZQ, Yin M: Perianal Rhabdomyosarcoma Misdiagnosed as Perianal Abscess: A Case Report (Titled in Chinese). Chin J Coloproctol 2011, 031:53.
11. Nie JL, Zhang YJ, Liu SY, Chen L: Perianal Embryonal Rhabdomyosarcoma: A Case Report (Titled in Chinese). Chin J Lab Diagn 2016, 081:681-682.
12. Liu HB, Song M, Wang LN, Liu JP, Ren XY: Primary Perianal Solid Alveolar Rhabdomyosarcoma: A Case Report (Titled in Chinese). Guangdong Med J 2016, 037:3172.
13. Zong JY, Yu YD, Ji XG, Ni DB: Rhabdomyosarcoma Misdiagnosed as Perianal Abscess: A Case Report (Titled in Chinese). The 12th academic conference of colorectal diseases of Chinese Association of traditional Chinese Medicine 2006:2.
14. Zhao W, Chen HM: A Case of Girl Perianal Rhabdomyosarcoma (Titled in Chinese). Chin Oncol 2013, 100-101.
15. Zhu MX, Zhu N: Experience of Misdiagnosis of Perianal Rhabdomyosarcoma: A Case Report (Titled in Chinese). J New Med 2007, 676.
16. Jin ML, Jiang J: A Case of Embryonal Rhabdomyosarcoma in Children (Titled in Chinese). Chin J Bases Clin General Surg 2005, 9.
17. Wang Y, Zou YR, Li JH: A Case of Perianal Pleomorphic Rhabdomyosarcoma in Children (Titled in Chinese). Sichuan J Cancer Control 2000, 29.
18. Yu L, Zhang PD, Zhao LZ: Primary Perianal Embryonal Rhabdomyosarcoma: A Report of 2 Cases (Titled in Chinese). Chin J Clin Oncol 2000, 3.
19. Jian NG, Zhou YY: Perianal Alveolar Rhabdomyosarcoma: A Case Report (Titled in Chinese). Chin J Coloproctol 2001, 21:28.
20. S. A: Rhabdomyosarcoma and other soft tissue sarcomas of childhood. Curr Opin Oncol 1994, 6:397-402.
21. Ferrari A, Dileo P, Casanova M, Bertulli R, Meazza C, Gandola L, Navarria P, Collini P, Gronchi A, Olmi P: Rhabdomyosarcoma in adults: A retrospective analysis of 171 patients treated at a single institution. Cancer-Am Cancer Soc 2003, 98:571-580.
22. Crist W, Gehan EA, Ragab AH, Dickman PS, Donaldson SS, Fryer C, Hammond D, Hays DM, Herrmann J, Heyn R, et a: The Third Intergroup Rhabdomyosarcoma Study. J Clin Oncol 1995, 13:610-630.
23. Lawrence WJ, Anderson JR, Gehan EA, Maurer H: Pretreatment TNM staging of childhood rhabdomyosarcoma: a report of the Intergroup Rhabdomyosarcoma Study Group. Children's Cancer Study Group. Pediatric Oncology Group. Cancer-Am Cancer Soc 1997, 80:1165-1170.
24. Sultan I, Qaddoumi I, Yaser S, Rodriguez-Galindo C, Ferrari A: Comparing adult and pediatric rhabdomyosarcoma in the surveillance, epidemiology and end results program, 1973 to 2005: an analysis of 2,600 patients. J Clin Oncol 2009, 27:3391-3397.
25. Okamura K, Yamamoto H, Ishimaru Y, Takayasu H, Otani Y, Yamagishi J, Takahashi A, Kuwano H, Nagashima K, Ikeda H: Clinical characteristics and surgical treatment of perianal and perineal rhabdomyosarcoma: analysis of Japanese patients and comparison with IRSG reports. Pediatr Surg Int 2006, 22:129-134.

26. Casey DL, Waxler LH, LaQuaglia MP, Meyers PA, Wolden SL: Patterns of failure for rhabdomyosarcoma of the perineal and perianal region, Int J Radiat Oncol Biol Phys 2014, 89:82-87.

27. Marcus RH, Stine RJ, Cohen MA: Perirectal Abscess. Ann Emerg Med 1995, 25:597-603.

28. Christison-Lagay ER, Hall JF, Wales PW, Bailey K, Terluk A, Goldstein AM, Ein SH, Masiakos PT: Nonoperative Management of Perianal Abscess in Infants Is Associated With Decreased Risk for Fistula Formation. Pediatrics 2007, 120:e548-e552.

29. Serour F, Somekh E, Gorenstein A: Perianal Abscess and Fistula-In-Ano in Infants: A Different Entity? Dis Colon Rectum 2005, 48:359-364.

30. Macdonald A, Storey DW, Munro F: Treatment of perianal abscess and stula-in-ano in children. Brit J Surg 2003, 90.

31. Blakely ML, Andrassy RJ, Raney RB, Anderson JR, Wiener ES, Rodeberg DA, Paidas CN, Lobe TE, Crist WM: Prognostic factors and surgical treatment guidelines for children with perineum or anus: A report of intergroup rhabdomyosarcoma studies I through IV, 1972 through 1997. J Pediatr Surg 2003, 38.

32. Fuchs J, Dantonello TM, Blumenstock G, Koszytla D, Klingebiel T, Leuschner I, Schuck A, Niggli FK, Koscielniak E, Seitz G: Treatment and outcome of patients suffering from perineal/perianal rhabdomyosarcoma: results from the CWS trials retrospective clinical study. Ann Surg 2014, 259:1166-1172.

33. Youssef AT: Use of Ultrasonography in Clarifying the Etiology of Anal Pain. J Med Ultrasound 2017, 25:208-214.

34. Mak CW, Chou CK, Su CC, Huan SK, Chang JM: Ultrasound diagnosis of paratesticular rhabdomyosarcoma. Brit J Radiol 2004, 77:250-252.

35. Anam A, Munden MM, Mehollin-Ray AR, Schady D, Browne LP: Extratesticular masses in children: taking ultrasound beyond paratesticular rhabdomyosarcoma. Pediatr Radiol 2015, 45:1382-1391.

36. Bahnson RR, Zaontz MR, Maizels M, Shkolnik AA, Firlit CF: Ultrasonography and diagnosis of pediatric genitourinary rhabdomyosarcoma. Urology 1989, 33:68-68.

37. Linea C, Sinagra E, Gioia F, Rimi C: Perianal embryonal rhabdomyosarcoma diagnosed by endoscopic ultrasound-guided fine needle aspiration. Endoscopy 2012, 44 Suppl 2 UCTN: E342-E343.

38. Agrons GA, Wagner BJ, Lonergan GJ, Dickey GE, Kaufman MS: From the archives of the AFIP: Genitourinary rhabdomyosarcoma in children: radiologic-pathologic correlation. Radiographics 1997, 17:919-937.

39. Tappouni RF, Sarwani NI, Tice JG, Chamathri S: Imaging of unusual perineal masses. Air Am J Roentgenol 2011, 196:412-420.

40. Fletcher BD, Kaste SC: Magnetic resonance imaging for diagnosis and follow-up of genitourinary, pelvic, and perineal rhabdomyosarcoma. Urologic Radiology 1992, 14:263-272.

41. Finelli A, Babyn P, Lorie GA, Bagli D, Khoury AE, Merguerian PA: The use of magnetic resonance imaging in the diagnosis and followup of pediatric pelvic rhabdomyosarcoma. J Urol 2000, 163:1952-1953.

42. Swami VG, Joseph K, Severin D, Tankel K, Usmani N, Nijjar T: Benefit of MRI scanning in the pretreatment assessment of anal canal carcinoma. Pract Radiat Oncol 2013, 3:59-510.

43. Roach SC, Hulse PA, Moulding FJ, Wilson R, Carrington BM: Magnetic resonance imaging of anal cancer. Clin Radiol 2005, 60:1119.

44. Ricard F, Cimarelli S, Deshayes E, Mognetti T, Thiesspe P, Giarmarile F: Additional Benefit of F-18 FDG PET/CT in the staging and follow-up of pediatric rhabdomyosarcoma. Clin Nucl Med 2011, 36:672-677.

45. Volker T, Denecke T, Steffen I, Misch D, Schönberger S, Plotkin M, Ruj J, Furth C, Stover B, Hautzel H: Positron Emission Tomography for Staging of Pediatric Sarcoma Patients: Results of a Prospective Multicenter Trial. J Clin Oncol 2007, 25:5435-5441.

Tables

table1: Clinical features in 15 patients from the Sixth Affiliated Hospital and the Cancer Center of Sun Yat-sen University
| Gender/Age | Presenting symptoms       | Misdiagnosis/Mistreatment | time interval from symptom onset to pathological diagnosis | Tumor site | Maximum diameter of tumor (cm) | Treatment* | Pathological subtype | IRS Sti |
|------------|--------------------------|---------------------------|----------------------------------------------------------|-----------|-------------------------------|------------|----------------------|---------|
| 1/10y      | Perianal mass            | None                      | 3d                                                       | Perineal  | 6.6                           | LRR(R0)+Chemotherapy | ERMS     | IV/ple Me            |
| 2/≥20y     | Perianal mass            | None                      | 1m                                                       | Perineal  | 4.5                           | APR(R0)+Chemotherapy | ARMS     | II/1                 |
| 2/≥20y     | Perianal mass            | None                      | 1m                                                       | Perineal  | 12.2                          | Chemotherapy         | ERMS     | III                  |
| 2/10-19y   | Perianal mass            | None                      | 1m                                                       | Perianal  | 6.8                           | Chemotherapy         | ERMS     | IV/ pel ret          |
| 2/≥20y     | Painful perianal mass    | Perianal abscess/abscessotomy | 2m                                                      | Perianal  | 10.0                          | APR(Rx)+Chemotherapy | ARMS     | II/1                 |
| 2/≥20y     | Painful perianal mass    | None                      | 7d                                                       | Perianal  | 4.7                           | APR(R0)+Chemotherapy | ARMS     | I/T                  |
| 2/10-19y   | Perianal mass            | None                      | 2m                                                       | Perineal  | 5                             | Inguinal lymph node dissection+chemotherapy | ERMS     | III                  |
| 2/≥20y     | Perianal mass            | Perianal abscess/Intravenous antibiotics | 2m                                                      | Perianal  | 8                             | LRR(Rx)+Inguinal lymph node dissection+Chemoradiation therapy | ARMS     | II/1                 |
| 2/10-19y   | Perianal mass            | None                      | 5m                                                       | Perianal  | 6.0                           | LRR(R0)+Chemotherapy | ERMS     | II/1                 |
| 1/10-19y   | Perianal mass; difficult defecation | None                        | 1m                                                       | Perianal  | 1.8                           | Chemotherapy         | ERMS     | IV/                  |
| 2/≥20y     | Perianal mass            | Perianal abscess/Abscessotomy+partial mass ectomy | 4m                                                      | Perianal  | 6.2                           | APR(R0)+Chemotherapy | ARMS     | II/1                 |
| 2/10-19y   | Painful perianal mass    | Abscessotomy               | 2m                                                       | Perianal  | 6.3                           | LRR(Rx)+Chemoradiation therapy | ERMS     | II/1                 |
| 2/10-19y   | Painful perianal mass; bloody stool | None                          | 2m                                                       | Perianal  | 7.5                           | Chemotherapy         | ARMS     | IV/ab                       |
| 2/10-19y   | Inguinal mass            | None                      | 3m                                                       | Perineal  | 5.9                           | LRR(Rx)+abdominopelvic and inguinal lymph node dissection+Chemoradiation therapy | ERMS     | II/1                 |
| 2/≥20y     | Painful perianal mass    | Abscessotomy               | 3m                                                       | Perianal  | 10.0                          | Chemotherapy         | ARMS     | III                  |

*R0: Microscopic negative margins; R1: Microscopic positive margins; Rx: Not evaluated

Abbreviations: y, year; m, month; d, day; ARMS, alveolar rhabdomyosarcoma; ERMS, embryonal rhabdomyosarcoma; NED, no evidence of disease; DOD, died of disease; AWD, alive with disease.
| **Table2: Data of 35 patients** |
|--------------------------------|
| **age**                        | 23m-56y (median, 23y) |
| 1-10y                          | 4 (11%)               |
| 10-19y                         | 13 (38%)              |
| ≥20y                           | 18 (51%)              |
| **gender**                     |                        |
| male                           | 10 (29%)              |
| female                         | 25 (71%)              |
| **symptoms**                   |                        |
| Perianal mass                  | 34 (97%)              |
| Pain                           | 20 (57%)              |
| Inguinal mass                  | 2 (6%)                |
| Bloody stool                   | 2 (6%)                |
| Difficult defecation           | 2 (6%)                |
| Fecal incontinence             | 1 (3%)                |
| **Misdiagnosis history/time interval of diagnosis** |                       |
| Misdiagnosis                   | 35 (3d-10m, 3.1m)     |
| No misdiagnosis                | 16 (10d-3m, 2.6m)     |
| **Pathological subtype**       |                        |
| Alveolar                       | 9                     |
| Embryonal                      | 14                    |
| Pleomorphic                    | 1                     |
| ND                             | 11                    |
| **IRS clinical group**         |                        |
| I                              | 1                     |
| II                             | 11                    |
| III                            | 8                     |
| IV                             | 5                     |
| ND                             | 10                    |
| **Stage**                      |                        |
| 2                              | 6                     |
| 3                              | 15                    |
| 4                              | 5                     |
| ND                             | 9                     |
| **Tumor site**                 |                        |
| Perianal                       | 26                    |
| Perineal                       | 9                     |
| **Tumor size**                 |                        |
| <5cm                           | 12                    |
| ≥5cm                           | 22                    |
| ND                             | 1                     |
| **Regional lymph node metastasis** |                    |
| N0                             | 7                     |
| N1                             | 15                    |
| ND                             | 13                    |
| **Distant metastasis**         |                        |
| M0                             | 17                    |
| M1                             | 5                     |
| ND                             | 12                    |
| **Surgical approach**          |                        |
| LRR                            | 12                    |
| APR                            | 7                     |
| No surgery or biopsy only      | 9                     |
| Outcome               | Survival time \( \geq 5\)y | NED | AWD | Survival time \( < 5\)y | NED | AWD |
|----------------------|-----------------------------|-----|-----|--------------------------|-----|-----|
| ND                   | 7                           |     |     | ND                       |     |     |
| NED                  | 3                           |     |     | AWD                      | 2   |     |
| AWD                  | 2                           |     |     | NED                      | 3   |     |
| DOD                  | 14                          |     |     | AWD                      | 1   |     |

Abbreviations: y, year; m, month; d, day; NED, no evidence of disease; DOD, died of disease; AWD, alive with disease; ND, not described

Table 3: Factors of misdiagnosis

| Features          | Misdiagnosis | P  |
|-------------------|--------------|----|
|                   | no           | yes|    |
| Pain              |              |    |    |
| no                | 12           | 3  | 0.010 |
| yes               | 7            | 13 |    |
| Gender            |              |    |    |
| male              | 5            | 5  | 0.519 |
| female            | 14           | 11 |    |
| Age               |              |    |    |
| \( \geq 20\)y     | 12           | 5  | 0.061 |
| \(< 20\)y        | 7            | 11 |    |
| Tumor site        |              |    |    |
| perianal          | 13           | 13 | 0.319 |
| perineal          | 6            | 3  |    |
| Tumor size        |              |    |    |
| \( \geq 5\)cm     | 11           | 11 | 0.285 |
| \(< 5\)cm        | 8            | 4  |    |
| Pathological subtype |          |    |    |
| Alveolar          | 5            | 4  | 0.239 |
| Embryonal         | 11           | 3  |    |
| IRS clinical group|              |    |    |
| I                 | 1            | 0  | 0.783 |
| II                | 7            | 4  |    |
| III               | 4            | 4  |    |
| IV                | 4            | 1  |    |
| Stage             |              |    |    |
| 2                 | 5            | 1  | 0.391 |
| 3                 | 8            | 7  |    |
| 4                 | 4            | 1  |    |