An Overview & Some Case Reviews On Rhabdomyosarcoma:

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Abstract: Rhabdomyosarcoma is a type of childhood sarcoma. Rhabdomyosarcoma can affect different places including the head and neck, the genitourinary system, and 35% of cases are in the head and neck. In contrast, India has an incidence rate of 8.9 per million cases of RMS in children aged 0–14 years. Histological types include alveolar rhabdomyosarcoma, which includes embryonal rhabdomyosarcoma, accounting for 70% of embryonal rhabdomyosarcoma and 20% of alveolar rhabdomyosarcoma cases. A variety of tests are performed along with physical tests such as CT scan, ultrasound, magnetic resonance imaging (MRI), biopsy, and blood tests. The gene responsible for rhabdomyosarcoma is the FOXO1 gene, which is thought to keep the PAX gene active, leading to the tumor. Shape. Treatment usually involves biopsies with adjuvant chemotherapy. Chemotherapy drugs such as vincristine, actinomycin-D, etoposide, cyclophosphamide, intravenous vincristine, and ifosfamide are administered in combination for months to years. Radiation therapy is also given for residual disease after 6-12 weeks of chemotherapy.

Keywords: rhabdomyosarcoma, fetal rhabdomyosarcoma, alveolar rhabdomyosarcoma, rhabdomyosarcoma stage, diagnosis, case study

Introduction:
Rhabdomyosarcoma (RMS) is the most common childhood soft tissue sarcoma, accounting for approximately 3–5% of all childhood malignancies [1,2]. Alveolar RMS (ARMS), pleomorphic and spindle cell and sclerosing RMS (ssRMS) [3,4]. According to a 1999 review by Dagger and Hellman, rhabdomyosarcoma (RMS) is a malignant tumor of mesenchymal origin and is thought to arise from cells committed to the skeletal muscle lineage [5]. Common sites of primary disease include head and neck (35%), genitourinary tract (22%) and organs (18%) [6,7]. Embryonic and alveolar variants are the most common histological types, accounting for 20% to 70% of cases [4]. According to the American Cancer Society, about four-fifths of these cancers are discovered before the cancer has visibly spread to other parts of the body. But even when this happens, very small tumors (that cannot be seen, felt, or detected by imaging tests) may have already spread to other parts of the body. This is why RMS usually requires surgery and other treatments [8].

Types:
Types of RMS have three histological subtypes: ARMS (alveolar), ERMS (embryonal), and PRMS (pleomorphic) [9]. PRMS occurs mainly in adults, while ARMS and ERMS subtypes occur mainly in children [10].

Embryonic rhabdomyosarcoma:
ERMS is defined as a malignant soft tissue tumor with embryonic skeletal muscle cell phenotype and biology [11]. About half of ERMS occurs in the head and neck and above half in the genitourinary tract [12,13]. Embryonic rhabdomyosarcoma (ERMS) Infants, the most common subtype a, account for more than two-thirds of all RMS [14,15]. The Otheroid form of ERMS has a rough (polypoid or grape-like) histological appearance (aggregation of tumor cells close to the epithelial surface/cambial layer) and accounts for about 6% of all RMS, % [11,16].

Alveolar rhabdomyosarcoma:
Alveolar rhabdomyosarcoma (ARMS) usually occurs during puberty. They are usually located in organs and have a high ability to metastasize [14,17]. By definition, it has a monomorphic population of primary cells with round nuclei, characterized by arrested myogenesis [11]. They are located between chromosomes 2 and 13, t(2;13) (q35;q14) and between chromosomes 1 and 13, t(1;13) (p36;q14), representing a specific type of chromosomal translocation. Number of cases [17]. The most common metastatic sites of ARMS include lung, brain and bone [18].

Pleomorphic rhabdomyosarcoma:
Pleomorphic rhabdomyosarcoma is the rarest type of rhabdomyosarcoma and is the least common and accounts for only 5% of all rhabdomyosarcomas. Unlike embryonal and alveolar forms, these tumors occur in adults over 40 years of age [19]. They usually appear on the limbs, with a preference for the thighs [20].

Primary intratesticular rhabdomyosarcoma is very rare. [21] Primary intratesticular rhabdomyosarcoma is rare and only 23 cases have been reported worldwide. [22]

Primary spindle cell rhabdomyosarcoma is a rare malignancy that usually presents early with lower urinary tract symptoms [23,24].

Diagnosis: The diagnosis of rhabdomyosarcoma should be based on careful physical examination, medical history, radiographic imaging, histology, laboratory and molecular tests. and pharyngeal structures of the front and back of the rhinoceros, ear
microscopy, endoscopy of the nasopharynx, hypopharynx and larynx, assessment of cranial nerve function, eye and lymph node examination. The main radiographic image for the diagnosis of head and neck RMS. This allows accurate localization and measurement of tumor size, local invasiveness assessment, visualization of lymph node metastasis, and visualization of brain tissue significance and invasion. It is also used to evaluate residual tumor burden after surgery and to detect tumor recurrence. Several reports show that positron emission tomography (PET) holds promise for imaging residual tumor burden [26]. Ultrasound, CT and MRI play an important role in diagnosing and identifying the mass [27].

**Tests for diagnosing and diagnosing rhabdomyosarcoma:** [8]

- Medical history and physical examination.
- Plain radiography
- Computed tomography (CT).
- Magnetic resonance imaging (MRI).
- Bone scan
- Positron emission tomography (PET) scan.
- Sonography
- Biopsy: surgical biopsy
  - Needle biopsy
  - Central needle biopsy
  - Fine needle biopsy (FNA).
  - Bone marrow aspiration and biopsy
- Blood test

**Stages of rhabdomyosarcoma:** [8]

The TNM stage is determined before starting treatment and is based on three key pieces of information:

- **T**: main characteristics of the tumor (location and size)
- **N**: Has the cancer spread to nearby lymph nodes (pea-sized clusters of immune system cells)
- **M**: Whether the cancer has spread to distant parts of the body (metastasized).

**Phase 1:**

Tumors start in favorable areas:
- Orbital (area around the eyes)
- Parameningeal areas (areas adjacent to the membrane that covers the brain, nasal cavity and adjacent sinuses, middle ear, and upper throat)
- Bladder or anywhere in the reproductive or urinary tract.
- Tumors can develop anywhere in the body and vary in size. It has spread to other parts of the body, such as the lungs, liver, bones, or bone marrow.

**Phase 2:**

The tumor has started in an unfavorable location:
- in the bladder or prostate
- parameningeal sites of the arm or leg (areas adjacent to the membrane covering the brain, such as the nasal cavity or adjacent sinuses, the middle ear, or the upper part of the brain). Throat
- Other body parts not listed in step 1

**Phase 3:**

The tumor has started in an unfavorable location:
- in the bladder or prostate
- parameningeal sites of the arm or leg (areas adjacent to the membrane covering the brain, such as the nasal cavity or adjacent sinuses, the middle ear, or the upper part of the brain). Throat
- Other body parts not listed in step 1

**Phase 4:**

Tumors can develop anywhere in the body and vary in size. It has spread to other parts of the body, such as the lungs, liver, bones, or bone marrow.

**Etiology of rhabdomyosarcoma:** [28]

Some genes control when cells grow, divide into new cells, and die. Genes that help cells grow, divide or survive are called oncogenes. Genes that slow down cell division or cause cells to die at the right time are called tumor suppressor genes. Cancer can be caused by DNA changes that turn oncogenes on or off.

Most RMS with ARMS histology contain FOXO1 by fusion, and SSRMS contain MYOD1 mutations or fusions of NCOA2 and VGLL2. ERMS shows a variety of genetic alterations, including loss of heterozygosity of chromosomal 11p15.5 and RAS-associated mutations, and is often associated with complex structural and numerical chromosomal changes [9].

- **Genetic changes in ARMS:** [28]
  - In these cancers, a small piece of chromosome 2 (or more commonly, chromosome 1) often ends up on chromosome 13. This moves a gene called PAX3 (or PAX7 for chromosome 1) right next to a gene called FOXO1, creating PAX/FOXO1. Fusion gene PAX genes play an important role in cell growth during the formation of embryonic muscle tissue, but these genes are usually turned off when they are no longer needed. Movement of one of these next to the FOXO1 gene activates the PAX gene, which is thought to lead to tumorigenesis. Clinically, ARMS behaves aggressively, and 25% to 30% of patients presenting with distant or local symptoms metastasize through lymphatic or hematogenous spread [9,29].

- **Gene changes in ERMS:**
  - Studies have shown that embryonal rhabdomyosarcoma (ERMS) develops in several ways. The cells of this tumor usually lose a small piece of chromosome 11 from the individual's mother and are replaced by a second copy of that piece from the father. It appears to overactivate the IGF2 gene on chromosome 11. The IGF2 gene codes for a protein that causes the proliferation of these tumor cells. Other genetic alterations may be important in these tumors [28]. Most ERMS tumors contain chromosomal regions such as TYROBP (tyrosine kinase tyrosine-binding protein), HCST (hematopoietic cell signal transducer), LRFN3 (fibronectin type III domain containing leucine-rich repeats and 3), and ALKBH6. Included (AlkB 6 homolog) [(19q13.12), [30] is increased or
decreased. ) morphological and biological studies have shown that RMS is a malignant neoplasm derived from immature myoblasts [31, 32]. Myocyte differentiation is an oncogenic process that contributes to the development of RMS [33].

Overexpression of insulin-like growth factor 2 was observed in 80%. samples and have been suggested to play an important role in this pathway of RMS biology [34]. Simultaneously, co-expression of IGF-1R and ALK was detected in ERMS and ARMS, indicating the combined inhibition of both pathways by an ALK inhibitor (NVP-TAE684, Novartis) and an anti-IGF-1R antibody (R1507, Roche). Is. field. String teeth. It has a synergistic cytotoxic effect on RMS cells [35]. Loss-of-function mutations in TP53 may be associated with approximately 10% of ERMS anaplasias [15].

Non-FOXO1Fusion change: SSRMS:
One subtype has been defined as congenital/infantile SSRMS with VGLL2/NCOA2/CITED2 rearrangements [36, 37]. Another subtype is known as MYOD1 mutant SSRMS p.Leu122Arg [38-41]. The third rare subtype is predominantly intraosseous RMS with EWSR1–TF2P2, FUS–TF2P2, or the MEIS1–NCOA2 rearrangement [42, 43].

Treatment:
Current front-line treatment for all RMS risk groups is a multimodal approach including chemotherapy, surgical resection, and/or radiation therapy. In North America, standard chemotherapy regimens include vincristine, actinomycin D, and cyclophosphamide (VAC) [44, 45]. In Europe, the backbone is ifosfamide, vincristine, and actinomycin D (IVA) [46].

Chemotherapy:
Chemotherapy is an important part of rhabdomyosarcoma (RMS) treatment. Even if surgery seems to remove all the cancer, it may come back without chemotherapy. For RMS, chemotherapy is usually given once a week for the first few months and then less frequently. The total duration of treatment usually varies from 6 months to 1 year [47].

The composition and dosage of these drugs depends on many factors, including risk group, histological type, completeness of primary resection, age and general condition of the patient. Child [48].

Low risk groups, the main medicinal compounds used are:
- VA: vincristine and dactinomycin (also known as actinomycin-D)
- VAC: vincristine, dactinomycin, cyclophosphamide [48]
- In the moderate risk group, the most common regimens are:
  - VAC: vincristine, dactinomycin, cyclophosphamide
  - VAC/VI: alternating vincristine, dactinomycin, cyclophosphamide

Vincristine and irinotecan [48] VAC mode is more commonly used in high-risk groups (including those with metastatic disease). These cancers can be difficult to treat, so doctors are also considering using more intensive chemotherapy, including several other drugs (eg, doxorubicin, ifosfamide, and etoposide) [48]. Cyclophosphamide (CPM)—28-day cycles of NLV 25 mg/m2 on days 1, 8, and 15, respectively, combined with 25 mg/m2 continuous oral CPM showed an interesting response rate in RMS [49].

Surgery: [47]
Surgery is an important part of rhabdomyosarcoma treatments. Most people with RMS do two things:
1. Biopsy to diagnose cancer
2. Surgical treatment to remove the tumor

Common side effects: Common side effects of many chemotherapy drugs include: [47]
1. Removal of excess hair
2. Stomatitis
3. Anorexia
4. Nausea and vomiting
5. Diarrhea

Side effects of some drugs: In addition to the risks mentioned above, some chemotherapy drugs are possible.

There are certain side effects (although these are relatively rare). For example: cyclophosphamide and ifosfamide can damage the bladder and cause hematuria. The risk of this happening can be reduced by prescribing medications that keep you well hydrated and a medication called Mesna that helps protect your bladder.

Vincristine can cause nerve damage. Some patients may experience tingling or numbness (called neuropathy), especially in the extremities. It often disappears or improves when treatment is stopped, but in some people it may take a long time.

Radiotherapy:
The radiation dose is usually 36 to 50.4 Gy, but this is a compromise, when aggressive treatment and patient safety are needed [50]. To improve the safety of radiation therapy, coordinated radiation therapy can be used because the risk of radiation exposure to surrounding healthy tissue is minimized. Intensity modulated radiation therapy (IMRT) and proton therapy [51, 52]. Radiation therapy is usually given to residual disease after 6 to 12 weeks of chemotherapy. Radiation is usually given five days a week for several weeks.

Case Study:
1. According to the study by Gay et al. (2022), in 44 patients with rhabdomyosarcoma out of 228 patients with soft tissue cancer, 34.1% of cases were performed in the limbs, 29.5% in the head and neck area, and 25 cases in the genitourinary area. % and 34 items are observed by type. ERMS (77.3%), PRMS 7 (15%), ARMS 3 (6.8%). The average observed tumor size was 7.45 ± 4.64 with a minimum of 2 cm and a maximum of 17 cm. Tumors ≥5 cm were observed in 15 patients (68.2%), while tumor size was less than 5 cm in 7 patients (31.8%). From the above research, it is clear that ERMS is the most common compared to other types. The authors also found a relationship between the type of tissue and the location in which it occurs [27].

2. GI Majid et al (2022) referred an 11-year-old patient with a 2-month history of a painless tumor of the left testicle, which was hypoechoic in the ultrasound of the scrotum and abdomen, measuring 8.0 x 7.5 x 6.0 cm. mass. Left scrotum. The patient
received bleomycin-etoposide-cisplatin chemotherapy after surgery. He said that radical orchiectomy followed by chemotherapy should be recommended, which can improve disease-free and overall survival [22].

3. Ploypailin Preechawetchakul et al (2022), November 2003 to September 2019. Male to female ratio was 2:3:1. Embryonic RMS was the most common histological subtype (40%). The location of the primary tumor was unfavorable in 33 children (79%). The tumor size at diagnosis was greater than 5 cm in 29 children (69%). 14 children (33%) had regional lymph node metastasis at diagnosis and 13 (31%) had metastatic disease at diagnosis. Age >10 years and metastatic disease at diagnosis were documented as poor prognostic factors [53].

4. DPE Aghabonon et al. (2021) reviewed the case of a 7-year-old boy with nasopharyngeal RMS who had a favorable initial response after treatment. He says this type of RMS has non-specific symptoms. If adjuvant therapy such as surgery, radiation, or chemotherapy must be used, radiation therapy can also be used with adjuvant chemotherapy to triple chemotherapy, such as vincristine, actinomycin D, and cyclophosphamide (VAC)[54].

5. In the study of Ashton et al. (2020) to determine whether MYXVA serp2 and ocracitinib can improve outcomes in ARMS, we used nude mice harboring ARMS mouse cells to generate tumors. Studies have shown that combination therapy is safe, with no viral DNA in off-target organs, but viral DNA detected in tumors of mice that received combination therapy [55].

6. Reniarti et al., (2020) This study was conducted at Hassan Sadikin General Hospital, a tertiary hospital in Bandung, West Java, Indonesia, using a cross-sectional descriptive design and global sampling method. Of the 30 data collected, most patients were male (57%), 1 to 5 years old (47%) and diagnosed by biopsy (63%). More than half of the patients (80%) had advanced disease and were treated with chemotherapy (83%). Most RMS patients had tumors (40%) in the head and neck region (40%), size more than 5 cm (70%) and a single node (43%). The remaining patients had a peripheral mass (17%), a skull (13%) or a neck node (27%) RMS [56].

7. In a study by McNeil et al. (2016) when a nude mouse model was used for treatment with oncolytic myxoma virus expressing red fluorescent protein (MYXV - red), a total of 11 mice were used in the study, resulting in 11 mice. The tumor burden in 8 of 11 mice and complete tumor remission in 5 of 11 mice. Therefore, MYX-red therapy may be beneficial for people suffering from RMS [57].

8. Connor et al. (Case Rev 2015,) presented a 36-year-old woman who presented with pelvic pain and vaginal masses based on ultrasound. It was confirmed to be a high grade embryonal rhabdomyosarcoma measuring 5.5 x 3.0 cm. She underwent laparoscopic hysterectomy and adjuvant chemotherapy and changed her VAC to etoposide and ifosfamide. After investigation, we concluded that this rare case of a 36-year-old woman may lack management and treatment guidelines following a conventional surgical approach with adjuvant chemotherapy [58].

9. Khosla et al (2015) analyzed 25 adult cases of RMS at their institution between 2000 and 2009. Diagnosis of these patients begins with medical history, physical examination of LFT, KFT and abdominal ultrasound. Combination chemotherapy alternated between VAC and IE regimens every 3 weeks. VAC included vincristine, actinomycin, and cyclophosphamide, and IE included standard doses of ifosfamide and etoposide. Radiation therapy included external beam radiation therapy. Doses ranged from 36 to 54 Gy with 1.8 to 2 Gy per fraction, with an average dose of 45 Gy. After completing the treatment, patients were followed up at 3-month intervals for the first 2 years, 6-month intervals for the next 3 years, and annually thereafter. For ten years, patients have been treated with relatively the same approach. Of the 25 patients, 15 patients had a complete response after first-line therapy, 8 patients had recurrent disease, including 3 patients with local recurrence, 2 with lymph node recurrence, and 3 with distant metastasis. Only 2 of the recurrences were successfully cured, and both recurrences were local. Five patients developed distant metastases and three patients developed distant metastases during their disease course. The most common site of metastasis was the lung (50%) followed by the brain (25%) [59].

10. Azam Al-Sadat Mousavi et al. (2010) presented a case report of a 14-year-old girl with botryoid sarcoma who presented with prolonged vaginal bleeding and increased cervical polyps. The patient's sister died at the age of 17 due to the same diagnosis. After a short investigation, they concluded that the two sisters were suffering from botryoid sarcoma, or that RMS might play a role as a possible genetic factor [60].

11. Francha et al. (2006) present two cases of oral RMS in adolescents: an 18-year-old Caucasian female with a 9-month history of a nodule in the left buccal mucosa and a 19-year-old Caucasian male with a known left posterior nodule. Upper jaw. With 4 months of progressive growth

Reference:


