Embryonal Rhabdomyosarcoma: Rare Case Reports with Middle Ear Location

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ABSTRACT

Background: Patients with embryonal rhabdomyosarcoma (EMRS) are dominated by boys. The peak incidence occurs in the small age group from one year to 4 years. Approximately 35% of all pediatric RMS occur in the head and neck. Case presentation: A 3-year-old male patient came to the ear, nose, throat-head (ENT-HNS) polyclinic at Dr. M. Djamil General Hospital Padang on February 25th, 2021, with complaints of a lump appearing in his right ear canal for 4 months. The patient also complained of slanting on the right side of his face and pain in his right ear since 2 weeks ago. History of bleeding from the ear 1 week ago. On the examination of House-Brackmann, the patient obtained a category House-Brackmann V. Histopathological results, microscopically visible pieces of tissue with part of the surface covered with keratinized squamous epithelium, part of the surface not keratinized. There are dense groups consisting of a proliferation of cells with round, oval nuclei, small to medium size, little cytoplasm, some cells with pleomorphic nuclei, hyperchromatic, irregular nuclear membranes, lots of eosinophilic cytoplasm, with the appearance of “tadpole”, atypical mitoses may be found. The underlying tissue stroma appears myxoid. Among them, fibrotic connective tissue septa containing partially hyperemic capillaries are visible. Necrotic areas and clusters of PMN leukocytes and cellular debris were also seen. This description is consistent with EMRS. Conclusion: The patient was diagnosed with right middle ear EMRS stage III with right peripheral facial nerve paresis House-Brackmann V.

1. Introduction

Embryonal rhabdomyosarcoma (EMRS) is a subtype of rhabdomyosarcoma (RMS) that is most commonly found in children. Patients with EMRS are dominated by boys. The peak incidence occurs in the small age group from one year to 4 years. Approximately 35% of all pediatric RMS occur in the head and neck. The most common sites involved are the orbit (approximately one-third of cases), the mouth and pharynx (29%), and the face and neck area (24%), whereas the involvement of the ear and temporal bone in RMS is rare and accounts for less than 10% of all cases of head and neck tumors. Based on the location of the tumor in the head and neck, RMS is classified into 3 subtypes, namely: orbital, parameningeal (ear, mastoid, nasal cavity, nasal sinus, infratemporal fossa, pterygopalatine fossa), and non-orbital non-parameningeal. EMRS is a pediatric neoplasm of the middle ear that is malignant and aggressive but responds well to treatment.1,2

Computed tomography scan (CT scan), magnetic resonance imaging (MRI), histopathology, and immunohistochemistry are supporting examinations that are very helpful in confirming the diagnosis of RMS. CT scan examination is better in bone analysis compared to MRI. Rhabdomyosarcoma usually shows aggressive bone destruction with obliteration of the landmark normal skull base. Meanwhile, MRI provides a better image for assessing cranial involvement, jugular veins, and carotid arteries compared to CT.
scans. Histopathological examination is the gold standard to confirm the diagnosis of RMS. Immunohistochemistry can differentiate rhabdomyosarcoma from small round cell neoplasm, such as lymphoma (CD 20, CD 3 positive), Ewing’s sarcoma, and primitive neuroectodermal tumor sarcoma (CD 99 positive). The RMS will give positive results for desmin and myogenin, as well as negative for other markers.\textsuperscript{3,4}

The goal of management in RMS is to achieve control loco-regional and prevent distant metastases. Chemotherapy with loco-radiotherapy regional is the mainstay of RMS therapy. Management in EMRS is multimodal. Chemotherapy and radiation provide good results when given simultaneously and increase overall survival rates, especially in EMRS that have not metastasized far. Surgical management of RMS is considered, especially for small, non-orbital, non-parameningeal, and localized tumors (without intracranial extension or distant metastases). Chemotherapy and radiation can provide a cure rate of up to 91\% in non-metastatic tumors. However, surgery for RMS is usually limited to biopsy for histopathological examination. Despite the use of multimodality therapy, survival of pediatric middle ear RMS patients is low. Overall survival was 59\%, and disease-free survival was 63\%. In addition, all deaths in RMS occur on average within 3 years from the time the diagnosis is made. This is because this tumor has the ability to develop rapidly, so it often gives a poor prognosis.\textsuperscript{5,6} This study aimed to present one’s case embryonal rhabdomyosarcoma stage III right middle ear with right peripheral facial nerve paresis House-Brackmann V in a 3-year-old boy.

2. Case Presentation

A 3-year-old male patient came to the ear, nose, throat-head neck (ENT-HNS) polyclinic at Dr. M. Djamal General Hospital Padang on February 25\textsuperscript{th}, 2021, with complaints of a lump appearing in his right ear canal for 4 months. The patient also complained of slanting on the right side of his face and pain in his right ear since 2 weeks ago. History of bleeding from the ear 1 week ago. There was no previous history of discharge from the ear. There is no history of severe headaches, seizures, or vomiting. There is no fever, cough, or cold. There is no history of allergies, no history of atopy, no history of malignant disease. There is no family history of this disease. There is no history of exposure to radiation. The patient was born normal at term. The patient had previously received an extirpation biopsy at a private hospital with the impression that the histopathological examination was tissue epithelial polyp. Two months after the procedure, the lump appeared again, filling the ear canal, and was accompanied by a slanted face. The patient was then referred to Dr. M. Djamal General Hospital Padang.

Physical examination revealed a moderate general condition, cooperative compositional consciousness, pulse rate 86x/minute, respiratory rate 16x/minute, and temperature afebrile. Physical examination of the right ear revealed that the ear canal was covered with granulation tissue, a mass appeared to fill the ear canal, the tympanic membrane could not be assessed, and secretions were (+). The left ear canal is wide, the tympanic membrane intact, light reflex (+), and secretions (-). Heart, lung, and abdominal examinations were within normal limits.

Figure 1. Mass in the right ear canal.
On the House-Brackmann examination, the patient obtained a category House-Brackmann V. The patient was diagnosed with a suspected malignant right ear canal tumor complicated by paresis of the right peripheral facial nerve House-Brackmann V. The patient went home on prednisone tablet therapy tapering off starting with a dose of 1x25mg and decreasing every 3 days for 2 weeks. The patient is then planned to undergo an examination of high-resolution computed tomography (HRCT) Scan mastoid and deep extirpation biopsy anesthesia general. Control after 2 weeks of administration of high-dose corticosteroids, no visible improvement in facial nerve paresis (House-Brackmann V). On examination, the right ear was visible pasta in the right ear cavity that is getting bigger. There is no secretion, and there is no blood.

An HRCT scan of the mastoid was carried out on March 15th, 2021, and an image was obtained of soft tissue mass that fills the external ear canal and extends to the middle ear canal, parapharyngeal space, and right side of the nasopharynx, which covers the musculus veli palatini, fossa Rosenmuller, and torus tubarius on the right side, the visible destruction of the mastoid bone, temporal wall, the anterior wall of the mastoid, part of the auditory ossicles and air cell mastoid. From inspection, the CT scan got an impression of soft tissue mass in the right ear canal with extension to the right parapharynx and nasopharynx. Examination impression CT Scan Mastoid is a soft tissue mass in the right ear canal with extension to the right side of the parapharynx and nasopharynx.

Figure 2. HRCT scan mastoid patient. (A) axial-coronal section bone setting, (B) axial-coronal section soft tissue setting.
The results of the patient's laboratory examination on March 17th, 2021 were hemoglobin 13.8 g/dl, leukocytes 12,870/mm³, hematocrit 45%, platelet count 512,000/mm³, prothrombin time (PT) 10.9 seconds, activated partial thromboplastin time (APTT) 28.7 seconds, Na 129 mmol/L, K 4.0 mmol/L, Cl 112 mmol/L, SGOT 26 U/L, SGPT 7 U/L, urea 13 mg/dl, and creatinine 0.35 mg/dl. The patient was diagnosed with a suspected malignant tumor of the right ear canal with extension to the nasopharynx and right parapharynx accompanied by complications of right peripheral facial nerve paresis House-Brackmann V.

On March 30th, 2021, a biopsy of the right ear canal mass was performed. The tissue taken was sent to the anatomical pathology laboratory for histopathological examination (Figure 3).

![Figure 3. Mass biopsy of the right ear canal.](image)

The first day after surgery, the pain in the surgical wound was still there. The surgical wound was calm, there were no signs of infection, and there was no bleeding. The patient was allowed to go home and given Amoxicillin syrup 3x250 mg and paracetamol syrup 3x1 tsp orally. The patient is asked to control the ENT polyclinic 1 week later.

Histopathology results on April 1st, 2021, macroscopically visible pieces of brownish white tissue, firm and chewy, measuring 2.5x2x1 cm. Microscopically, a piece of tissue appears with part of the surface covered with keratinized squamous epithelium. Part of the surface is not keratinized. There are dense groups consisting of a proliferation of cells with round, oval nuclei, small to medium size, little cytoplasm, some cells with pleomorphic nuclei, hyperchromatic, irregular nuclear membranes, lots of eosinophilic cytoplasms, with the appearance of "tadpole", atypical mitoses may be found. The underlying tissue stroma appears myxoid. Among them, fibrotic connective tissue septa containing partially hyperemic capillaries are visible. Necrotic areas and clusters of PMN leukocytes and cellular debris were also seen. This description is consistent with EMRS (Figure 4). Block paraffin was sent for an IHC desmin examination to confirm the diagnosis. The results of the CPI examination are available, as seen in Figure 5.

![Figure 4. Histopathological features of EMRS. (A) Tissue with a surface covered with squamous stratified epithelium (4x magnification). (B) Bluish round cells and tadpole" (40x magnification).](image)
Figure 5. The microscopic image of IHC desmin on EMRS shows a positive smear for desmin in the cytoplasm diffusely. (A.40x magnification, B.100x magnification).

On control, 1 week after surgery, a mass appeared to fill the right ear canal, accompanied by necrotic tissue and pain. Lumps were seen in the right parotid region, right submandibular region, and right retroauricle up to the right colli region with a fixed solid mass. The staging was carried out with the results of the patient being categorized as EMRS right middle ear stage III with right peripheral facial nerve paresis House-Brackmann V. The patient was then referred to the pediatric hemato-oncology subsection.

Control at the pediatric hemato-oncology subsection on April 9th, 2021, the patient was diagnosed with EMRS stage III and planned to undergo chemotherapy. The patient is then prepared for repeat laboratory examinations and chemotherapy. The patient died at home before chemotherapy was administered. One week before he died, he experienced complaints of difficulty swallowing, followed by complaints of shortness of breath before the patient died.

3. Discussion

Embryonal rhabdomyosarcoma macroscopically correlates with the primary location, where large tumors are usually found in the abdomen and extremities with sizes exceeding 6-8 cm. Tumors are generally in the form of soft, shiny gelatinous tissue, and on the surface, you will see a gray-white surface with or without areas of bleeding or necrosis. Generally, tumors have firm boundaries with or without a tissue capsule. In this case, pieces of solid brownish-white tissue measuring 2.5x2x1 cm were visible. The tumor is small due to the location of the tumor in the ear cavity. Microscopic EMRS features can resemble various variations of normal skeletal muscle embryogenesis but are more variable, ranging from poorly differentiated tumor cells that are difficult to detect and diagnosed without immunohistochemical examination to good differentiation with a picture resembling fetal muscle. Histological features generally consist of (1) varying degrees of cellularity with dense clusters, areas hypercellular, and a loose myxoid area. (2) a mixed picture of cells with poor orientation, small, undifferentiated, hyperchromatic, round, or spindle-shaped, with varying numbers of differentiated cells with eosinophilic cytoplasm characteristic of rhabdomyoblasts, and (3) a matrix that contains a small amount of collagen and varying amounts of myxoid material. Description cross-striations are seen in 50-60% of cases. Similar to skeletal muscle cells, EMRS contains primitive mesenchymal cells at various stages of myogenesis with varying numbers of rhabdomyoblasts.

Rhabdomyoblasts are characterized by eosinophilic and elongated cytoplasm, manifesting as tadpoles, straps, and spiders. In terminal differentiation, cells can be seen with a bright eosinophilic appearance, with peripheral and multinucleated nuclei and cross-striation in the cytoplasm. In this case,
microscopically, a piece of tissue appears with part of the surface covered with keratinized squamous epithelium and part without keratin. Below it appears a dense group consisting of a proliferation of cells with round, oval nuclei, small-medium size, little cytoplasm, some cells with pleomorphic nuclei, hyperchromatic, irregular nuclear membranes, lots of eosinophilic cytoplasm, with the appearance of tadpole, atypical mitoses may be found. In this case, in general, the microscopic picture looks quite impressive from EMRS, but the IHC examination is still carried out for confirmation reasons because the location of the tumor is quite rare.11-13

RMS cells usually show involvement in skeletal muscle lineage specification and/or differentiation as evidenced by light or electron microscopy and/or IHC or molecular evidence for skeletal muscle gene expression such as muscle-specific actin and myosin, desmin, myoglobin, Z-band protein, and MyoD1 or myogenin. Immunohistochemistry is necessary to differentiate RMS from small round cell neoplasm others such as lymphoma (CD20, CD3 positive) and Ewing’s sarcoma/PNET (CD99 positive) because RMS is negative for these markers and diagnostically positive for desmin. EMRS therapy is multimodal, including chemotherapy, radiation, and resection. Recent trends suggest that concurrent chemotherapy and radiation work well and improve overall survival in cases of EMRS that have not metastasized. The chemotherapy regimens currently used are VAC (vincristine, actinomycin D, cyclophosphamide), VIE (vincristine, ifosfamide, etoposide), and VAI (vincristine, actinomycin D, ifosfamide). Surgical removal of the tumor is often difficult in cases of head and neck tumors, so the main treatment modality in these cases is chemoradiotherapy. In this case, the patient was planning to receive treatment in the form of chemotherapy, but the patient deteriorated very quickly and died before receiving it. Prognostic factors for children or adolescents with RMS relate to patient age, location of tumor origin, tumor size (widest diameter), resectability, presence of metastases, presence or absence of lymph node involvement, and histopathological subtype. Based on subtype, EMRS has the best prognostic factors, and AMRS is the subtype with the worst prognosis. Parameningeal tumors, especially the middle ear and mastoid, have a poor prognosis due to their location close to the brain.14-18

4. Conclusion
Rhabdomyosarcoma is an aggressive soft tissue sarcoma that is most commonly found in children. Embryonal rhabdomyosarcoma is the most common subtype, with a good prognosis. However, EMRS with parameningeal tumor locations, especially in the middle ear and mastoid, has a poor prognosis due to the close location to the brain. Accuracy and speed of diagnosis, as well as treatment in the form of a combination of chemotherapy and radiotherapy, are important to prevent tumor progression and increase life expectancy.

5. References


