POST-TRAUMATIC Rhabdomyosarcoma: An Unfortunate Red Herring

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ABSTRACT

Rhabdomyosarcoma (RMS) is a relatively rare malignancy but the most common cause of soft tissue sarcoma in children. It can present anywhere in the body, but most seen in the extremities, head, neck and genitourinary organs. The two most common types of RMS are embryonal RMS and the more aggressive kind, the alveolar RMS. Development of RMS occurring after trauma is uncommon but as children are readily prone for lumps and bumps due to their adventurous and playful nature, it is much important to always keep in mind the possibility of malicious causes of swelling as any delay in diagnosis directly affects the outcome of the disease. Here we present an infant who presented with symptoms suggestive of post trauma swelling but later was confirmed as embryonal RMS. The child underwent chemotherapy as the treatment of option.

Keywords: Rhabdomyosarcoma; Pediatric tumour; Head And Neck; Post Trauma

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Introduction

Rhabdomyosarcoma (RMS) is the most common malignant solid tumour in children after neuroblastoma and nephroblastoma (Wilms tumor) [1] and the most common soft tissue sarcoma in children, comprising 4.5% of all childhood cancer with an annual incidence of 4.5 cases per 1 million children [2]. It can be classified into two main histological subtypes with distinct appearances and clinical behaviours. Embryonal rhabdomyosarcoma (ERMS), the most common type, is usually seen in children less than 5 years old and mostly present within the head and neck area (40%) or genitourinary area (~20%) [3]. It shows a less aggressive clinical behaviour than alveolar rhabdomyosarcoma (ARMS) which is a relatively rarer type. ARMS can present at any age and arises mainly in the extremities and the trunk (20%) [3]. It is known to have worse prognosis and higher disease stage at the point of diagnosis.

RMS tends to present as an expanding mass, resulting in pain and symptoms related to the compression of nearby structures. Metastases can lead to pain in the bones, difficulty with respiration due to lung nodules or pleural effusion, anaemia, thrombocytopenia, and neutropenia, with a 5-year survival rate less than 30% [3]. In contrast, a confined disease treated with combined surgery, radiation and chemotherapy has a 5-year survival rate of over 80% [4]. The incidence of rhabdomyosarcoma is 6 cases per 100,000 per year in the United States, and approximately 87% of patients are under 15 years of age [4]. The prognosis...
for RMS depends strongly on tumour size, location, staging, and child’s age [5]. In general, ERMS has a more favourable outcome, whereas the mortality rate remains high in patients with ARMS, because of its aggressive nature and metastatic tendencies. Therefore establishing an early, prompt diagnosis with its histological type is most vital in treating cases of RMS and achieving the best possible outcome [5].

The Case

A 1-year-old infant was brought in by her mother to the emergency department and subsequently referred to our clinic due to sudden onset of swelling near the left side of the nose which was thought to be a simple case of bruising. A week earlier, a bicycle had fallen on top of the child while playing and later on noted by mother a bluish discoloration over the left nasomaxillary groove. The traumatized area subsequently developed into a small pea-sized swelling which was mildly tender and firm on touch. It then slowly increased in size extending medially into the left vestibule area (Figure 1a). Despite the progress, the child remained active, afebrile with no nasal symptoms. In view of history of trauma and its location, she was treated for left vestibulitis with differential diagnosis of abscess or hematoma. As swelling was within danger area of the face, she was admitted for close observation and intravenous antibiotics. After 48 hours of no response to treatment, the child was arranged for incision and drainage under general anaesthesia via endoscopic approach intranasally at the vestibule area. Intraoperatively, no pus collection seen but tissue was edematous with minimal bleeding and no suspicious lesions within. Swab cultures taken later returned with no organisms isolated.

Post operatively, the firm swelling expanded causing more deformity over left side of the nose until maxillary area, hence an urgent ultrasound was performed and showed a vascular lesion suggestive of haemangioma or Arterial-Venous (AV) malformation. The swelling was aggressive as it drastically increased in size over the subsequent weeks (Figure 1b). She remained active, cheerful and pain free on rest and play. A follow-up CT angiography (CTA) was then obtained and showed a lobulated enhancing mass within left subcutaneous layer of left maxilla representing a left nasomaxillary soft tissue with no evidence of vascular malformation (Figure 2a & 2b). An endoscopic incisional biopsy was performed via previous incision site and the histopathology reports confirmed the swelling to be malignant, which is embryonal rhabdomyosarcoma (Figure 3a & 3b). In view of the poor surgical plane within the nasomaxillary area, which would likely be cosmetically impairing and radiotherapy might also cause more complications, it was concluded after oncology consultation that the child, who was stratified as ‘Standard-risk’, would be started on chemotherapy alone.

She was prescribed chemotherapy following the European Paediatric Soft Tissue Sarcoma Study Group (EPSSG) 2005 protocol for Subgroup D comprising of 9 courses of Ifosfamide, Vincristine and Actinomycin D (IVA) with 3 weekly intervals. Imaging mid-cycle chemotherapy had showed good treatment response with 75% reduction of tumour bulk and no distant metastases. Despite febrile neutropenia, she was able to complete the regimen with full resolution of the left nasomaxillary swelling (Figure 4). Local treatment (radiotherapy±surgery) at 13 weeks as per protocol was not done for the patient upon re-assessment. However, she had developed a new swelling at left submandibular area which was initially treated with antibiotics for lymphadenitis. Simultaneously, positron emission tomography (PET) scan done 2 months post treatment showed increased focal uptake of fluorodeoxyglucose (FDG) only at left submandibular nodes, suspicious of nodal metastases. Treatment was then escalated by oncology team to ICE chemotherapy (comprising of Ifosphamide, Carboplatin and Etoposide). The swelling clinically resolved after 2 cycles of ICE chemotherapy before further management was able to be performed as planned and child is doing well. A repeat PET scan was scheduled after completion of 3rd cycle of ICE.
Figures

Figure 1a. Child image at the time of presentation. 1b. Two weeks post operation

Figure 2a. CECT of the face in soft tissue setting, axial view. 2b. CECT of the face in soft tissue setting, coronal view

3a. Tumour cells arranged in lobules, displaying round nuclei with high N/C ratio and moderate eosinophilic cytoplasm. Mitosis present (white circle). H&E 400x

3b. The tumour cells are diffusely positive for MyoD1 (nuclear brownish staining). MyoD1 400x
Discussion

In cases where there is a convincing background history of trauma which later lead to the diagnosis of infected hematoma/vestibule abscess within the facial area, an urgent drainage may be planned as per treatment protocol. Infection or collection around the danger area is readily known for its nature of spread which can lead to more dire consequences such as intracranial infection. But when there is lack of or inappropriate response to initial treatment, further investigation is required to rule out other causes, and in this case turned out to be hostile. While most cases of paediatric RMS are sporadic, risk factors to look out for include neurofibromatosis, Li-Fraumeni syndrome, Costello syndrome, Noonan syndrome, Beckwith-Wiedemann syndrome, and parental use of cocaine or marijuana [1,5]. A study by Li H et al in 2021 which involved 615 newly diagnosed children with RMS showed seven percent had pathogenic or likely pathogenic variant in a cancer pre-disposition gene [6].

Although there has been previously reported scalp RMS post head injury, there is still a lack of report regarding post trauma RMS in the facial region such as in this case. Currently it is still inconclusive regarding the role of trauma as a definite factor causing tumour development but it is believed that occurrence of tumours has three associations in that it (i) results from natural causes irrelevant to trauma; (ii) acquired factor from trauma as it can result in local tissue degeneration, necrosis and immune clearance, new cell proliferation, repair which ultimately may lead to malignant transformation and (iii) both congenital factors and acquired factors together play a role in the formation of tumour. Tumour cells may germinate during the embryonic period but triggered during the trauma leading to rapid proliferation and differentiation [7]. Nevertheless, an urgent tissue diagnosis with the appropriate accompanying imaging (CT /MRI) is promptly needed if swelling fails to respond to initial treatment and/or accompanied with rapid deterioration. The time of identification of RMS and its subtypes is important as the rarer type, ARMS has been reported to have a poor prognosis and to be associated with a greater frequency of disseminated metastases. But we must bear in mind due to the plethora of presentations and variable prognosis, prediction of RMS outcome has become a complicated undertaking.

EPSSG 2005 protocol is the treatment of choice for non-metastatic RMS. The aim is to give homogenous (local and systemic) treatment according to the risk of local and metastatic relapse in patients categorized as Low, Standard, High and Very High risk. A combination of post-surgical stage, presence of metastasis, site of origin, age of the patients and most importantly histologic (alveolar vs non-alveolar) and genetic properties of the tumour is taken into account to further stratify RMS into the four risk groups. Urgent review by the local pathologist to diagnose ERMS will help determine eligibility of patients in each risk group strategy like in our patient. The treatment option are then further divided into Subgroups B, C and D [8].
The standard therapy includes chemotherapy combined with radiotherapy ± surgery, or both for local control, if indicated [8]. Further discussions among managing teams must be done to determine the best approach as not all tumours are suitable for resection or radiotherapy like in this case. These modalities have not improved survival rates in patients with metastatic disease; however, new agents active against RMS are currently being sought, which include oncolytic viruses and immunotherapies, such as monoclonal antibodies and dendritic-cell vaccines [9,10]. It is noted that generally younger patients tend to have a more favourable prognosis, for unknown reasons [11]. Over 90% of patients with low-risk localized disease can be cured with multi-modal therapy, but overall survival rates of patients with metastatic or recurrent disease remain dismal at 21% and 30%, respectively [11-13].

Conclusion

There is still lack of reports on ERMS developing after trauma, but the occurrence is always possible. Time of histological diagnosis of RMS and its subtype is vital to predetermine the outcome hence tissue biopsy should not be delayed and to be done upon first intervention. Not only does it benefits the patient, it is highly time and cost effective. Local control is necessary to cure those with localized RMS via surgery and/or radiotherapy unless complete clearance is unlikely and excision may cause even more harm. It should however, be re-considered after patient lack response to chemotherapy. Continuous discussions among teams and caretaker must be done to achieve consensus on best treatment option.

References


