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Case Report

Unusual Presentation of Juvenile Rhabdomyosarcoma in the Temporomandibular Area: A Case Report

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Abstract: Rhabdomyosarcoma frequently affects the craniofacial region with a rapid growing pattern that usually results in swelling of the interested area. The present paper describes a peculiar occurrence of rhabdomyosarcoma in a 12-year-old boy and the importance of a careful evaluation of clinical history to choose the correct diagnostic strategy. The patient was evaluated in the orthodontics section of the Dental School of the University of Bologna by an orofacial pain specialist, with a compliance of excruciating pain around the right ear that occurred 4 months earlier after a sports trauma. The patient had been previously evaluated by a pediatrician and an ENT specialist who requested a computerized tomography that did not show pathological conditions in the head/neck district. The drug therapy for pain control was not effective. The clinical examination showed a severe limitation of mouth opening, periauricular paresthesia and mandibular hyperalgesia on the right side. The patient reported intermittent, very intense stabs of pain occurring every 5 min, with a continuous dull pain in the temporal area. A nuclear magnetic resonance was requested and showed the presence of a solid expansive lesion in the right pterygoid area that eroded the cranial base and the medial portion of the mandibular condyle. An incisional biopsy led to the diagnosis of embryonal rhabdomyosarcoma. This case report emphasizes the importance of not underestimating the presence of pain in young subjects, suggesting a proper approach to apparently simple clinical cases.

Keywords: rhabdomyosarcoma; pediatric; orofacial pain; TMJ

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1. Introduction

Rhabdomyosarcoma (RMS) is a malignant soft tissue neoplasm deriving from embryologic skeletal muscle precursor cells frequently affecting the craniofacial region. It accounts for 6% of all malignancies in children younger than 15 years and represents about the 60% of all soft tissue sarcomas, with a slight male predilection [1]. This tumor is generally characterized by neoplastic mesenchymal cells showing features of not completely developed muscle, and the most recent WHO classification describes four subtypes of RMS, viz., embryonal rhabdomyosarcoma (ERMS), alveolar rhabdomyosarcoma (ARMS), pleomorphic rhabdomyosarcoma (PMRMS) and spindle cell/sclerosing rhabdomyosarcoma (SSRMS) [2,3], with additional description of a few novel subtypes. ERMS is a malignant, primitive, soft tissue tumor that recapitulates the biological and phenotypical features of embryonic skeletal muscle, occurring in equal proportion in the head and neck and the genitourinary system. It is the most common subtype of rhabdomyosarcoma, and it is more frequent in males than females [3,4]. ARMS is a cellular malignant neoplasm characterized by a monomorphous population of primitive cells with round nuclei and aspects of arrested myogenesis. It occurs less frequently than ERMS at all ages but more often in adolescents and young adults than in younger children [3,5], with no gender predilection. ARMS commonly affects the extremities, the paranasal sinuses, and the paraspinal and perineal regions with rapid growth. PMRS occurs almost exclusively in adults; it consists of peculiar

polygonal, round spindle cells that display aspects of skeletal muscle differentiation with no embryonal or alveolar components. It mainly affects men around in their 60s and 70s [6]. PMRS present as a rapidly growing, painful swelling occurring more frequently in the deep soft tissues of the lower extremities but have been described in a large variety of other locations [7,8]. First described in 2002, SSRMS represents a heterogeneous variant associated with disparate prognosis [9]. It can present as painless masses or can cause symptoms due to compression. Usually well circumscribed, this spectrum of the tumor shows some areas with a grey/white whorl-cut surface. SSRMS shows different microscopic morphologies [3]. The risk factors that have been associated with RMS are parental smoking, maternal age over 30, use of antibiotics before or during pregnancy, exposure to X-rays in utero, and drug abuse during pregnancy [10]. Despite most of the cases seeming to be sporadic, genetic alterations emerged to play a role in RMS development; pathologies such as Type-1 Neurofibromatosis, Noonan and Li–Fraumeni syndrome showed an association [1,11]. RMS frequently occurs in the head and neck district (35–40% of all RMS), where it generally originates from the orbit (25%) and the middle ear. The temporal bone is not frequently affected by RMS in the adults, but it is the most common temporal bone neoplasm in children [1]. The main clinical features of RMS are a rapidly growing, non-ulcerated swelling, sometimes multilobular or exophytic. The prognosis depends on the stage of the disease when the diagnosis is performed, the anatomic localization, histology and genetic mutations [12]. The present manuscript describes an unusual presentation of RMS, which affects the temporomandibular joint (TMJ).

2. Case Report

A 12-year-old male was referred to the Unit of Orthodontics and Dental Sleep Medicine in the Department of Biomedical and Neuromotor Sciences of the University of Bologna to be evaluated by an orofacial pain specialist. The patient reported intermittent very intense stabs of pain occurring every 5 min, with a continuous dull pain around the ear, in the temple and in the jaw on the right side. A limitation in mouth opening was also reported. The patient associated the onset of the symptoms to a hit on the face received during water polo training 4 months earlier. The pain worsened over time and did not respond to drug therapies. The clinical examination was performed following the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) [13]. The non-assisted mouth opening presented a severe limitation (24 mm) and a mandibular deviation on the right side. The assisted and passive mouth opening were 35 and 40 mm, respectively, and exacerbated the pain in the right temporomandibular area and in the temple. The palpation of the right masseter and temporalis muscles caused severe pain to the patient, while no muscle pain was registered on the left side. Paresthesia in the right temporomandibular joint (TMJ) area and hyperalgesia in the right side of the mandible were also registered. No acute dental conditions, periodontal inflammations, nor intra- and extra-oral swelling were detected. The patient had been previously evaluated by other colleagues: a pediatrician prescribed analgesics and non-steroidal anti-inflammatory drugs (paracetamol and ibuprofen) for pain control, obtaining scarce success. An ENT specialist prescribed steroidal anti-inflammatory drugs that were also not effective in pain reduction and requested for a computerized tomography (CT) that did not show significant problems affecting the facial bones and the TMJ. Further investigating the history, a discomfort related to the jaw movement previous to the facial trauma was also reported by the patient: it started about one year earlier as an impairment and worsened over time. The clinical aspects and the evaluation of the anamnesis suggested a request for a Nuclear Magnetic Resonance (NMR) of the skull and of the TMJs. The NMR revealed a solid expansive lesion without hypervascularization in the right pterygoid area with a diameter of 61 × 40 mm in the axial plane and a craniocaudal extent of 59 mm. The upper portion of the lesion eroded the skull base invading the intracranial area. The lateral portion reached the mandibular ramus extending from the angle to the condyle, that appeared reduced to in size due to the erosion of its medial portion by the tumor. The retro-lateral lymph nodes appeared enlarged (Figure 1).

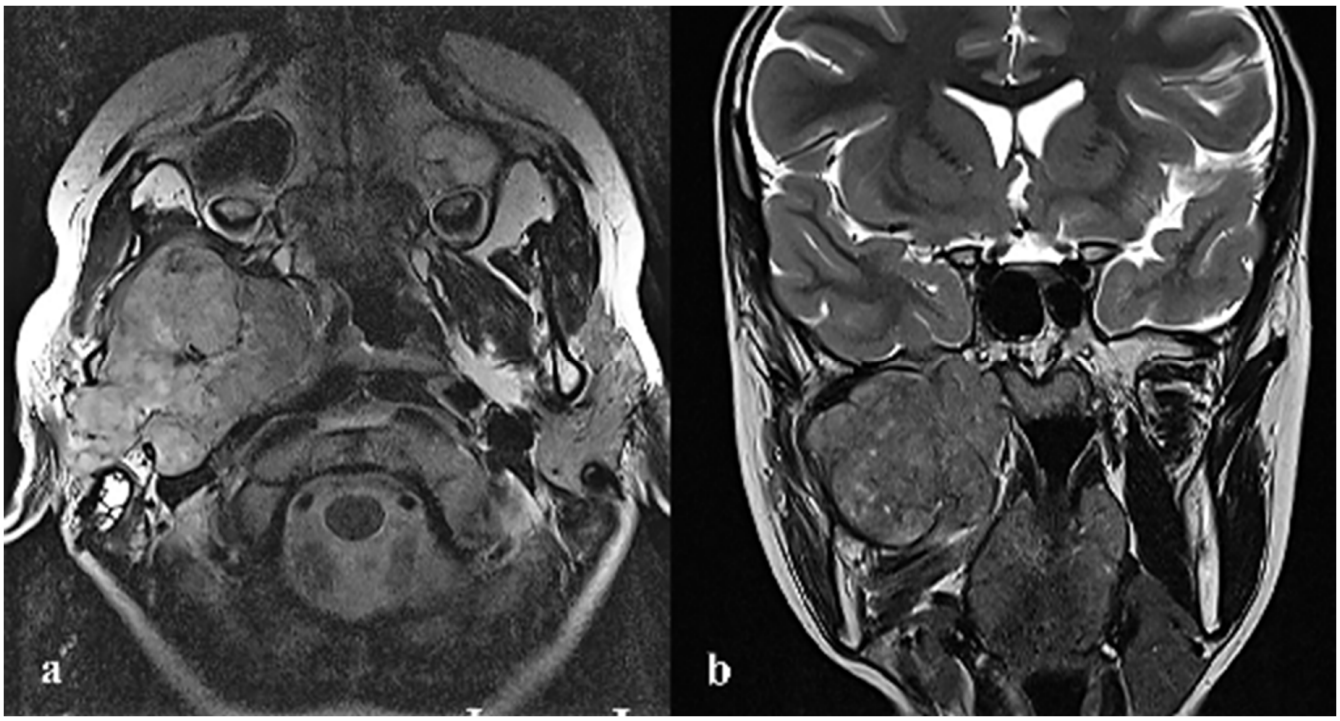

Figure 1. NMR: coronal (**a**) and transverse (**b**) sections of the RMS showing the extent of the tumor.

An incisional biopsy was performed and the histological examination revealed the presence of epithelioid and spindle cells with pleomorphic, hyperchromatic nuclei with eosinophilic cytoplasm, arranged in nests and chains, with perivascular thickening (Figure 2). Immunohistochemistry was performed for Ki-67, muscle actin, S100, CD34, CD45, CD30, desmin, CD99 and myogenin. Desmin and Ki-67 showed high positivity. CD99 and myogenin revealed patchy positivity, and broad-spectrum cytokeratin was focally positive (Figure 3). The fluorescent in situ hybridization (FISH) technique was used to evaluate the rearrangement of FOX01: the translocation was negative. Based on these characteristics, the tumor was classified as ERMS. The young patient underwent chemotherapy which had a poor prognosis due to the large size of the tumor mass.

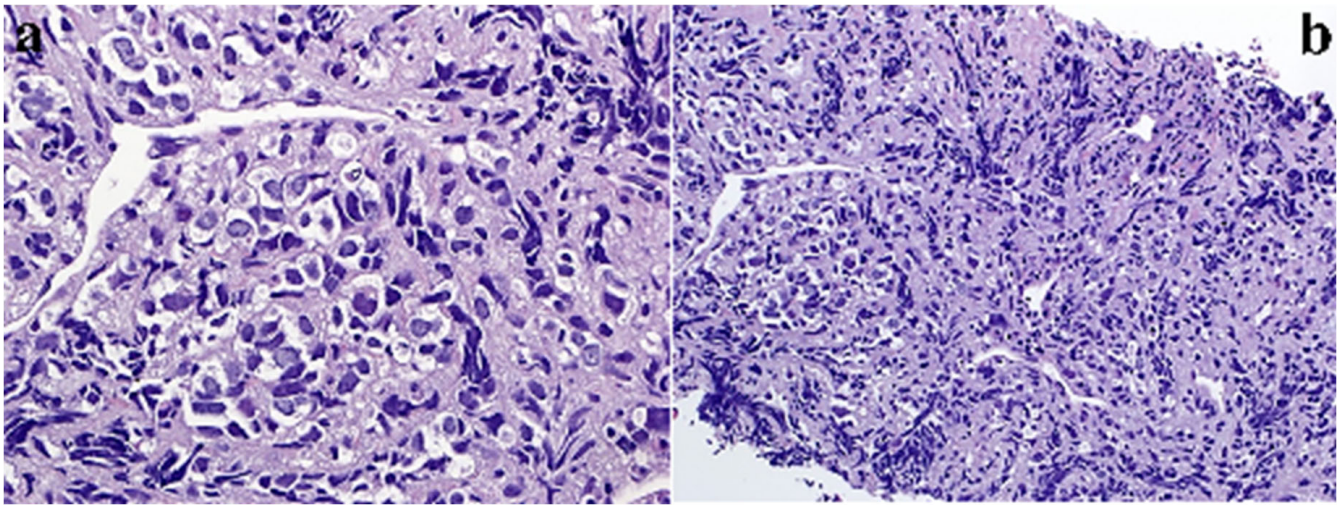

Figure 2. Hematoxylin–eosin stain of the tumor mass in the temporomandibular area: (**a**) high magnification microscope view (400×). Cell proliferation organized in nests and chains. Presence of eosinophils and clear cytoplasm; (**b**) medium magnification microscope view (100×). Epithelial-like and spindle cells with pleomorphic and hyperchromatic malignant nuclei.

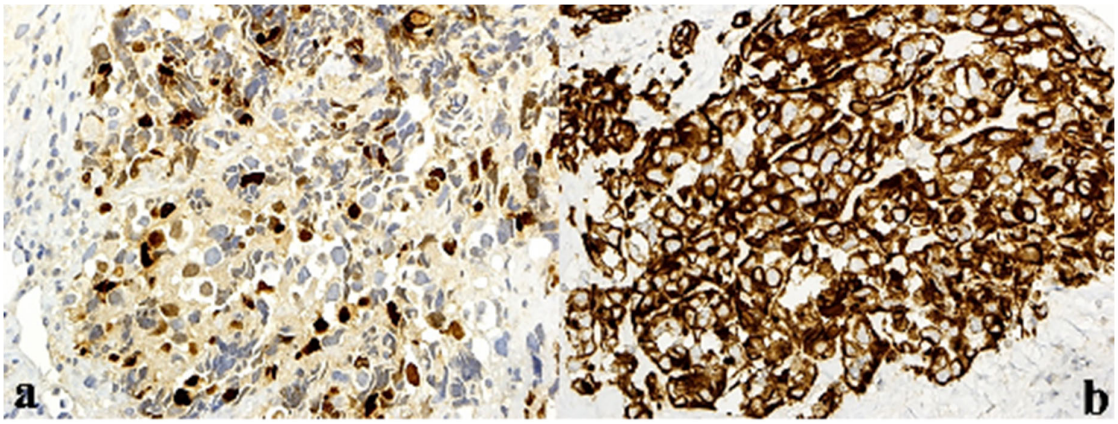

Figure 3. Immunohistochemistry: (**a**) diffuser staining of *desmin*; (**b**) patchy positivity for *myogenin.* (Original magnification 400×).

3. Discussion

RMS is an aggressive malignancy composed of neoplastic mesenchymal cells, with varying degrees of striated muscle differentiation. It is characterized by rapid growth through bone erosion. The RMS of the head and neck region is usually associated with facial swelling and symptoms such as sore throat, nasal airway obstruction and pain. These non-specific symptoms are responsible for a diagnostic delay that is crucial for the prognosis [14]. Durve and coworkers [15] reported a mean time interval of 21 weeks from symptom onset to diagnosis; this is a very important aspect since the prognosis is directly related to the stage of the disease as well as to the anatomical location and histological aspect. Concerning the case described in this report, it took four months to reach a correct diagnosis after the onset of symptoms. Some confounding factors, such as the temporal association between the onset of pain and the trauma and the presence of limited mandibular function, caused a delay of the appropriate diagnostic process by clinicians, who were first oriented toward a TMD. Furthermore, despite the increase in pain and dysfunction, no facial asymmetry or swelling occurred over time, since the tumor involved the right TMJ area and grew intracranially, causing compression-related symptoms. Similar clinical aspects can be found in the presence of acoustic neuroma, which, however, is frequently associated with monolateral deafness, vertigo and tinnitus, which were not present in the patient of the present paper. Another pathology that must be excluded is the trigeminal neuralgia (TN), which manifests itself as a sudden pain, usually unilateral, severe, brief, stabbing, recurrent and localized in the area of distribution of one or more branches of the fifth cranial nerve: these characteristics are very similar to the signs and symptoms of our patient. However, TN is a rare disease in children [16], and other pathologies commonly affecting the head and neck district in young subjects, such as fibrosarcoma, leiomyosarcoma, neurofibrosarcoma, RMS [17], lymphatic-venous malformations [18] (that can grow and become clinically apparent only after the onset of respiratory infections), must be ruled out by radiological and histological examination [19].

In this case report, a more accurate anamnesis and the careful evaluation of the peculiar pain characteristics led to further investigation. The patient referred to discomfort for a year before receiving the correct diagnosis: occasional, intermittent or mild symptoms may be underestimated or misdiagnosed, but it is essential to properly evaluate the presence of pain in children as in adult subjects, even if not associated with functional limitation.

In addition to the clinical aspects, the imaging plays a fundamental role in the diagnostic process of RMS. A joint task force of the Children's Oncology Group and the Society for Pediatric Radiology investigated the current landscape of medical imaging for children with cancer, providing an overview of the risks and benefits associated with commonly used modalities. The authors underline that MRI is superior to CT in evaluating regions involving predominantly soft tissue and is preferred for imaging of the head and

neck [20]. Dohar and coworkers [19] reported a similar case of RMS in the infratemporal fossa showing how CT scans failed to detect a mass that MRI delineated well. It appears that tumors involving sites such as the infratemporal fossa and TMJ may be difficult to evaluate by CT, due to severe interference from bone artifact and limited section planes. Although CT is considered the best method for evaluating bone erosions or fractures, MRI can also show these lesions. Furthermore, artifacts caused by metallic dental restorations sometimes produce serious diagnostic problems in CT examinations of malignant tumors of the oral and maxillofacial region. On the other hand, the incidence of artifacts that seriously disturb image interpretation on MRI is only half that associated with CT. In cases where artifacts severely interfere with CT image interpretation, further evaluation with MRI is recommended, which also delineates tumor boundaries accurately [19,21]. CT is a faster examination than MRI, providing high quality data. It is less expensive than MRI and well tolerated by the patients that rarely need sedation; however, CT scans entail the exposure to ionizing radiations. MRI evaluations are time intensive, and in order to acquire high-quality images, the children often need sedation, which has its own associated with risks and costs. Technological advancements are allowing for MRI scans to be acquired in a shorter time and not exposing patients to ionizing radiations makes this examination very important in pediatric settings [20]. Early diagnosis is crucial in defining the prognosis and treatment modality of RMS [22]. Surgical excision is rarely effective because RMS is characterized by an early diffusion and because it often involves important anatomical structures. Destructive behavior and bone invasion are frequent, and chemotherapy is the main treatment modality regardless of whether surgery or radiotherapy are performed [23]. All the treatments carry morbidity risks; therefore, a multidisciplinary approach is mandatory for a better quality of life. Despite the patient receiving the treatments recommended by the literature, it was too late for a surgical intervention, and the tumor did not respond positively to chemotherapy, leading to the patient's death after 4 months from initial biopsy.

This case report describes an uncommon presentation of RMS and the accurate evaluation of the patient's clinical history, allowing for the correct diagnosis to be made. This suggests possible improvements in the diagnostic process if a more accurate and comprehensive clinical evaluation were to be performed. The absence of swelling was very peculiar in this case and represents a rare manifestation of RMS that must be taken into account.

Cancer in children is a very challenging issue due to the burden of emotions it brings about as well as the complexity of its management. The diagnosis is often far from being easy to make, due to the children's difficulty in telling a clear history; therefore, a thorough examination is crucial to understand the entity of the problem. Continuous, non-specific signs and symptoms, such as limited mouth opening and pain during function, that is not modified by pharmacological treatments, should alert the pediatrician and the dentist even if patients do not show facial swelling or asymmetry. The presence of pain deserves the utmost attention and must be evaluated by experts with all the tools available to reach a correct diagnosis.

4. Conclusions

Accurate evaluation of clinical history and knowledge of possible, and even unusual, presentations are crucial to suspect RMS. Continuous pain both spontaneous and function related, should suggest further investigations. The choice of proper imaging together with the histopathologic evaluation can provide the diagnosis of RMS.

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