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Adult Neuromuscular Choristoma in the Intraconal Region of the Orbital Muscle: A Case Report

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Abstract

Background: Neuromuscular choristoma is a rare benign peripheral neuropathy composed of ectopic mature muscle fibers and nerve bundles, usually involving large nerve roots or trunks, such as brachial plexus and sciatic nerve. NMC usually occurs in childhood, and some cases are congenital. Here, we report a case of adult orbital intraconal NMC. The resected specimens were fish-like and tough. Histological pathology suggested that the specimen was composed of mature skeletal muscle tissue interspersed with peripheral nerve bundles. Histopathological examination revealed that the left orbital mass was composed of mature skeletal muscle tissue interspersed with surrounding nerve fascicles. Immunohistochemistry: S-100 protein was positive. In general, postoperative histopathological examination ultimately determined the diagnosis of NMC in the intraconal region of the orbital muscle. **Case Presentation:** A 51-year-old female patient was admitted to the hospital due to periocular pain for 2 weeks. Orbital CT scan showed an irregular soft tissue density in the left orbital muscle cone area, and the boundary between the local and the left lateral rectus muscle was unclear. Magnetic resonance imaging showed that there was an oval abnormal signal in the posterior lateral space of the left eyeball, with a clear edge and a size of about 22 mm × 8 mm. The boundary between the local area and the left lateral rectus muscle was unclear, and the optic nerve was compressed to the right side. The T1 WI showed low signal, T2-FS showed high and low mixed signal, and the enhanced scan showed continuous obvious enhancement. Eventually, the patient underwent surgical resection of the lesion. **Conclusions:** NMC is a rare benign peripheral neuropathy, especially NMC in the orbital muscle cone. There is no specificity in

clinical and imaging examinations. Accurate diagnosis before surgical resection is very challenging for clinicians and radiologists. Importantly, we can differentiate orbital NMC from other types of orbital tumors.

Keywords

Neuromuscular Choristoma, Desmoid-Type Fibromatosis, Orbit, Case Report

1. Introduction

Neuromuscular choristoma (NMC) is a rare benign peripheral nerve lesion caused by the aberrant growth of normal embryonic tissue. It primarily involves peripheral nerves, with the sciatic nerve being the most commonly affected, followed by the brachial plexus. Its histological characteristics are manifested as the presence of ectopic differentiated and mature skeletal muscle fibers embedded within nerve fascicles. The principal symptoms experienced by patients with NMC include pain, deformities of soft tissue or bone, and related neurological abnormalities, with variable disease courses. Notably, symptomatology appears similar between children and adults. Desmoid-type fibromatosis (DTF) is a tumor composed of myofibroblasts. Despite lacking metastatic potential, it demonstrates local aggressiveness and invasive growth, with a significant propensity for occurrence near nerves and recurrence after resection. NMC is frequently associated with DTF. Neuromuscular choristoma-associated desmoid-type fibromatosis (NMC-DTF) typically occurs following iatrogenic injury but can also arise spontaneously [1]. NMC and NMC-DTF share the same CTNNB1 mutation and abnormal nuclear localization of the β-catenin protein [2] [3]. CTNNB1 mutations in peripheral nerves or skeletal muscles may prevent normal development, and specific types of CTNNB1 mutations are correlated with more aggressive clinical manifestations [1]. CTNNB1 is a proto-oncogene encoding the β-catenin protein, which is involved in intercellular adhesion and can function as a transcriptional activator within the cell nucleus. Activation of the CTNNB1 gene leads to the accumulation of the β-catenin protein within the cell nucleus, promoting DNA transcription and cell proliferation. Commonly, CTNNB1 gene mutations are related to tumorigenesis and development, and high expression of this protein can be observed in other tumor tissues such as liver cancer [4].

CTNNB1 mutations were previously thought to be limited to DTF. Recently, the first case of a soft tissue tumor with three morphological components has been reported, and more importantly, all three regions contain the same mutated CTNNB1, which suggests that the morphological spectrum of CTNNB1-mutated soft tissue tumors is gradually expanding [5]. This also suggests that we should carefully observe the surrounding tissues when diagnosing CTNNB1-mutated tumors to rule out the possibility of CTNNB1-mutated mixed tumors. However, the etiological mechanism between NMC and DTF is still unclear [6]. However,

previous studies have shown that NMC originates from a pluripotent mesenchymal progenitor cell that carries a CTNNB1 mutation and can initiate the development of adjacent myofibroblasts into DTF [1].

Given the connection between these two diseases, it provides clinical insights for the diagnosis and treatment of patients. Additionally, close follow-up and reexamination should be emphasized for NMC, particularly for the nerve regions affected by NMC. According to the available data and clinical experience, NMC patients need close follow-up, and the recommended frequency is 1 - 3 years 1 time. The incidence of NMC is low, and it lacks specific clinical manifestations, laboratory examination indicators, and imaging features, making accurate preoperative diagnosis challenging. This article reports a case of Neuromuscular choristoma in the intraconal region of the orbit in our hospital, providing experience in the diagnosis and treatment of orbital NMC and a brief review of NMC, with the hope of providing a reference for future clinical diagnosis and treatment.

2. Case Presentation

The patient, a 51-year-old female, was admitted to the hospital due to periorbital pain for 2 weeks. The patient experienced intermittent periorbital pain, each episode lasting for approximately several seconds, which could resolve spontaneously and was triggered when bending down. Other than that, the patient had no headache, dizziness, blurred vision, or amaurosis, and no positive findings were noted during the physical examination. The patient had no history of trauma, hypertension, diabetes, or coronary heart disease. There was no history or family history of NMC, DTF, or other tumors. Orbital CT plain scan of the patient indicated an irregular soft tissue density shadow in the intraconal region of the left orbit, with indistinct boundaries with the left lateral rectus muscle locally, and a calcified nodular shadow was visible at the anterior edge of the lesion (**Figure 1(a)**). Magnetic resonance imaging showed an oval abnormal signal shadow in the intraconal space of the left lateral posterior globe, with a clear edge, approximately 22 mm × 8mm in size, indistinct boundaries with the left lateral rectus muscle locally, the optic nerve was compressed and displaced to the right, presenting low signal on T1WI, mixed high and low signal on T2-FS, and showed continuous and significant enhancement on enhanced scan (**Figures 1(b)-(d)**).

Based on the CT and MRI enhanced scans, the preliminary preoperative imaging diagnosis was hemangioma with hemorrhage, and the differential diagnosis was inflammatory pseudotumor. Considering the location and size of the lesion, and the patient's desire to voluntarily remove the tumor, it was decided that surgical resection would be performed. The procedure involved transcranial resection of a left orbital space-occupying lesion utilizing neuro-navigation techniques combined with microscopy for precision surgery along with dural repair and lumbar cistern drainage procedures. The patient was positioned supine while an arc-shaped incision was made over her left frontal and temporal regions using a pterional approach; subsequent incisions through scalp tissues followed by muscular dissection allowed for suspension of dura mater before lifting up her frontal lobe,

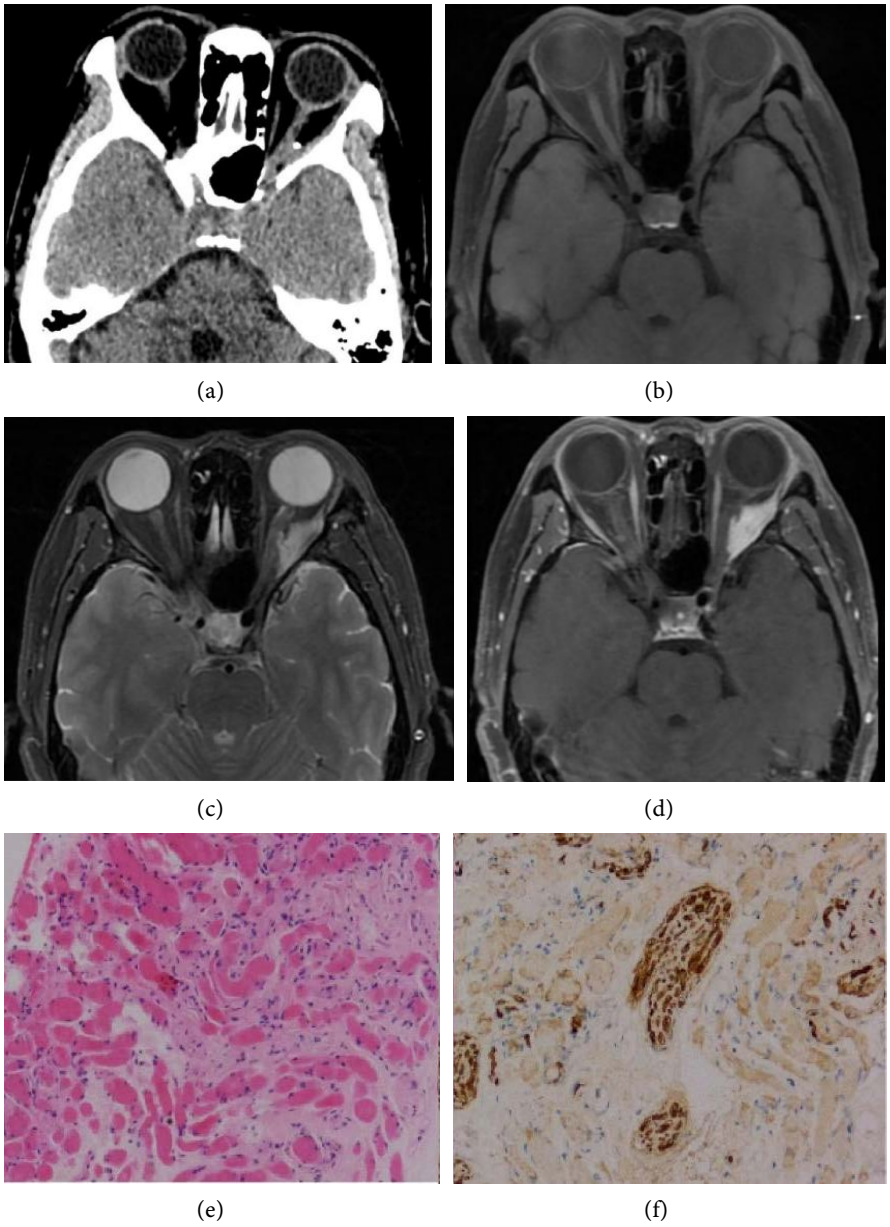

Figure 1. (a) Orbital CT plain scan; (b)-(d) Brain Magnetic Resonance plain scan and enhanced scan; (e) & (f) Pathological tissue section: hematoxylin and eosin staining (e, ×100), immunohistochemistry (f, ×100).

the orbital roof was exposed, the bone of the orbital roof was ground, the dura was incised, the tumor appeared fishy, with indistinct boundaries from the adjacent muscles. The tumor was resected piece by piece along its pseudo-boundary, hemostasis was performed meticulously, the dura was repaired, and the muscles and skin were sutured. Postoperative pathology: Hematoxylin and eosin (H&E) sections revealed mature skeletal muscle tissue interspersed with peripheral nerve bundles under the microscope (Figure 1(e)). Immunohistochemistry: S-100 protein was positive (Figure 1(f)). Combined with imaging examinations, it was consistent with Neuromuscular choristoma (NMC). It has been 6 months since the

tumor resection in this patient. During the follow-up, the patient had no obvious clinical symptoms. However, no imaging examination has been performed for reevaluation.

3. Discussion and Conclusions

This case represents a NMC located in the intraconal region of the adult orbit, unrelated to large nerve trunks such as the sciatic nerve or brachial plexus. Since its first report in the late 19th century, fewer than one hundred cases have been documented to date. Most of the reported cases occurred in large nerve roots or trunks such as the sciatic nerve or brachial plexus, and there have also been reports of trigeminal NMC and esophageal NMC [7] [8]. To our knowledge, no adult intraconal neuromuscular choristoma in the orbital muscle cone has been reported before. The primary clinical symptoms of NMC patients are pain, deformities of soft tissue or bone, as well as related neurological abnormalities. Disease courses can vary significantly—from several months to several years—while some patients may exhibit foot varus deformity or congenital hip dysplasia. These symptoms were within the range of the affected nerves [9]. This is the first reported case of adult intraconal neuromuscular choristoma in the orbital muscle cone, which is different from the imaging manifestations of neuromuscular choristoma occurring in the sciatic nerve, including the affected nerve exhibited fusiform thickening with distinct boundaries, and all sequence signals were analogous to those of skeletal muscle, presenting a T1WI signal and a slightly higher signal on T2WI. The enhancement scan indicated no enhancement or slightly uneven enhancement [6]. In this instance, the MR manifestations of NMC in the intraconal region of the orbital muscle demonstrated low signal on T1WI, a high and low mixed signal on T2-FS, and obvious and persistent enhancement on the enhanced scan. It can be observed that there is a significant difference in the reinforcement patterns. Therefore, the imaging diagnosis of the disease is more challenging.

Based on the location of this lesion, it should be differentiated from other space-occupying lesions in the intraconal region: 1) Cavernous hemangioma: It is the most common primary benign tumor in the adult orbit, being round or oval. CT shows isodensity, clear boundaries, and small punctate calcifications may be visible within the mass. The lesion is clearly demarcated from the optic nerve, and the optic nerve and ocular muscles are compressed, with no significant expansion of the optic nerve canal. MR plain scan shows long T1 and long T2 signals, clear boundaries, compression of surrounding tissues, and clear fat spaces. Enhanced scan shows progressive and filling-type significant enhancement of the lesion. 2) Inflammatory pseudotumor: It is a granulomatous lesion formed by non-specific chronic inflammation of the soft tissues within the orbit of unknown cause. This case is mainly differentiated from the inflammatory mass type of inflammatory pseudotumor: CT plain scan shows an irregular or regular soft tissue mass in the orbit, with blurred or clear edges. The mass is located anteriorly and often adheres to or envelopes the eyeball and attachment points of the rectus muscles, accompanied by thickening of the ocular ring. MR shows that the morphology and

boundary of the lesion are the same as those on CT, with a lower signal on T1WI and a higher or lower signal on T2WI. The signal of the lesion is related to the degree of fibrosis of the lesion. In addition, inflammatory pseudotumor is considered an autoimmune disease and is responsive to hormone therapy. 3) Neurilemmoma is more common in young and middle-aged women, presenting as oval or quasi-circular. CT shows isodensity, mostly homogeneous density, and cystic changes can be seen in a few cases. Enhancement is mostly heterogeneous. MR shows slightly long T1 and T2 signals, heterogeneous signals, and small cystic change areas with long T1 and long T2 signals can be seen. This patient was admitted with periorbital pain. The clinical manifestations, laboratory tests, and imaging examinations were non-specific. Therefore, it is highly challenging for clinicians and radiologists to provide an accurate diagnosis at the initial visit of the patient. A clear diagnosis requires postoperative pathological examination and further immunostaining after surgical resection.

Previous studies have investigated whether the CTNNB1 gene mutation status is related to DTF in 5 cases of NMC. The results show that the CTNNB1 mutations in NMC and DTF-related lesions and sporadic DTF are similar, which not only strengthens the relationship between the two diseases, but also indicates a common pathogenic mechanism: the characteristic of desmoid-type fibromatosis is the CTNNB1 exon 3 mutation, leading to abnormal nuclear localization of β-catenin and dysregulation of the classical WNT signaling. The CTNNB1 gene mutations exist in both NMC and NMC-DTF, which may be a common molecular genetic abnormality in the pathogenesis of the disease [10]. Some DTF patients, although initially not diagnosed with NMC, were later found to be hidden cases of NMC [9]. Currently, it is uncertain whether NMC within the orbital muscle cone region is associated with the development of DTF. Given the characteristics of NMC, clinicians should consider this condition in their differential diagnosis when evaluating patients with orbital space-occupying lesions to avoid misdiagnosis and ensure comprehensive imaging studies such as CT and MRI are conducted. As there have been no prior reports on orbital NMC, further investigation into its natural course is warranted through additional case studies. With ongoing research into its biological behavior, NMC has been classified as a benign disease; only a small number of cases exhibit progression [11]. In most instances, complete surgical resection of the tumor can lead to cure. Clinicians should enhance their awareness regarding NMC to prevent misdiagnosis or overtreatment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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