Case Report

Paraphayngeal Salivary Duct Carcinoma Involving the Cavernous Sinus

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Salivary duct carcinoma (SDC) is a relatively uncommon malignant tumor of the salivary gland derived from the excretory duct reserve cells of the salivary glands. The authors report a case of SDC in a 34-year-old man who presented with trismus and left sided headache, radiologically by a left parapharyngeal mass involving into the left cavernous sinus and histologically by intraductal growth pattern with a cribriform appearance and comedonecrosis. Perineural invasion of the mandibular branch of trigeminal nerve is demonstrated. Clinical and pathologic features with relevant literatures are reviewed.

Keywords: *Salivary duct carcinoma, Parapharynx, Cavernous sinus*

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Salivary duct carcinoma (SDC) is an uncommon, highly aggressive malignant salivary gland tumor demonstrating the formation of relatively large cell aggregating resembling distended salivary ducts, which is characterized by a combination of cribriform, looping (Roman bridging) and solid growth patterns, often with central necrosis[1-3]. SDC most commonly affects the major salivary glands and is characterized histologically by multiple epithelial nests reminiscent of ductal carcinoma of the breast[1-3]. Clinically, SDC is characterized by a high rate of recurrence and significant mortality.

The purpose of this report was to illustrate the clinical, radiological, and pathological findings of parapharyngeal SDC invading into the cavernous sinus, which first presented clinically as trismus and the left sided headache.

Case Report

A 34-year-old Thai married male patient living in Surin province, Thailand was admitted to Ramathibodi Hospital in June 2004, because of trismus of one-month duration together with left sided headache of two years duration. The patient had no history of significant illness in the past. There was no history of tuberculosis and cancer among the members of the families. Physical examination revealed mild bulging of the left parapharynx. The left eye showed lateral rectus palsy. The visual field and papillary light reflex were normal. There was sensory loss in the distribution of the mandibular branch of the left trigeminal nerve. The limitation of movement and atrophy of the left masseter muscle was noted. The cervical lymph node could not be palpated. The radiological findings revealed an ill-defined inhomogenous enhancing isosignal-T1, mixed iso/hypersignal-T2 tumor occupying the left infratemporal parapharyngeal fat space, left carotid space, which extended superiorly through the left foramen ovale into the left cavernous sinus and Meckel's cave (Fig. 1A-D). The ill-defined enhancing isosignal-T1 and hypersignal-T2 change of the muscles of mastication representing denervative change due to perineural tumor extension along the mandibular branch (V3) of the trigeminal nerve were observed. The left parapharyngeal lesion was biopsied under general anesthesia. The diagnosis was parapharyngeal salivary duct carcinoma involving the left cavernous. He

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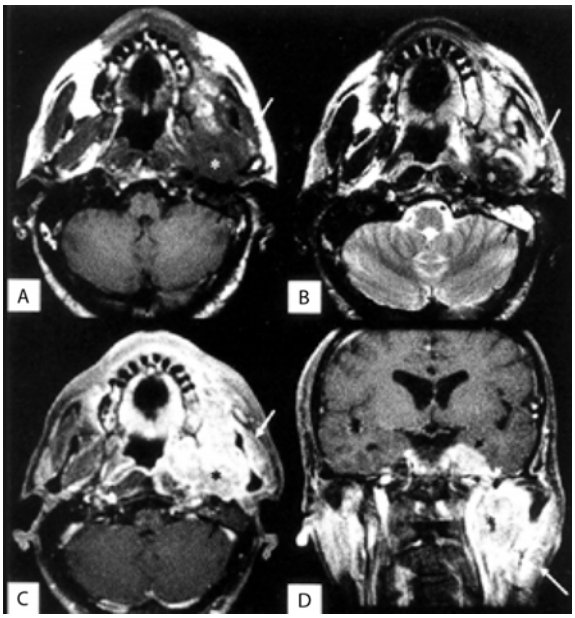

Fig. 1 Axial T1W (A), T2W (B) and post gadolinium axial and coronal T1W with fat suppression MR imaging study around the skull base reveals an ill-defined inhomogenous enhancing isosignal T1, mixed iso/persignal T2 mass locating at the left infratemporal parapharyngeal fat space (small white and black asterix in A, B, C and D) extending superiorly through the foramen ovale (white arrowhead in D) into the left cavernous sinus and Meckel's cave (black arrowhead), also observed is il l-defined enhancing isosignal T1 and hypersignal T2 change of the muscles of mastication (white arrows in A, B, C and D) representing denervative change due to perineural tumor extension along the V3 segment of the trigeminal nerve, secondary otomastoid retention is seen due to eustachain tube compression (small black arrows in A, B and C)

received post operative radiotherapy over the left parapharyngeal area including the base of the skull with the total dose of 51 Gy. At the end of the treatment, an improvement in trismus and left sided headache were observed. Thirty-six months of follow-up, he is well and there is no evidence of metastasis.

Pathological findings

The sections of the left parapharynx revealed multiple foci of round, well-circumscribed nodule of neoplasitc ductal epithelium forming cribriform architecture. Comedonecrosis is evident in the central area of the cytic nodules of tumor (Fig. 2). The necrotic material has slightly retracted from the surrounding

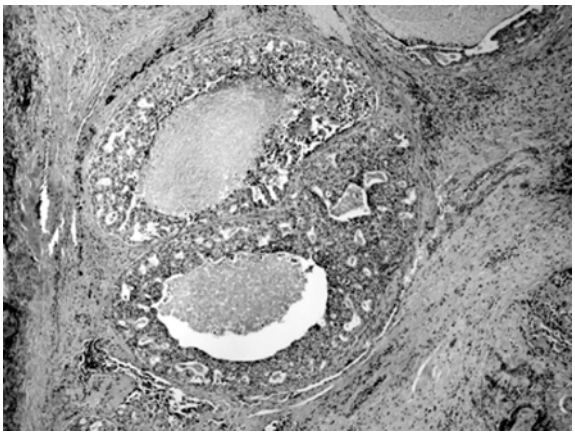

Fig. 2 The section of the left parapharynx reveals multiple foci of round, well-circumscribed nodule of neoplasitc ductal epithelium forming cribriform architecture with comedonecrosis, H&E, X40

epithelium. A few mitotic figures with moderate cytologic atypia are apparent. Perineural invasions, infiltration of vascular and lymphatic spaces are noted. Immunohistochemical stains showed tumor cells to be positive with epithelial cell markers, including cytokeratin, and epithelial membrane antigen (EMA) confirming the epithelial origin of the tumor. Tumor cells were negative for estrogen and progesterone receptors, E-cadherin, gross cystic disease fluid protein 15, HER-2/neu and prostatic specific antigen (PSA) excluding metastatic mammary and prostatic carcinoma. The malignant epithelial cells showed negative signal for Epstein Barr virus (EBV)-encoded Ribonucleic acid (EBER) (DAKO) by in situ hybridization (ISH).

Discussion

Salivary duct carcinoma is a relatively uncommon, high-grade malignant salivary gland neoplasm composed of structures that resemble expanded salivary gland ducts[1-3]. SDCs originate from the excretory duct reserve cells of the salivary glands[3]. This tumor shows a male predilection of approximately 2.5:1[3]. The average age at presentation occurs principally during the sixth to seventh decade[2,3]. The age of patients range from 22 to 91 years old [2]. The tumors are usually found mostly in the parotid glands, although cases with involvement of the submandibular glands and the minor salivary glands have been reported[2]. Salivary duct carcinomas usually remain asymptomatic until they produce a mass effect, or neural invasion. The routine initial laboratory investigations are noncontributory. The imaging procedures such as com-

puted topography, and magnetic resonance image may allow early recognition of malignant primary SDCs.

Diagnosis often is delayed because of protean nonspecific and diverse clinical manifestations at presentation with resultant poor outcome resulting from advanced locally invasion and metastatic disease. The most common sites of metastases are lymph node (59%) and distant sites (46%)[3]. The most frequent distant sites include the lungs, bones, liver and brain[2]. This tumor has a high mortality rate due to its rapid local relapse and a high incidence of systemic metastasis[2,3]. The tumor size ranges vary from 1 to larger than 7 cm (average 3 cm)[2,3]. The microscopic findings demonstrate pleomorphic cells forming both aggregates resembling distended ducts, papillary, cribriform, and solid patterns with central necrosis[1-5]. Neoplastic cells are round, clear nuclei, and eosinophilic cytoplasm with numerous mitotic figures[1-5]. Perineural and periglandular soft tissue infiltration is a common finding[2]. Previous immunohis to chemical studies have reported that SDC stained positive for keratin, variable positive for the EMA, and negative for PSA, and estrogen receptor[2-6]. The immunohistochemical results of the presented case are compatible with these reports[2-6].

Cavernous sinus involvement is a unique presentation of the salivary gland malignancy. SDC and adenoid cystic carcinoma involving the cavernous sinus have been reported[7,8]. The mechanisms of involvement include the neural invasion, the lymphovascular invasion, and direct extension. Our patient presented with an advanced lesion, which involved the cavernous sinus. Retrograde spread along trigeminal nerve is the most likely hypothesized, which can result in neuropathy and involvement of the cavernous sinus. The picture of intracranial trigeminal nerve invasion was demonstrated by histopathology and radiography, as seen in the presented case.

Perineural invasion is frequently noted with adenoid cystic carcinoma and SDC. The division of the trigeminal nerve has extensive neural branches and connections involving the parapharyngeal structures, masticator spaces, and cavernous sinus. Therefore, SDCs involving multiple and varied regions of the parapharynx and masticator space have multiple opportunities to gain access to neural pathways. When peripheral branches of trigeminal nerve are involved, tumor may spread retrogradely and eventually reach the cavernous sinus. Perineural invasion are generally characterized by an indolent course and has considerable implications for prognosis and treatment. Therefore, the early and accurate detection of perineural invasion may enhance surgical planning and appropriate use of adjuvant therapy.

The differential diagnoses of the cavernous sinus tumor include directly invasive nasopharyngeal carcinoma (NPC), meningioma, schwannoma, or metastasis. NPC originates from the mucosal space of the Rosenmuller fossa and can spread along the preexisting vulnerable routes or direct invasion to the adjacent structures. Patients previously reported with NPC (World Health Organization grade II, III) had been identified EBV- Ribonucleic acid by ISH in the neoplastic cells[9]. Furthermore, there are few reports in the literatures documenting the elevated titers of IgA antibodies to EBV capsid antigen[10]. It is suggest that EBV infection may be a factor in the development of these NPCs. Negative results of ISH for EBER and histopathology may be helpful in excluding NPC in the presented patient. Meningioma arises from the lateral wall of the cavernous sinus[11]. It may cause intracavernous cranial nerve palsies by invading or compressing the cavernous sinus. Schwannoma of the cavernous sinus can arise from differentiated neoplastic Schwann cells of the intracavernous cranial nerves[12]. The other nonmeningeal tumors of the cavernous sinus have been reported[12]. However, the histological features of the differential diagnoses of tumor in cavernous sinus were not found in the presented case.

Wide surgical excision and neck dissection remains the cornerstone of surgical management of SDC, since it improves survival, but there is almost always recurrence[13]. Complete surgical resection is rarely possible for the SDCs of the minor salivary glands involving the cavernous sinus. The adjunctive treatments include radiotherapy and systemic therapy[13]. However, the tumor may recur even after radiotherapy and the patient may die of metastatic disease. The overall life expectancy is 56 months after receipt of initial treatment[14].

This is a case of salivary duct carcinoma in a 34 year-old man of a clinically, radiologically, and pathologically identical SDC involving the cavernous sinus. Antegrade spread along the neural pathway and invaded the cavernous sinus is demonstrated. Radiotherapy is recommended for the treatment of unresectable SDC.

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มะเร็งท่อน้ำลายที่ข้างคอหอยลุกลามเข้า *cavernous sinus*

นพดล ลาภเจริญทรัพย์, ยุวดี เลี่ยวไพรัตน์, จำรูญ ตั้งกีรติชัย, จิรพร เหล่าธรรมทัศน์

มะเร็งท่อน้ำลายเป็นเนื้อร้ายที่พบน้อยโดยเกิดจากเซลล์ต้นแหล่งของท่อน้ำลาย คณะผู้รายงานเสนอผู้ป่วยชายไทยอายุ 34 ปี มาพบแพทย์ด้วยอาการอ้าขากรรไกรไม่ได้ร่วมกับอาการปวดศีรษะข้างซ้าย ตรวจทางรังสีวิทยาพบก้อนที่บริเวณข้างคอหอยด้านซ้าย ลุกลามเข้า cavernous sinus ด้านซ้าย ตรวจทางพยาธิวิทยาพบเป็นเซลล์มะเร็งในท่อน้ำลายที่มีการจัดเรียงเป็นรูปตะแกรง และพบกลุ่มเซลล์มะเร็งลุกลามเข้าแขนงของเส้นประสาทสมองคู่ที่ 5 นอกจากนี้ คณะผู้รายงานได้รวบรวมวิเคราะห์ลักษณะแสดงทางคลินิกและพยาธิวิทยาที่เกี่ยวข้อง
