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A review of the application of MRI in the diagnosis of salivary gland malignancies

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Abstract

Salivary gland tumors are an important group of pathological lesions of the head and neck and are often seen in adults. Clinically, salivary tumors are often asymptomatic and may become apparent over time. Malignant tumors of the salivary glands are not very common. The most common site of these tumors is the parotid gland, and in many studies these tumors have been reported to be more common in women than men. Radiographic techniques in the diagnosis of salivary gland diseases include conventional radiography, sialography, ultrasonography, scintigraphy, computed tomography (CT) scan, magnetic resonance imaging (MRI), and nuclear medicine. The above radiographic techniques are very useful in distinguishing between infectious and neoplastic diseases, identifying and locating salivary gland stones, and showing the morphology of the secretory ducts. In addition, with these radiographic images, the anatomical position of a tumor, whether it is benign or malignant, and the relationship between the tumor and adjacent tissue can be determined. Depending on the nature of the lesion, a special imaging technique is used. Conventional radiographs do not play much role, but are used to examine stones and the effect of salivary tumors on adjacent bone structures. Sialography is the method of choice in examining the salivary gland ducts. CT scan is the method of choice for examining inflammatory lesions of the salivary glands. Ultrasound and MRI are used for salivary gland tumors, and nuclear medicine is used to evaluate salivary gland function in autoimmune diseases. The aim of this study was a review of the application of MRI in the diagnosis of salivary gland malignancies.

Keywords: Salivary glands, tumor, malignancy, imaging, MRI.

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1. Introduction

Various lesions can affect the salivary glands. Salivary gland tumors are not very common and make up 3 to 5% of head and neck neoplasms [1] and only 0.5% of all malignant tumors match these types [2]. The incidence of all salivary gland tumors varies between 0.11 to 4 per 100,000, population [5-3]. Salivary gland tumors originate less frequently in the submandibular, sublingual and minor salivary glands. Tumors in the parotid gland account for approximately 70% of SGT, the submandibular gland accounts for around 10% and the sublingual gland less than 1%, thus the minor glands are affected by about 20% [6]. In the parotid gland, approximately 80% of neoplasms are benign while 20% are malignant. In the submandibular gland, 50% of neoplasms are benign while 50% are malignant. As in the parotid gland, the most common benign neoplasm is the pleomorphic adenoma, constituting 85% of all benign submandibular gland neoplasms. Tumors of the sublingual gland were rare, but all were malignant. In the sublingual and minor salivary glands, 80%–90% of neoplasms are malignant [7, 8]. Malignant tumors are generally less common than benign tumors in the large salivary glands [7, 8]. Although tumors are less common in the minor glands about 50% are malignant, compared to only about 20% in the major glands [6, 8]. The palate is the most common site of minor salivary gland tumors in 33.3 to 67% of cases [9, 10], followed by the upper lip and buccal mucosa. The 5-year predicted overall survival rate was 86%, and the disease-specific survival rate was 94% at 5 years [8].

The prevalence of these tumors seems to be related to geographical areas as well as race [9]. Clinically, the symptoms that predict the benign or malignant nature of the lesion are unreliable, but low-grade benign malignancies present as painless, slow-growing masses [1, 9]. Progressive malignancies or inflammatory lesions are associated with pain and rapid growth [11]. In about one-third of patients, pain is one of the early symptoms [12, 13]. Facial nerve involvement strongly suggests a malignant process. Other symptoms that may be associated with malignancy include trismus, cervical adenopathy, numbness, loose teeth, and bleeding [10, 14]. Preoperative diagnostics are mainly based on imaging methods and pathological findings, especially fine-needle aspiration cytology (FNAC) [4, 7]. The sensitivity of FNAC for the diagnosis of salivary

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malignancies is 60 to 73%. FNAC is very useful for deciding how to perform surgery and consulting the patient before surgery [15]. There is disagreement about preoperative imaging of parotid tumors. Some studies suggest that superficial parotidectomy without imaging is sufficient if the mass is completely on the parotid surface and FNAC proves that the tumor is benign, but others emphasize preoperative imaging.

Various imaging techniques have been studied to evaluate tumors, which include conventional radiography, sialography, ultrasonography, scintigraphy, computed tomography, and magnetic resonance imaging (MRI). These techniques are very useful in distinguishing between infectious and neoplastic diseases, identifying and locating salivary gland stones, and showing the morphology of the secretory ducts [16, 17]. Ultrasound, MRI and contrast-enhanced computed tomography (CT) scan are the most commonly used imaging modalities to evaluate salivary gland lesions [18, 19]. Ultrasound remains the basic diagnostic imaging procedure, especially when occurring in parotid glands. As a low cost, non-invasive modality, ultrasound provides excellent localization of the tumor in the gland and enables differentiation from the cystic mass [4, 7], however, this method is only able to show superficial tumors and the relationship of the mass with adjacent structures is unexplored. But it is used as a low-cost and non-invasive method [20, 21]. CT scan is especially useful for assessing the location and extent of the disease, especially in cases of deep parotid lobe involvement and parapharyngeal areas [22, 23]. MRI is preferable to soft tissue scan over CT scan but is unable to identify bone marrow landmarks [24, 25].

The methods of diagnosis primarily depend on the location of lesions. FNAC and ultrasound are mainly applied to lesions of the superficial glands. For lesions of the small salivary glands, lower lobes or suspected cases of malignancy, other methods like MRI or CT should be used. One of the advantages of MRI and CT techniques is the ability to gauge the extent and invasion of the tumor, which can be additionally used for diagnosis [26, 27]. Several MRI techniques have been applied to differentiate between benign and malignant salivary gland tumors. Of these, dynamic contrast-enhanced (DCE) and diffusion-weighted (DW) MRI have been the most frequently evaluated for that purpose [28, 29]. Studies have shown that analyses using time-intensity curves (TICs) that are obtained by DCE imaging and apparent diffusion coefficients (ADCs) obtained by DW imaging could be potential tools for the differentiation of tumor types. The single use of these MRI techniques has yielded acceptable results, but the diagnostic efficacy was not high [28, 30].

Due to the importance of identifying tumors and malignancies of the salivary glands and the need for deep and accurate knowledge of its imaging methods, especially MRI imaging, we aimed to review the application of MRI in the diagnosis of salivary gland malignancies.

2. Methods

Studies in the English language literature investigating the diagnosis accuracy of MRI to diagnosis benign and malignant salivary gland tumors were the focus of this review study. The PubMed, ScienceDirect, and Web of Science databases were searched to find relevant publications up to March 2022, with the keywords Salivary glands, tumor, malignancy, imaging

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and MRI as well as their abbreviations and synonyms and all the possible combinations. To ensure a more complete literature search, references of the retrieved articles were also reviewed to cover all relevant studies.

3. Findings

3.1. Salivary Gland Imaging Techniques

Before discussing salivary gland lesions, it is important to review the strengths and weaknesses of the various imaging modalities available. Conventionally, radiography and sialography were the workhorse of salivary gland imaging due to their ability to detect calcifications and exquisitely visualize the ductal system. Although sialography is still used for certain indications (i.e., identifying sialoliths or dilating strictures in cases of chronic sialadenitis), these modalities cannot adequately visualize the vast majority of salivary gland neoplasms and have largely been replaced by cross-sectional imaging, namely ultrasound, CT, and MRI [6].

Ultrasound is a quick and relatively inexpensive modality that can accurately depict the vast majority of salivary gland neoplasms. Due to their superficial location, the margins of most salivary gland neoplasms can be delineated through the use of high-frequency transducers (7–10 MHz). This allows the radiologist to not only determine the size of the lesion but also help guide the site of biopsy/aspiration, especially in cases where a lesion demonstrates mixed cystic/solid components. However, as with all modalities, ultrasound carries significant limitations. It is heavily operator dependent, provides limited visualization of the deep lobe of the parotid gland, and often has difficulty distinguishing benign from malignant neoplasms. It is for these reasons that ultrasound is not commonly used unless there is limited access to other advanced imaging techniques such as CT or MRI.

CT is frequently the first test to identify a salivary gland lesion due to the fact that many lesions are often incidentally discovered on CT performed for other reasons. Compared to other cross-sectional imaging, CT is an extremely fast imaging technique, but carries the risk of ionizing radiation. CT is very good at identifying salivary gland lesions, but is particularly useful for identifying lesions with calcifications (i.e., phleboliths in venous malformations). However, due to relatively poor soft-tissue contrast, defining tumor extent and attempting to differentiate benign from malignant neoplasms can be quite challenging.

MRI is currently the test of choice in evaluating salivary gland lesions. Not only can it identify and properly size most lesions, but its higher soft tissue resolution allows for better identification of internal tumor characteristics, better definition of tumor margins, and most importantly, identification of perineural spread. In addition, advanced MRI techniques such as DWI have proven helpful in better characterizing various lesions (i.e., identifying malignant transformation of a pleomorphic adenoma as areas of low apparent ADC signal in an otherwise hyperintense mass) [6]. The application of MRI in discriminating between benign and malignant salivary gland tumors presented a pooled sensitivity of 0.80 (95% CI 0.67–0.89) and a pooled specificity of 0.90 (95% CI 0.83–0.95) [19] .

3.2. MRI view of salivary glands

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Parotid gland is a relatively fat-rich structure in adults that includes components such as the facial, arteries, veins, and duct system. In MRI images, the fat component is the parotid, which determines its signal strength, which is usually a medium to high signal in T1 images and a low to medium signal in T2 images. The T1 image is usually inhomogeneous. Areas with low signal include ducts and interstitial tissue and branches of the facial nerve. The facial nerve can be seen in a high-resolution MRI image (1.5 Tesla with coil neck and head). Although some researchers believe that the use of contrast with MRI is necessary to obtain diagnostic images, other authors believe that contrast is not necessary. Because the presence of contrast material reduces the visibility of the lesion due to the loss of contrast between the lesion and normal parotid adipose tissue. It is generally believed that T1 images are useful for showing tumor location and T2 images are more useful for showing tumor boundaries, and T1 .T2 images are both necessary for accurate evaluation [31]. The submandibular gland has fewer fat components than the parotid gland. As a result, it is seen in T1 images with fewer signals and in T2 with more signal than parotid. After contrast injection, both submandibular glands should have the same amount of contrast, and if this is not the same, usually the gland that has shown the most contrast has an abnormal data function [32]. The sublingual gland has been studied less than the other two major glands. This indicates that inflammatory and tumor processes in this gland are rare. The sublingual gland is located on the lingual surface of the anterior third of the mandible. In MRI images, at T1, there are fewer signals than surrounding fat but more signals than muscle, and at T2, there are a higher signal. With age, the parotid signal in T1 images increases, but not in the sublingual and submandibular glands [33, 34].

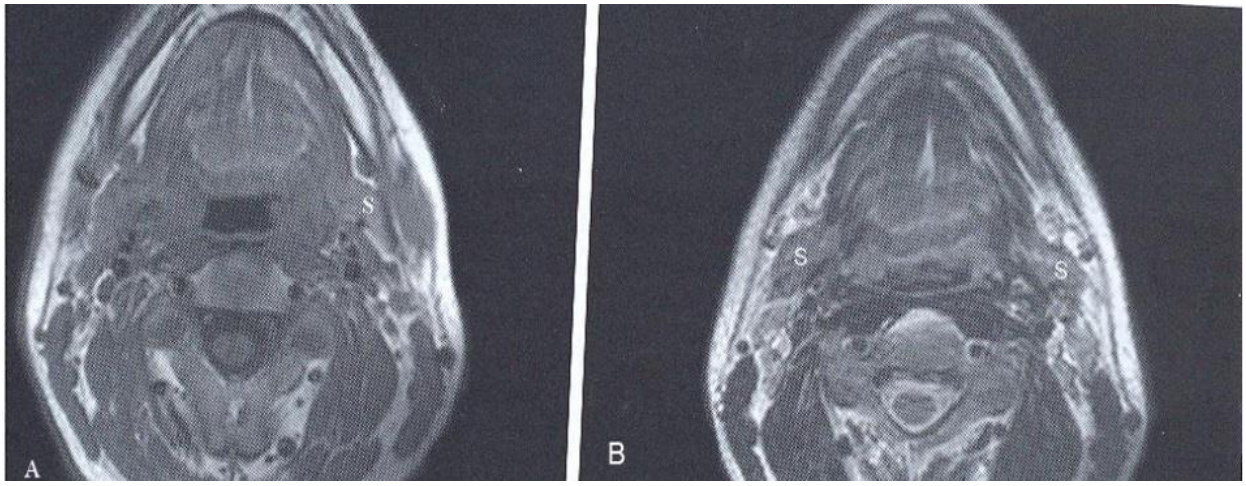

Figure 1: MRI image of the submandibular gland (A, B). Figure A shows the T1 view and B the T2 view of the submandibular gland (S) [32].

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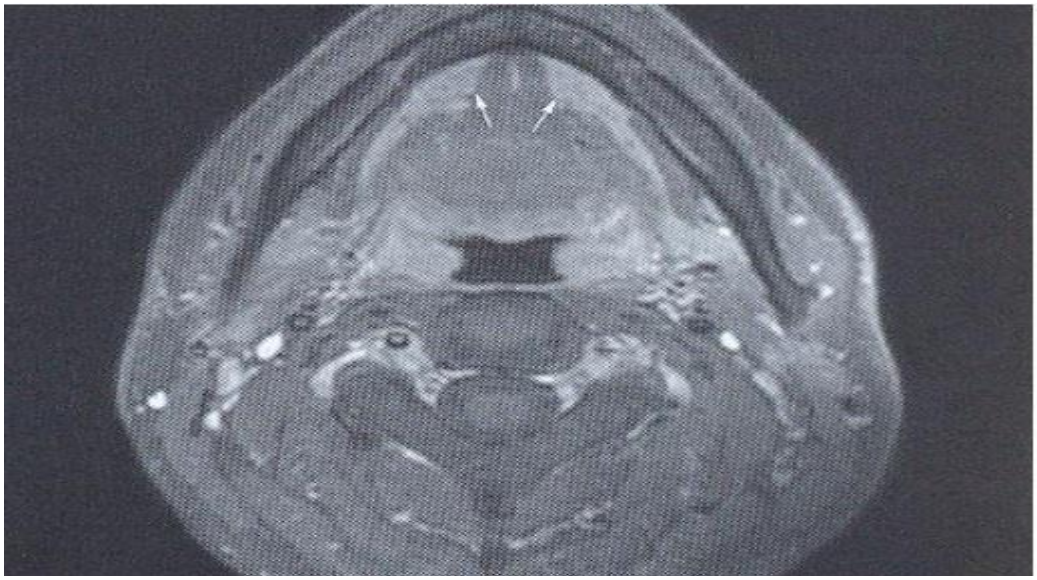

Figure 2: T1 image on MRI in the axial section of the sublingual gland (arrows) [32].

One of the pathological changes in salivary glands is tumor changes. In the following, we will examine the imaging scenes of the most common salivary gland tumors. For easier evaluation and better classification, we examine tumors in benign and malignant categories.

3.3. Benign tumors

Salivary gland tumors are often benign or low-grade malignancies, and are more common in the parotid gland. Their imaging findings usually confirm their benign nature. They usually have certain boundaries and do not destroy adjacent structures.

3.3.1. Pleomorphic adenoma

Pleomorphic adenoma is the most common salivary gland tumor, which accounts for about 70-60% of all parotid tumors, 40-60% of submandibular gland tumors and 70-40% of secondary salivary gland tumors. 84% of cases occur in the parotid gland and in an age range from the first decade to the tenth decade; the highest prevalence is in the third and fourth decades. Parotid tumors are usually in the superficial lobe. (90% of cases) but 10% are located in the deep lobe or in the parotid gland. The ratio of men to women is 0.7 to 1 [35]. These tumors are hard and mobile in the main salivary glands as a painless mass. Deep lobe tumors are not palpable, but may present as an intraoral mass or appear on examination as a superficial lobe mass. These tumors in the minor salivary glands are painless submucosal swelling and are usually 6 to 2 cm in size, although they can be very large if left untreated [7, 8, 36, 37].

Microscopic examination of this tumor consists of mesenchymal and epithelial components in which the appearance of tissues such as chondroid, myxoid, osteoid, etc. can be seen, the reason for its name is the same histological manifestations [8, 9]. The recurrence rate of this tumor is between 1-5% and is directly related to primary surgery. Also, the more chondroid and myxoid

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tumors there are, the more recurrent it is. The recurrence of this tumor is usually multifocal [10, 11].

Imaging findings

On MRI, they usually have a low signal in T1 images but a high signal in T2. The tumor capsule is seen as a low signal area in T2 images but is not easily seen on CT scan. Small masses in images T2 and T1 are homogeneous, but larger tumors are usually heterogeneous. The hemorrhagic regions in T1 and T2 are manifested as high-signal regions. The necrotic regions have a low signal in T1 and a high signal in T2 (Figure 3). MRI is particularly good to evaluate deep lobe masses, to differentiate parapharyngeal space masses, and to evaluate the condition of the facial nerve in relation to the tumor and surgical considerations [1, 2, 4, 5].

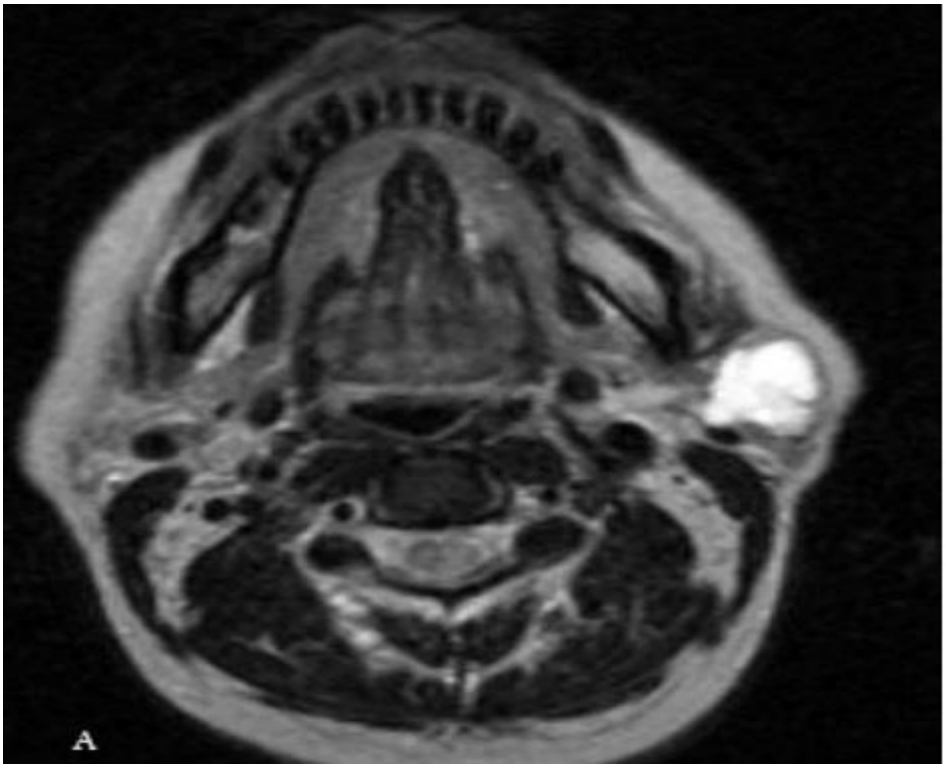

Figure 3: T2 image in the axial section, which shows a mass with a definite limit and a strong signal (pleomorphic adenoma) [32].

3.3.2. Wartin tumor

The second most common benign parotid tumor is after pleomorphic adenoma occurs exclusively in the parotid gland. It is usually seen in the lower part of the parotid gland at the angle of the mandible. Rare cases of involvement of the submandibular gland, palate, lips, larynx, maxillary sinus, and buccal space have been reported [12, 27]. Patients often complain of swelling. Their age range is 92 to 2.5 years, but its highest prevalence is in the seventies. In previous studies, the ratio of men to women was 10 to 1, but recently this ratio has become 1 to

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1, which confirms the etiology of smoking in the pathogenesis of this tumor. Radiation exposure is another etiological factor for this tumor. The most common salivary gland tumor is multifocal, or bilateral. The percentage of masses is bilateral. 25% of them occur simultaneously and 75% have different occurrences. On microscopic examination of this tumor, it is composed of variable ratios of lymphoid stroma and epithelium, which are located around the cystic spaces and are in the form of granolaraosinophilia. Malignant changes in this tumor are very rare [13, 14].

Imaging findings

In MR images, these tumors are usually in the form of a mass with defined boundaries or inhomogeneous lobules, which have a weak to moderate signal in T1 images and a high signal in T2 images. Wartin tumor may be indistinguishable from parotid gland cysts [2, 5].

3.3.3. Oncocytoma

Oncocytic tumors are relatively rare (about 1% of parotid tumors). The main salivary glands are their most common sites, occurring about 86% in the parotid gland, 11% in the submandibular, and 5% in cervical lymph nodes. They do not tend to a particular gender. Most patients complain of a painless unilateral mass. These tumors are rare in patients under 5 years of age and are most common in the 7-9 decade. Exposure to radiation is evident in 20% of patients. Oncocytoma can be multifocal or bilateral, accounting for about 7% of cases. Bilateral diffuse parotid involvement is very rare. It arises from the proliferation of oncocytes and these cells are rich in mitochondria [20, 21].

Imaging findings

Both T1 and T2 images on MRI have a weak signal due to the lack of tumor secretory components [2, 16].

3.3.4. Hemangiomas:

The most common neoplasm originates in the soft tissue of the salivary glands, accounting for 50% of cases and 85% in the parotid gland. Parotid hemangiomas account for 1.5% of all salivary gland tumors. But the most common neoplasm of the salivary glands is in children. Involvement of the submandibular glands is rare. Hemangiomas are tufts of extra blood vessels that commonly occur in capillaries or cavernous vessels (large vessels with smooth endothelial cells). These lesions are usually discovered shortly after birth and are unilateral and soft to the touch, most patients are not older than 16 years. Hemangiomas are tufts of extra blood vessels that commonly occur in women and are more common in women than men. Most of these tumors regress spontaneously [8, 17].

Imaging findings

On MRI, most of them have low to moderate inhomogeneous signal in T1 images and high signal in T2 images (Figure 4). The high signal areas in T1 and T2 are due to previous hemorrhage and low vascular flow, and if the blood flow is high, they are depicted as signal void areas. Because of the risk of tumor bleeding during surgery, more accurate methods such as

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digital subtraction MR angiography are suggested. This method is able to assess the vascularity of the tumor and estimate the risk of intraoperative bleeding. Unlike clinical examinations and simple MRI, the procedure is highly safe, accurate, and non-invasive, and reduces the risk of intraoperative bleeding [18, 19].

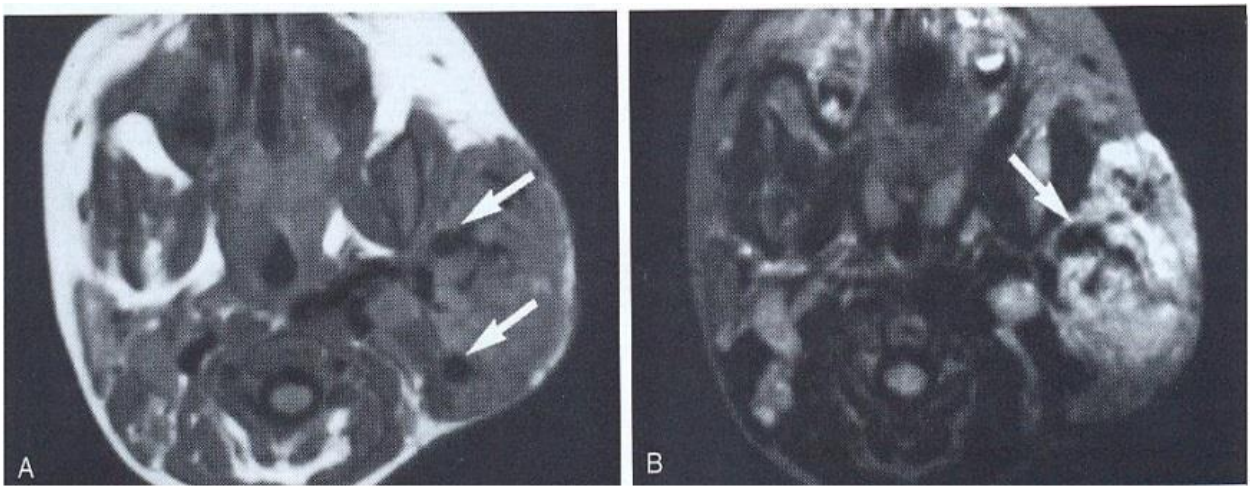

Figure 4: MRI view of hemangioma (B, A). Figure A shows T1 and B shows T2 in the axial section of a soft tissue mass in the left parotid. A weak signal is observed in T1 and a high signal in T2. Vascular streaks are seen inside the lesion (arrows) [32].

3.3.5. Lipoma

Lipoma is rare in the salivary glands. About 1.5% of all parotid tumors are present and usually occur in women. In the clinical picture, they appear as painless swelling with slow growth. Sometimes they may be in the form of infiltration of adipose tissue until it is a real mass. Histopathology shows a nodule with a capsule that is composed of mature adipose tissue and puts pressure on the parenchyma of the salivary glands [8].

Imaging findings

MRI has a high signal in T1 images and a moderate signal in T2, which can be heterogeneous. An important diagnostic point is that when the lipomatous mass has a general heterogeneous matrix, it may be a sign of a liposarcoma [2].

3.4. Malignant tumors

3.4.1. Mucoepidermoid carcinoma

Mucoepidermoid carcinoma has an annual prevalence of 1 in 100,000, accounting for 15.5-2.8% of salivary gland tumors and 12-29% of malignant salivary gland tumors. Mucoepidermoid Carcinoma is the most common malignant tumor of the salivary glands. About 56-53% occurs in the main salivary glands. Of these, 80-95% are in the parotid gland, 8-15% in the submandibular gland and 2-4% in the sublingual gland. If the salivary glands are involved, the most common site is the palate, but a significant number also occur in the retromolar region, the floor of the

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mouth, the buccal mucosa, the lips, and the tongue. This tumor can initially affect the mandible or maxillary trunk. In fact, mucoepidermoid carcinoma is the most common central tumor of salivary gland origin. Its highest prevalence is in 35-35 years old. Although it can occur at any age. Mucoepidermoid carcinoma is the most common malignant tumor in children and adults under 20 years of age and is slightly more common in women than men. About 60% of the infected are women. The most common cause was radiation. It has also been reported to occur simultaneously with myasthenia gravis. Clinically, they are usually slow-growing masses that are usually hard to the touch and indistinguishable from pleomorphic adenomas. Pain is uncommon, but if present, it is usually associated with tumors with a high degree of malignancy. On microscopic examination, the tumor contains different proportions of squamous cells, goblet mucin-secreting cells, and cells of intermediate type. This tumor is graded according to the predominance of the constituent cells. High-grade tumors contain mostly squamous and intermediate cells and are more likely to infiltrate the lung parenchyma. Imaging findings of these tumors depend on the degree of tumor malignancy [15, 22, 24, 25, 38].

Imaging findings

On MR images, these tumors have a signal similar to that of a pleomorphic adenoma. In MR images, it has a low to moderate signal in phase T1 and low in T2 [1, 2, 4, 5].

3.4.2. Adenoid cystic carcinoma:

Adenoid cystic carcinoma develops over a wide age range from the first decade to the ninth decade. The female-to-male ratio is 3 to 2. It is usually a slow-growing, highly invasive tumor that tends to spread through the nerves. Tumor retrograde spread to the base of the skull occurs through the facial or mandibular nerve. Patients usually have pain. It constitutes 4-8% of salivary gland tumors. 6-2% of parotid tumors, 12% of submandibular gland tumors and 15% of sublingual gland tumors, 30% of subarachnoid tumors and 50% of lacrimal gland tumors are adenoid cystic carcinoma. Like other malignant tumors, it tends to metastasize, and in one case, multiple skin metastases have been reported that are very rare [15, 27].

Imaging findings

Imaging findings of this tumor based on the tumor differentiation rating may be benign or malignant. Parotid tumors are usually benign and have definite limits, while submucosal salivary gland tumors usually have indefinite spreads. MR images are more sensitive than CT scans in showing small degrees of tumor neuronal invasion. In contrast-enhanced MR images, increased

nerve contrast is often seen even at a slight nerve enlargement. MR images are also very useful in showing postoperative recurrence [2, 4, 5] (Figure 5).

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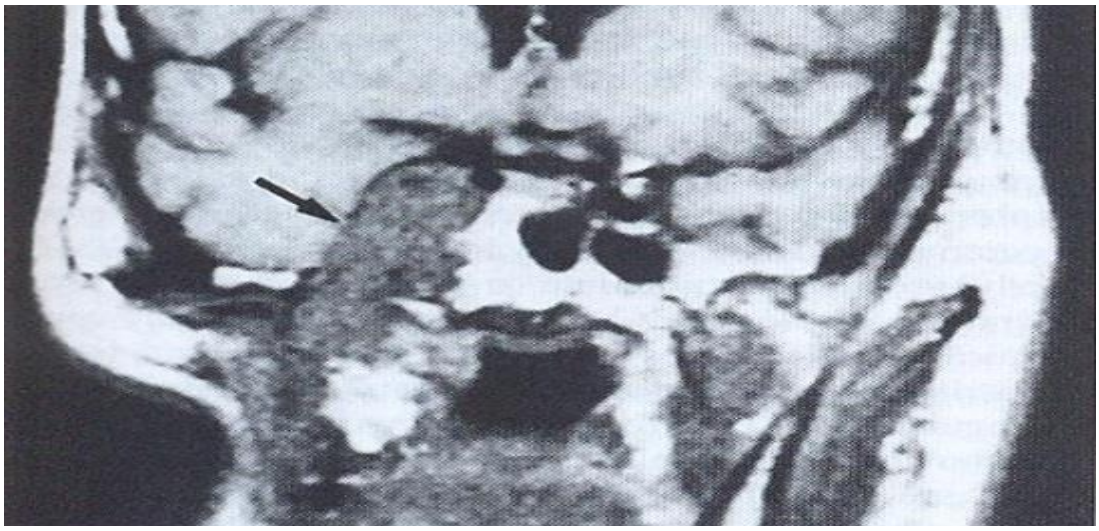

Figure 5: T1 image of the coronary section of adenoid cystic carcinoma. Tumor spread from the oval hole into the cavernous sinus is evident.

3.4.3. Acinic cell carcinoma

Acinic cell carcinoma (ACC) is a low-grade malignant neoplasm of salivary glands. After Mucoepidermoid Carcinoma and adenoid cystic carcinoma, the most common malignant tumor of salivary glands is the ACC, which consist 17% of primary salivary gland malignancies. The parotid gland is the most common site of involvement and accounts for about 50% of cases. Submandibular gland and the palate area each contains about 15% of the adenocarcinoma. It usually occurs in the four to eight decades with an average age of 58 years and has a slight tendency for women. Most are asymptomatic swellings, but about 25% of cases of paresthesia and pain are reported in the tumor area. Metastasis to different areas including the skin, brain and lungs can occur. A case of myocardial metastasis has also been reported [26, 27].

Imaging findings

Imaging findings of ACC vary according to the degree of malignancy. The findings of this tumor are usually similar to other malignant tumors and its manifestations are not specific [2].

3.4.4. Malignant oncocytoma:

Malignant oncocytoma is a malignant type of oncocytoma. It occurs mostly in the parotid gland and in about 10% of cases in the submandibular gland. So far, 50% of cases have been reported. The average age is 60 years old. The ratio of male to female is 2 to 1. The most common clinical finding is slow-growing swelling, often accompanied by pain and facial paralysis. Imaging findings are similar to other malignant and nonspecific tumors. And T2 have a weak signal [2].

3.4.5. Lymphoma:

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Primary salivary gland lymphoma is rare. The parotid gland was involved in 80% and the submandibular gland in 20% of cases. These lymphomas are classified as MALT (mucosa associated lymphoid tissue). Their average age is 66 years old. And patients often complain of swelling and pain in the body. Autoimmune diseases are associated in 21% of patients. Its diagnosis is based on showing lymphocyte colony and its morphology. These lymphocytes are usually group B, with plasma cell differentiation and low grade. The prognosis is usually very good. In imaging, there is a diffuse nodular view in the gland. Lymphoma can also secondarily affect the parotid gland, which is usually a high-grade diffuse lymphoma with a poor prognosis [6, 39]. Imaging usually shows multiple nodules, with definite boundaries inside the gland. These nodules are usually homogeneous and show an increase in contrast shortly after injection of the contrast agent. On MRI, there is a moderate signal in all sections, and on ultrasound, lymph nodes in the parotid region can be seen [2, 5, 19].

3.5. Discussion and conclusion

Routine precontrast and postcontrast MR imaging is essential for initial diagnosis and accurate localization and locoregional extension of salivary gland tumors. Advanced MR imaging, such as diffusion and dynamic contrast MR imaging, provides additional tissue characterization when combined with standard MR imaging. Various imaging techniques can be used to examine and diagnose salivary gland lesions. These techniques include routine radiography, ultrasound, CT scan, MRI, and nuclear medicine. Depending on the nature of the lesion, a special imaging technique is used. Conventional radiographs do not play much role, but are used to examine stones and bone lesions from salivary gland lesions. Sialography is the method of choice in examining the salivary gland ducts. CT scan is the method of choice for examining inflammatory lesions of the salivary glands. Ultrasound and MRI are used for salivary gland tumors, and nuclear medicine is used to evaluate salivary gland function in autoimmune diseases.

Conflicts of interest

None to declare.

Author contributions

All the coauthors critically revised the manuscript.

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