PET/CT of Salivary Gland Tumors

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1 Common Malignant Tumors of the Salivary Gland

Salivary glands are exocrine glands that produce and secrete saliva. They include three paired major glands (parotid gland, submandibular gland, and sublingual gland) and minor salivary glands that widely exist in the entire respiratory and digestive tract. Many minor salivary gland tumors are located on the hard palate. The global annual incidence of salivary gland tumors is 0.4/100,000–13.5/100,000, and that of malignant tumors is 0.4/100,000–2.6/100,000, accounting for 0.7%–1.6% of all malignant tumors and 2.3%–10.4% of head and neck malignant tumors. Most of the salivary gland tumors are benign, but about 20% of parotid gland tumors are malignant; the incidence of submandibular gland and minor salivary gland malignant tumors is about 50% and 80%, respectively. Nearly 80% of salivary gland tumors occur in the parotid gland, most commonly in the superficial lobe, less than 1% in the sublingual gland, and 9%–23% in the minor salivary glands. The proportion of malignant tumors is different in different parts: 20%–30%, 45%–60%, and 70%–85% in the parotid gland, submandibular gland, and sublingual gland, respectively; 80%–90% of salivary gland tumors in the tongue, floor of the mouth, and retromolar area are malignant. Salivary gland tumors are slightly more common in women, with the peak age of onset ranging from 50 to 70 years, but the peak age of pleomorphic adenoma, mucoepidermoid carcinoma, and acinus cell carcinoma is 20–40 years. Among all salivary gland tumors, pleomorphic adenoma is the most common, accounting for about 50%, usually occurring in young adults aged 30–50 years without significant gender difference. The second most common is Warthin tumor (adenolymphoma), which is common in men over 50 years old; it is usually multiplex or bilateral, mostly located in the inferior superficial lobe of the parotid gland; almost all of Warthin tumors come from the parotid gland or peripheral lymph nodes. Others such as hemangioma, lymphangioma, and lipoma are rare. The most common malignant tumor is mucoepidermoid carcinoma.

The cause of salivary gland tumors is currently unclear. Many studies have shown that ionizing radiation is one of the main risk factors for salivary gland tumors. Radiation from radiotherapy, especially head and neck radiation, significantly increases the risk of salivary gland cancer. When ^{131}I is used to treat thyroid disease, radioiodine is also concentrated in the salivary gland, which may increase the risk of salivary gland tumor. It has been recognized that smoking is closely related to Warthin tumor. Clinically, it is suggested that all current smokers should quit smoking and those who have ever smoked should continue to quit smoking. Furthermore, it may also be related to vitamin A deficiency and exposure to smoke, dust, and chemicals.

The persistent pain in patients clinically diagnosed with salivary gland cancer often indicates a poor prognosis. Compared with patients without pain, their 5-year survival rate drops from 68% to 35%. The overall 10-year survival rate of patients with salivary gland malignant tumors is close to 50%.

1.1 Mucoepidermoid Carcinoma

1.1.1 Clinical Overview

Mucoepidermoid carcinoma of the parotid gland is the most common malignant salivary gland tumor. It is mainly composed of mucous cells, epidermoid cells, and intermediate cells. Based on the ratio and differentiation of the three kinds of cells, they can be divided into three types: well differentiated, moderately differentiated, and poorly differentiated. The parotid gland is the most common site (about 45%), followed by the submandibular gland (about 7%). The minor salivary glands are more common in the palate and buccal mucosa. The disease can occur at any age, mostly in people

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aged 30–50 years old, with more females than males, while malignant tumors of the parotid gland in children are usually of this type. Clinically, the well-differentiated type is usually a slow-growing painless mass with medium texture and clear edge; the poorly differentiated type is characterized by fast growth, hard texture, unclear boundary, poor mobility, and adhesion or even fixation with surrounding tissues, it may invade the facial nerve to cause facial paralysis, and it is easy to relapse and metastasize, and the prognosis is poor.

1.1.2 PET/CT Diagnostic Points

Well-differentiated mucoepidermoid carcinoma has the characteristics of general benign tumor, which is similar to pleomorphic adenoma, while poorly differentiated mucoepidermoid carcinoma has the characteristics of general malignant tumor, which is difficult to differentiate from other salivary gland malignant tumors. PET/CT plain scan shows soft tissue density masses. The well-differentiated type often has clear edge and may have cystic degeneration or bleeding. The poorly differentiated type often has unclear edge, is prone to cystic degeneration and bleeding, and is often accompanied by peripheral lymph node metastasis; ^{18}F-FDG uptake shows mild to moderate increase, and it may significantly increase and it is uniform or inhomogeneous.

1.1.3 Typical Cases

A 60-year-old female patient with right facial paralysis gradually aggravated for 1 year and right hemifacial pain for 2 months. She was a case of mucoepidermoid carcinoma of the right parotid gland involving the peripheral nerve wall of V, VI, and VII cranial nerves (Fig. 19.1).

1.1.4 Differential Diagnosis

1. Pleomorphic adenoma: Patients often have a long history of salivary gland masses. The mass develops slowly, with no obvious symptoms or only mild pain. Generally, it is a round or quasi-round mass with clear edge, uniform density, and clear boundary. When the tumor is large, it can push the surrounding tissues.
2. Warthin tumor of the parotid gland: It is more common in middle-aged and elderly men. The lesions are mostly located in the posterior lower pole of the parotid gland, bilateral or multifocal. A history of tumor growth is one of the prominent clinical features of Warthin tumor. A cold or upper respiratory tract infection may induce tumor enlargement.
3. Lymphoma: It is mostly characterized by abnormally high metabolism of ^{18}F-FDG, with soft texture, relatively uniform density, and usually systemic involvement (Fig. 19.2).

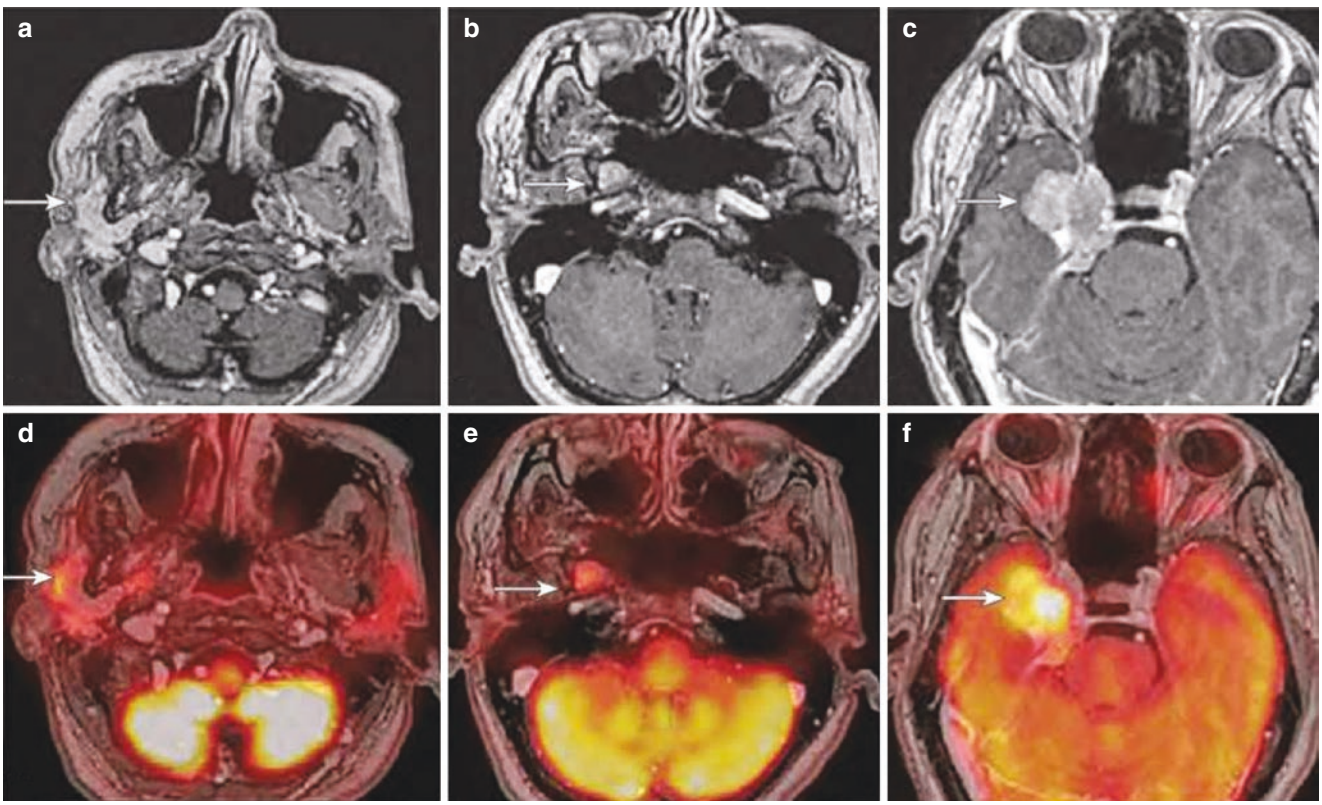


Fig. 19.1 ^{18}F-FDG PET/MR images of mucoepidermoid carcinoma. (**a–c**) Continuous transaxial MR images showed the lesion (arrow) was diffuse and has uniform enhancement, extending from the right parotid gland along the thickened mandibular nerve upward to the right middle cranial fossa (MCF) and anterior cistern. (**d–f**) Continuous transaxial fusion PET/MR images showed that FDG uptake increased in the nodular lesion with clear boundary of the right parotid gland, and continuous curvilinear FDG uptake was seen along the thickened mandibular nerve and extended upward to the mass lesion of MCF

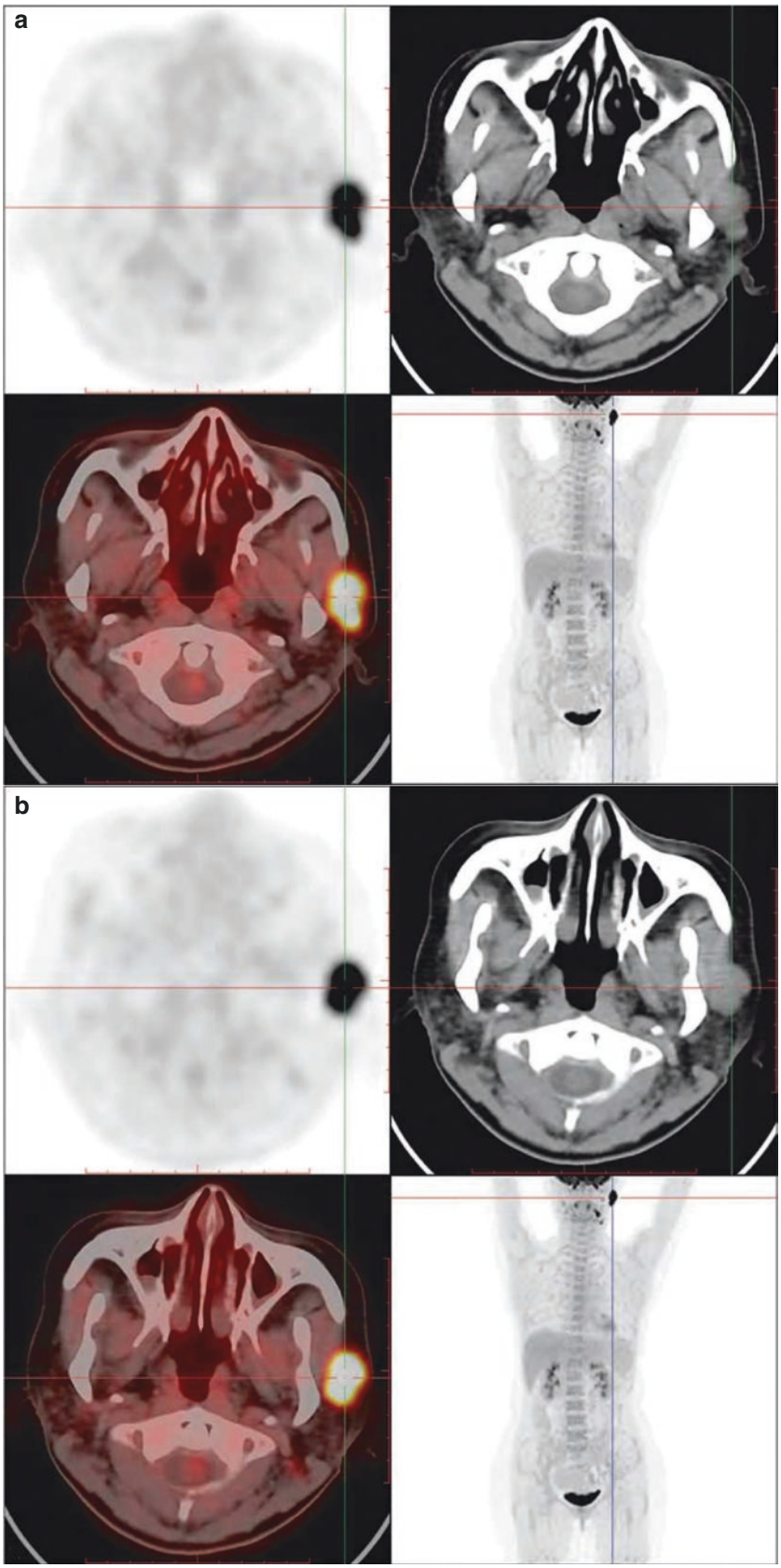


Fig. 19.2 ^{18}F-FDG PET/CT images of left parotid lymphoma. A 55-year-old female patient went to a doctor because a left preauricular mass was found 1 month ago. (**a**) PET/CT image of hypermetabolic nodule in the left parotid gland. (**b**) PET/CT image of hypermetabolic nodule in the left parotid gland. (**c**) PET/CT image of hypermetabolic nodule in the left parotid gland. PET/CT showed that there was a soft tissue mass in the left parotid gland area, which was not clearly separated from the surrounding tissues. Its size was 1.9 cm × 2.5 cm, density was relatively uniform, and shape was irregular, and the FDG uptake was intense (SUVmax 25.8). There were multiple enlarged lymph nodes in bilateral cervical Ib area and II area and left cervical III area. The larger one was about 0.8 cm in short diameter, and the radioactive distribution was concentrated in different degrees, and the SUVmax was about 23.4. Postoperative pathology: (left parotid gland) invasive B-cell lymphoma

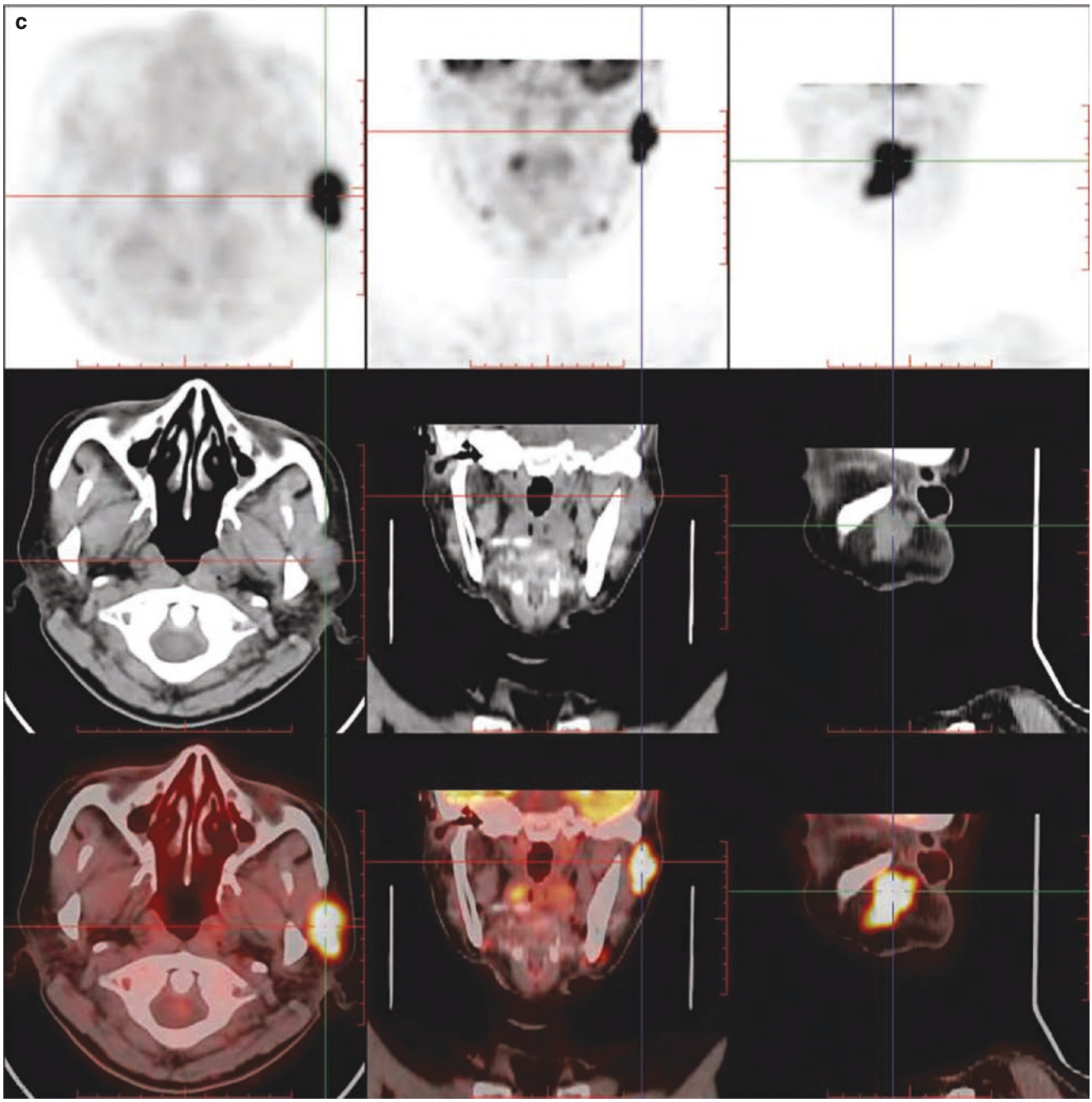


Fig. 19.2 (continued)

4. Adenoid cystic carcinoma: It is more common in the elderly. The tumor grows rapidly, which is fixed, is hard, and often has pain and facial paralysis.
5. Acinar cell carcinoma: Low-grade malignant tumor, similar to benign tumor.

1.1.5 Summary

Salivary gland mucoepidermoid carcinoma is more likely to occur in women or infants aged 30 to 50. FDG PET/CT images are characterized by salivary gland space-occupying lesions with signs of malignant tumor and increased FDG uptake.

1.2 Adenoid Cystic Carcinoma

1.2.1 Clinical Overview

Adenoid cystic carcinoma is a common malignant tumor of the salivary gland epithelium, which accounts for more than one-third of the malignant salivary gland tumors. It mainly occurs in middle-aged people (aged 35–45 years old). It may occur in the parotid gland, especially in the deep part or isthmus of the parotid gland, but it is more common in the submandibular gland, sublingual gland, and other minor salivary glands. The cause is unknown. It is believed that it is related

to environmental factors such as chronic injury, inflammatory stimulation, and radiation exposure, as well as internal spirit, immunity, and heredity.

The tumor does not have a complete envelope and originates from the epithelial cells of the salivary gland duct. There are often multiple fluid areas of different sizes within the tumor, and there may be fibrous septum. In the late stage, the tumor grows rapidly in various forms, and they are usually hard, fixed, and with invasive growth. It is low-grade malignancy in early stage, the tumor grows slowly, and it is not easy to differentiate from benign tumors surrounding tissues. It has the characteristics of infiltration and diffusion along the nerve. When the nerve is involved, the pain is obvious. The degree of pain is not directly proportional to the size and growth rate of the tumor. It is more common in middle-aged and elderly people. The early-stage patients have pain or numbness, which is often ignored and delayed in diagnosis, or there are masses in minor salivary gland, which are not taken seriously because of slower early growth. When the tumor is large, the local skin bulges, the mass is fixed, the texture is hard, and the surrounding and cervical lymph nodes may be enlarged. Adenoid cystic carcinoma of the parotid gland often invades the facial nerve, resulting in facial paralysis.

1.2.2 PET/CT Diagnostic Points

When the tumor is small, PET/CT scan shows enlarged salivary gland on the affected side, with the internal localized masses mostly in the size of 2–4 cm. Some masses could completely occupy the whole salivary gland and the shape is irregular, but a few of them could be quasi-circular, with unclear edge and inhomogeneous density. Most are patchy or large patchy low-density areas without incomplete shape in the masses. When the tumor is large, the cystic necrosis area may appear, the cyst wall has irregular shape, the thickness is different, and the edge is lobulated. It often invades superficial and deep lobes. ^{18}F-FDG uptake is often significantly increased, but it may be inhomogeneously increased. In addition, enhanced CT of the salivary glands, or CTS examination, can show signs of compression and displacement to the main duct and branch duct, interruption of erosion, and overflow of contrast medium, which can assist in the differentiation of benign and malignant tumors. Enlarged lymph nodes can be seen around the tumor, and necrotic low-density areas can also be seen in them. ^{18}F-FDG uptake shows a circular increase. Some tumors can destroy the ascending ramus of the mandible, resulting in the destruction and defect of the mandibular bone. Deep tumors can spread to the parapharynx, bulge the pharyngeal wall, and narrow the pharyngeal cavity; sometimes, it is the first symptom of patients, and it is easy to be mistaken for other tumors. At this time, we should pay attention to the position of the carotid sheath. Salivary gland tumors tend to push the carotid sheath backward, while neurogenic tumors in the carotid sheath usually compress the large blood vessels in the neck to move forward and medially.

1.2.3 Typical Cases

A 42-year-old male patient presented with swelling and pain in the right maxillofacial region for more than 2 months. Pathology: (right parotid gland) adenoid cystic carcinoma (Fig. 19.3)

1.2.4 Differential Diagnosis

The differential diagnosis of benign and malignant tumors of the parotid gland is mainly considered from three aspects: the edge, the density of the mass, and the presence or absence of enlarged lymph nodes. Whether the tumor boundary is clear is the key to differentiate between benign and malignant tumors. If the tumor is irregular and shows infiltrative growth and it is significantly enhanced after enhancement and multiple enlarged lymph nodes can be seen at the same time, it is the typical sign of malignant tumor. However, low-grade malignant tumors can also have a clear boundary, and some benign pleomorphic adenomas can also be lobulated or nodular, which should be paid attention to in the differentiation and should be comprehensively analyzed in combination with other clinical manifestations. Facial nerve involvement is also an important clinical symptom in differential diagnosis. Facial nerve paralysis can occur in 12%–14% of malignant tumors of the parotid gland, while facial nerve involvement in benign tumors is rare.

According to the image morphology, the masses in the parotid gland can be divided into three types: ① round or oval tumors, with clear boundary and envelope, more common in benign tumors and inflammatory lesions; ② lobulated tumors with clear boundary and envelope, mainly seen in benign tumors with local erosion and low-grade malignant tumors with slow growth; and ③ invasive tumors, with irregular shape, unclear boundary, and diffuse growth, mostly malignant.

Adenoid cystic carcinoma is a common epithelial malignant tumor of the salivary glands. It is more common in the elderly. The mass grows rapidly, which is fixed and hard, often with pain and facial paralysis. When the tumor is large, the signs are obviously easier to diagnose. When the tumor is small, it should be differentiated from the benign tumor of the salivary gland. It should be observed from the mass location, shape, density, adjacent bones, blood vessels, and peripheral lymph nodes. Benign tumors are characterized by regular shape, uniform density, clear boundary, vascular migration, and no lymph node enlargement, while adenoid cystic carcinoma is characterized by irregular shape, inhomogeneous density, blurry boundary, wrapping or eroding blood vessels, and lymph node enlargement.

1.2.5 Summary

The imaging findings of adenoid cystic carcinoma are diverse, and FDG uptake is increased obviously in the tumor. The important clinical features are neurotropic growth and early hematogenous metastasis.

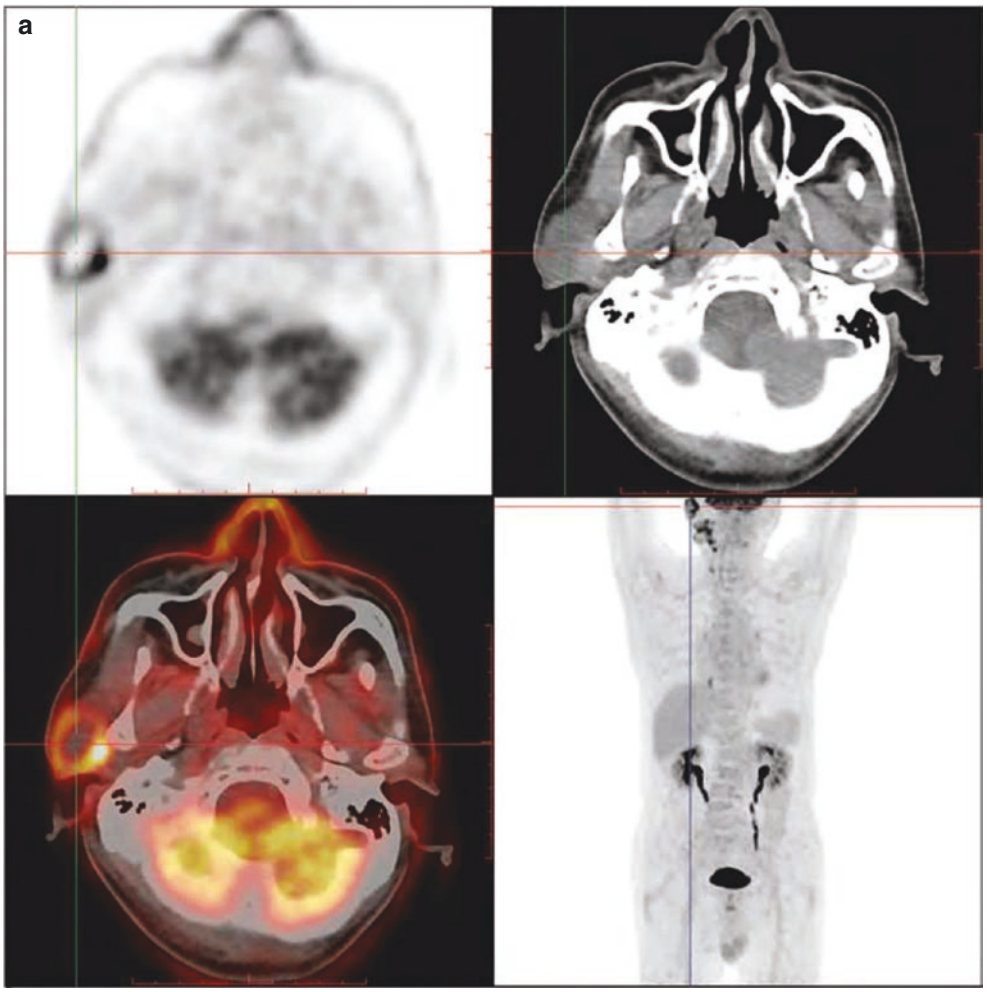


Fig. 19.3 ^{18}F-FDG PET/CT images of adenoid cystic carcinoma of the right parotid gland. (**a**) PET/CT image of hypermetabolic nodules in the right parotid gland; (**b**) PET/CT image of hypermetabolic nodules in the right parotid gland. PET/CT showed that the right parotid gland was enlarged with a cystic and solid nodule (about 3.5 cm × 1.9 cm in size). The nodule was slightly lobulated, irregular in shape with unclear margin, and inhomogeneous density, and it showed intense FDG uptake (SUVmax 14.7). There was necrosis area in the center of the nodule without FDG uptake. Multiple enlarged lymph nodes were found on the right side of the neck, the larger one was about 0.8 cm in short diameter, and there was increased FDG uptake (SUVmax 5.1)

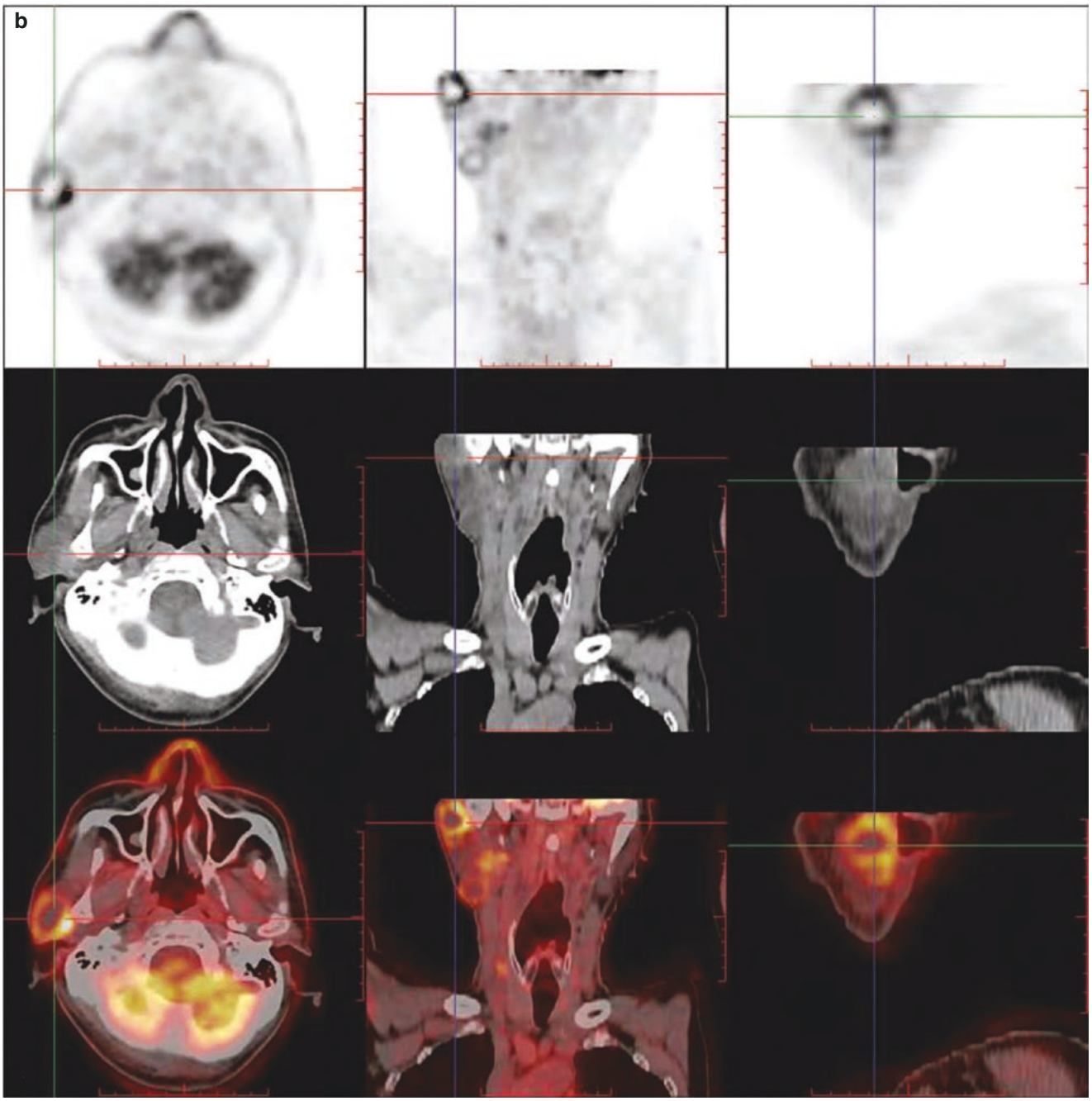


Fig. 19.3 (continued)

1.3 Malignant Mixed Tumor

1.3.1 Clinical Overview

Malignant mixed tumors account for 2%–5% of mixed tumors. Most of them originate from benign transformation, and a few are primary. Patients often have a history of mass in the salivary glands for many years. The patient will go to a doctor due to the mass growing rapidly or pain or facial paralysis. If the tumor occurs in the deep lobe of the parotid gland, the mass tends to protrude into the pharynx and soft palate, causing neck and ear pain, hearing loss, dysphagia, or dyspnea. When the tumor invades the masticatory muscles, the mandible, and the temporomandibular joint, it is difficult to open the mouth. The salivary gland is enlarged, and its internal mass has unclear boundary, with poor activity, tenderness, and hard texture, and some enlarged lymph nodes are palpable.

1.3.2 PET/CT Diagnostic Points

PET/CT scan shows soft tissue mass shadows with unclear boundary, irregular contour, and inhomogeneous density in the salivary gland area. The mass is generally large in size and can involve the deep and superficial parotid gland. Necrosis and liquefaction area can be seen in some tumors with low density. ^{18}F-FDG uptake increases inhomogeneously or increases in a circular shape. When the tumor invades the adjacent muscle, the fat space between the tumor and muscle disappears, the muscle edge becomes blurred, and the density may increase. When the tumor invades the mandible and temporomandibular joint, bone destruction and defect can be seen. It is often accompanied by enlarged lymph nodes around the parotid gland or neck.

1.3.3 Differential Diagnosis

Malignant mixed tumors are mostly caused by malignant transformation of benign mixed tumors. The tumor grows rapidly with pain and adjacent enlarged lymph nodes. Imaging findings show masses in the salivary glands, mostly irregular in shape and inhomogeneous in density, and the boundary between them and the normal salivary glands is not clear. It should be differentiated from benign mixed tumor and chronic abscess of the salivary gland.

1. Benign mixed tumor: Patients with benign mixed tumor often have a long history of mass in the salivary gland area. The mass of benign mixed tumor develops slowly, and the symptoms are not obvious or there is only slight pain; on PET/CT scan, it shows a round or quasi-round mass with clear edge, uniform density, and clear boundary; and large tumor can push and press the surrounding tissues. The mass of malignant mixed tumor grows fast, with obvious pain; the imaging findings show a mass with inhomogeneous density and irregular edge; and sometimes large patchy low-density necrosis in the mass often invades surrounding tissues, with lymph node enlargement.
2. Salivary gland abscess: It is caused by inflammation of the salivary gland. The patients often have a history of painful swelling of the salivary gland in the affected area. The local skin is red with high skin temperature and tenderness. Imaging findings show that the salivary gland is enlarged and there is hypodensity and there is irregular or circular necrotic area in the gland. ^{18}F-FDG uptake is annularly increased in the lesion, with extensive edema surrounding.

1.4 Salivary Duct Carcinoma

1.4.1 Clinical Overview

Salivary duct carcinoma (SDC) is a rare, highly malignant tumor that occurs from the epithelium of the salivary duct. It is classified as an independent tumor in the new WHO classification of salivary gland tumors. This tumor is highly malignant, with significantly more males than females, with a male-to-female ratio of 3:1, and the onset peak age is between 51 and 70 years old. The parotid gland is the most common site, followed by the submandibular gland, and minor salivary glands are rare. The clinical manifestations include that it has strong infiltration; it has invaded the surrounding tissues during early stage, with symptoms of neural paralysis; it is easy to metastasize through lymph and blood circulation; it has a high rate of cervical lymph node metastasis; it often involves in each group of deep cervical lymph nodes; it is prone to distant metastasis; and lung metastasis is the most common, followed by liver and bone metastasis. The tumor grows rapidly, the disease period is short, and most of them are in the advanced stage when they go to a doctor. Most patients have neurological symptoms. Patients with parotid gland tumor mostly have facial paralysis of varying degrees. Patients with submandibular gland tumor may have tongue numbness or tongue dyskinesia and often have local pain.

Its histopathological features are similar to those of breast ductal carcinoma, and the tissue is derived from the reserve cells of the excretory duct. Under the light microscope, the cancer cells are cubic or polygonal, with acidophilic cytoplasm, and may be accompanied by apocrine, with obvious cell atypia; the characteristic structures including papillary, cribriform, solid, and comedo exist alone or in combination, and tumor masses commonly infiltrate extensively around. Some scholars performed immunohistochemical analysis on it and found that S-100 antibody staining is negative and keratin and epithelial membrane antigen reaction is positive; in addition, other studies have confirmed that the tissue source of salivary duct carcinoma is the reserve cells of the salivary gland excretory duct through other special examinations. The treatment of salivary duct carcinoma is mainly surgery. Because of its strong invasion and easy metastasis through lymph and blood, extensive local resection is necessary. Facial nerve is not generally retained for tumors located in the parotid gland. Even if lymph node metastasis is not suspected clinically, cervical lymphatic dissection should be performed, which is supplemented by radiotherapy and chemotherapy to prevent distant metastasis.

1.4.2 PET/CT Diagnostic Points

Salivary duct carcinoma can occur in the gland or outside the gland. The tumors outside the gland are almost enlarged lymph nodes around the gland. Most of the tumors are characterized by diffuse growth of irregular masses with blurred edge and unclear contour and small adjacent fat or fascia space and mostly accompanied by abnormal hypermetabolism of ^{18}F-FDG. The rate of cervical lymph node metastasis is high, and it often involves the deep cervical lymph nodes in each group, with abnormal high metabolism of ^{18}F-FDG.

1.4.3 Typical Cases

Case 1: Male patient, 68 years old. Pathology: poorly differentiated carcinoma of the right parotid gland, which was consistent with salivary duct carcinoma (Fig. 19.4)

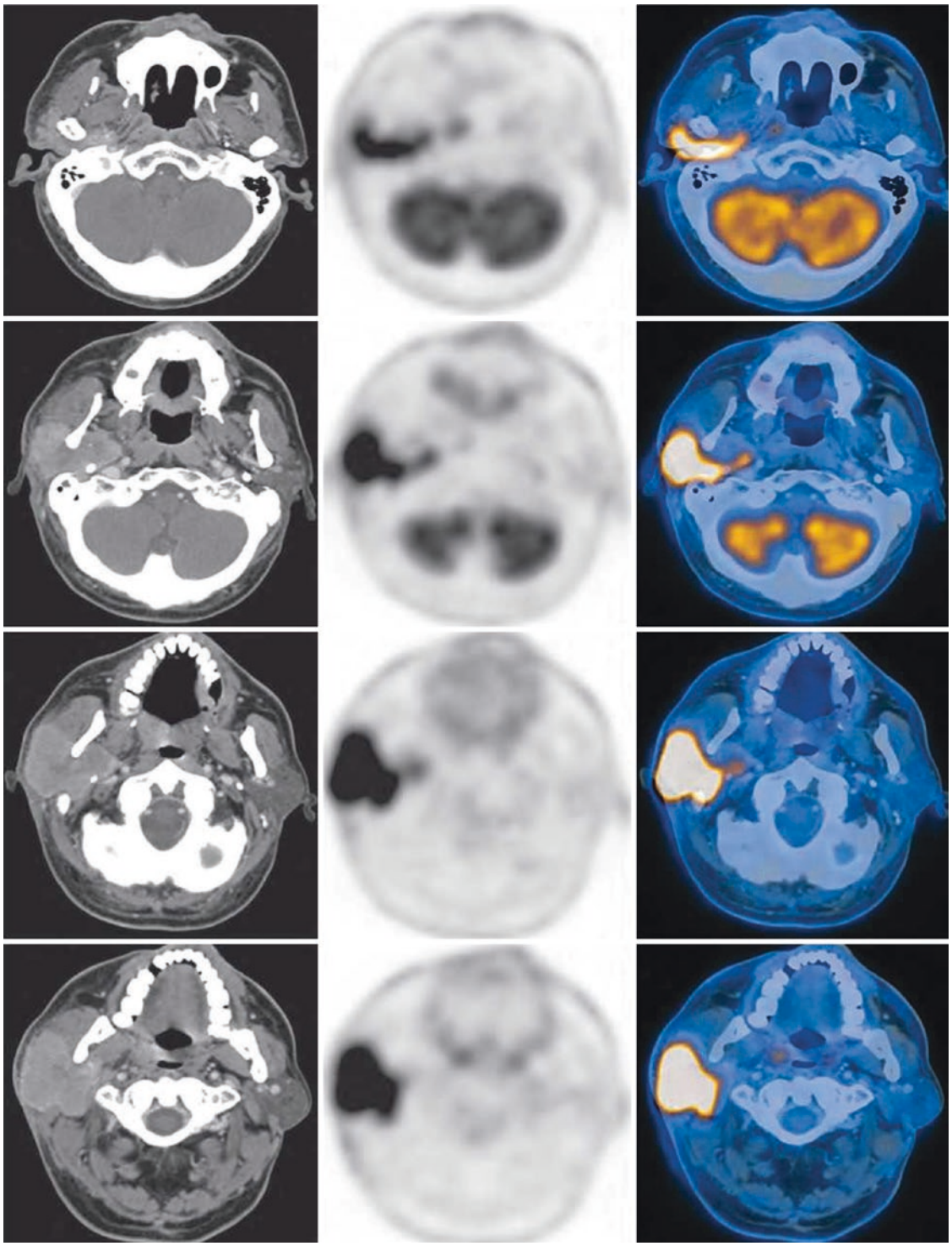


Fig. 19.4 ^{18}F-FDG PET/CT image of right salivary duct carcinoma. The lobulated soft tissue density mass of the right parotid gland showed intense FDG uptake. The SUV was about 17.7, and the largest layer was about 4.6 cm × 5.4 cm. There were low-density necrosis areas and small punctate calcifications with sparse radioactive distribution, and the enhanced scan showed obvious inhomogeneous enhancement. The lesions invaded the right parapharyngeal fat space, and the boundaries with the right masseter muscle, the right medial pterygoid muscle, and the right sternocleidomastoid muscle were not clear. It wrapped the right mandibular ramus and styloid process and pushed the blood vessels in the right carotid sheath area (This case was provided by Lin Xiaoping and Fan Wei from Sun Yat-sen University Cancer Center)

Fig. 19.4 (continued)

Case 2: Male patient, 65 years old. The left preauricular nodule has been found for more than 60 years, and the nodule has increased rapidly in the past 6 months. Pathology: (left parotid gland) salivary duct carcinoma with interstitial collagenization, calcification and massive necrosis, and metastasis or infiltration into the (left cervical) fiber and adipose tissue (Fig. 19.5)

1.4.4 Differential Diagnosis

1. Inflammatory mass or parotid abscess: Chronic inflammation of the parotid gland can form local mass or show inhomogeneous density change, similar to tumor. The typical manifestation is that the parotid gland is generally enlarged and the density is increased, but the shape of the parotid gland is still maintained. If the inflammation involves soft tissue and the edge is blurred, it is difficult to differentiate (Fig. 19.6).
2. Salivary ductal carcinoma: It has the characteristics of most malignant tumors, and it is difficult to differentiate from other malignant tumors of the salivary gland. Its malignant degree is relatively high and metastasis occurs early.

1.4.5 Summary

It should be clear, firstly, whether it is derived from the submandibular gland and, secondly, whether it is the mass inside or outside the submandibular gland. If the plain scan shows there are masses in the submandibular gland and enlarged lymph nodes outside the gland and the FDG uptake is abnormally increased, it mostly is the malignant tumor.

1.5 Papillary Cystadenocarcinoma

1.5.1 Clinical Overview

Papillary cystadenocarcinoma is rare in salivary gland tumors, accounting for 5–7% of salivary gland epithelial tumors. It is often considered as a subtype of adenocarcinoma. Papillary cystadenocarcinoma originates from the salivary duct epithelium. Its pathological morphology resembles mixed tumors, which is round or nodular, mostly without envelope. The cystic cavity is common in the tumor section. The inner wall of the cavity is not smooth, and there may be some papillary processes or granules. The tumor cells vary in size and are columnar or cuboid and form various irregular adenoid structures. Many of the glandular cavities are significantly enlarged to form cysts. The cells are arranged disorderly, although they are arranged in a single layer or multiple layers, and the cancer cells are extremely proliferated, forming single or dendritic papillae, protruding into the cyst cavity. There is a small amount of fibrous tissue interstitium between cancer cells or in the papilla, often infiltrated by inflammatory cells, but no lymphoid tissue. Tumor envelope is incomplete, and sometimes tumor cells invade the internal or surrounding tissues. The growth rate of papillary cystadenocarcinoma varies. It can metastasize along blood and lymphatic channels and also invade nerves, but it is relatively rare.

Papillary cystadenocarcinoma is the most common in the parotid glands, followed by the minor salivary glands in the palate and submandibular glands. It may also occur in the

minor salivary glands in the buccal mucosa, floor of the mouth, tongue, and upper lip. The age of onset is 12–72 years old, most common in 30–50 years old, and the ratio of male to female is about 2:1.

The tumors resemble malignant mixed tumors. The common symptom is local painless masses, some of which are larger and nodular. The gland cavity is significantly enlarged to form a cystic shape, and hemorrhage and necrosis can occur, so cystic degeneration often occurs. The palpation part is soft, and bloody secretion can be drawn out by puncture. Generally, there is no obvious adhesion in the early stage and it can be moved.

1.5.2 PET/CT Diagnostic Points

On PET/CT scan without contrast agents, papillary cystadenocarcinoma can be seen as cystic and solid nodules with blurred edge and unclear outline, and the adjacent fat or fascia space is narrowed. ^{18}F-FDG shows a circular metabolic increase, and the circular shape is not obvious or metabolism is not high when the lesion is small.

1.5.3 Differential Diagnosis and Summary

How to differentiate papillary cystadenoma from papillary cystadenocarcinoma is the biggest challenge in histopathological diagnosis. It is often difficult to confirm whether it is

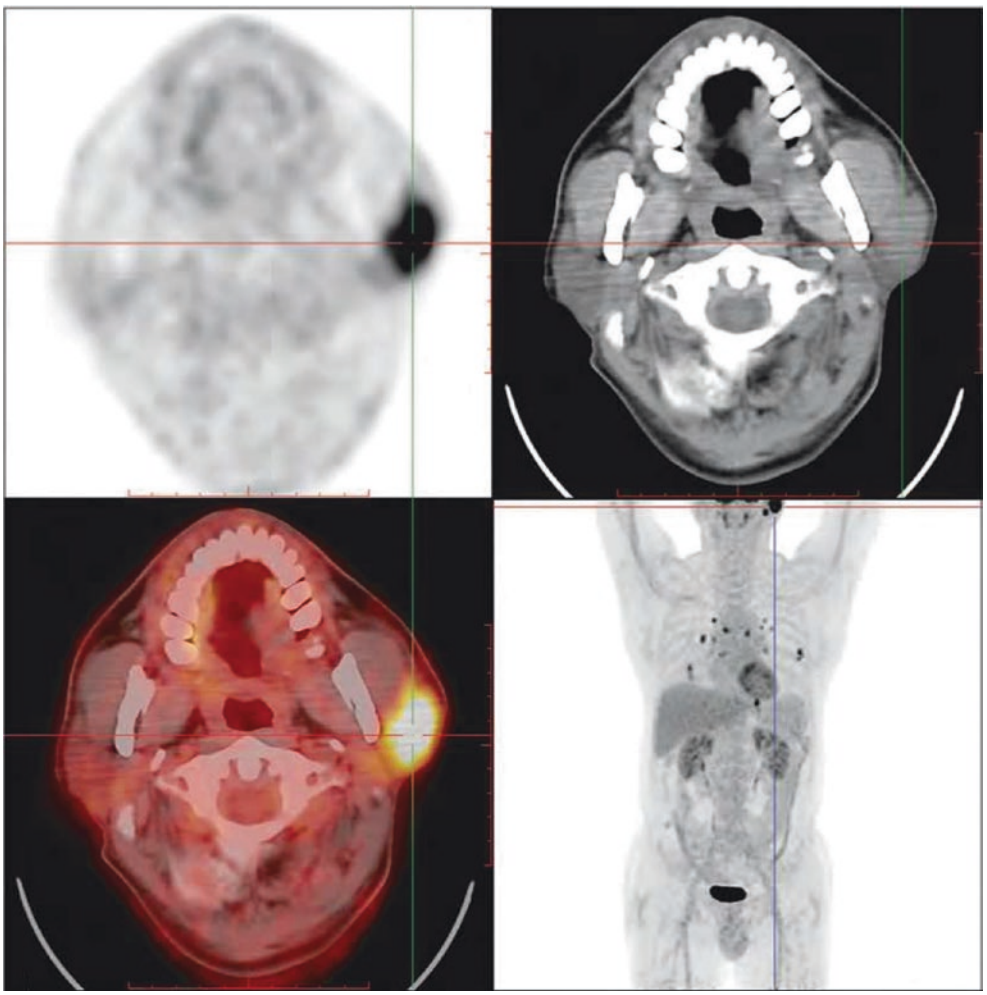


Fig. 19.5 ^{18}F-FDG PET/CT images of left salivary duct carcinoma. A round soft tissue mass was found in the left parotid gland area. Its internal density was inhomogeneous and the boundary was not clear. The size was about 3.8 cm × 2.5 cm. The radioactive distribution was abnormally concentrated, and the SUVmax was about 15.2

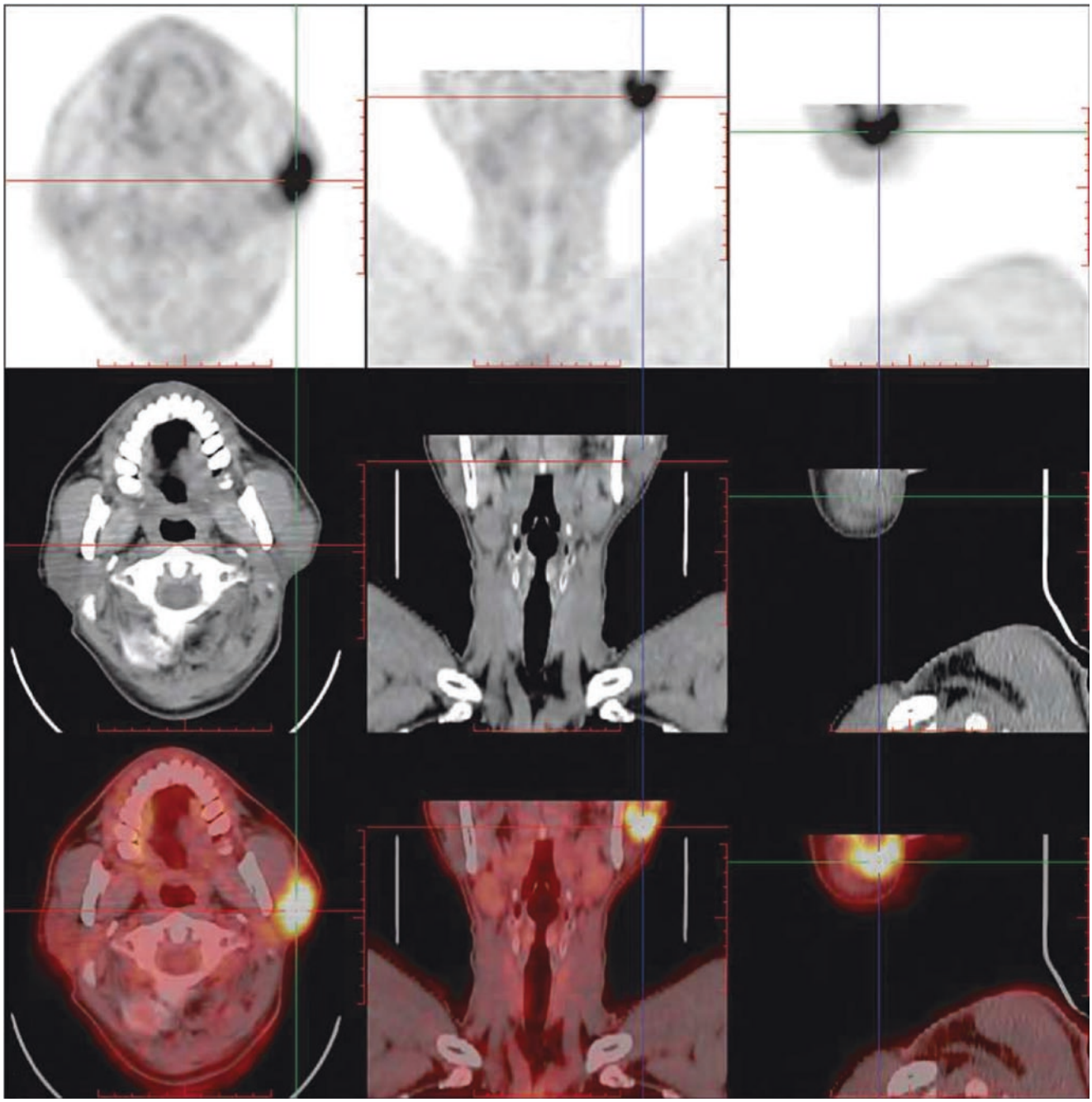


Fig. 19.5 (continued)

benign or malignant due to the similarity between the two in histopathology and cell morphology, especially in some cases of papillary cystadenoma with tumor cells invading the envelope and adjacent glands. However, the main determinant of malignancy is its extensive invasive growth and pleomorphism of cells and nuclei. Clinical symptoms should also be considered. If there are signs of spontaneous pain, recent growth acceleration, facial nerve palsy, etc., malignancy should be considered.

Papillary cystadenocarcinoma of the salivary gland has the characteristics of common malignant salivary gland tumors, so it is difficult to differentiate each other from imaging examination alone.

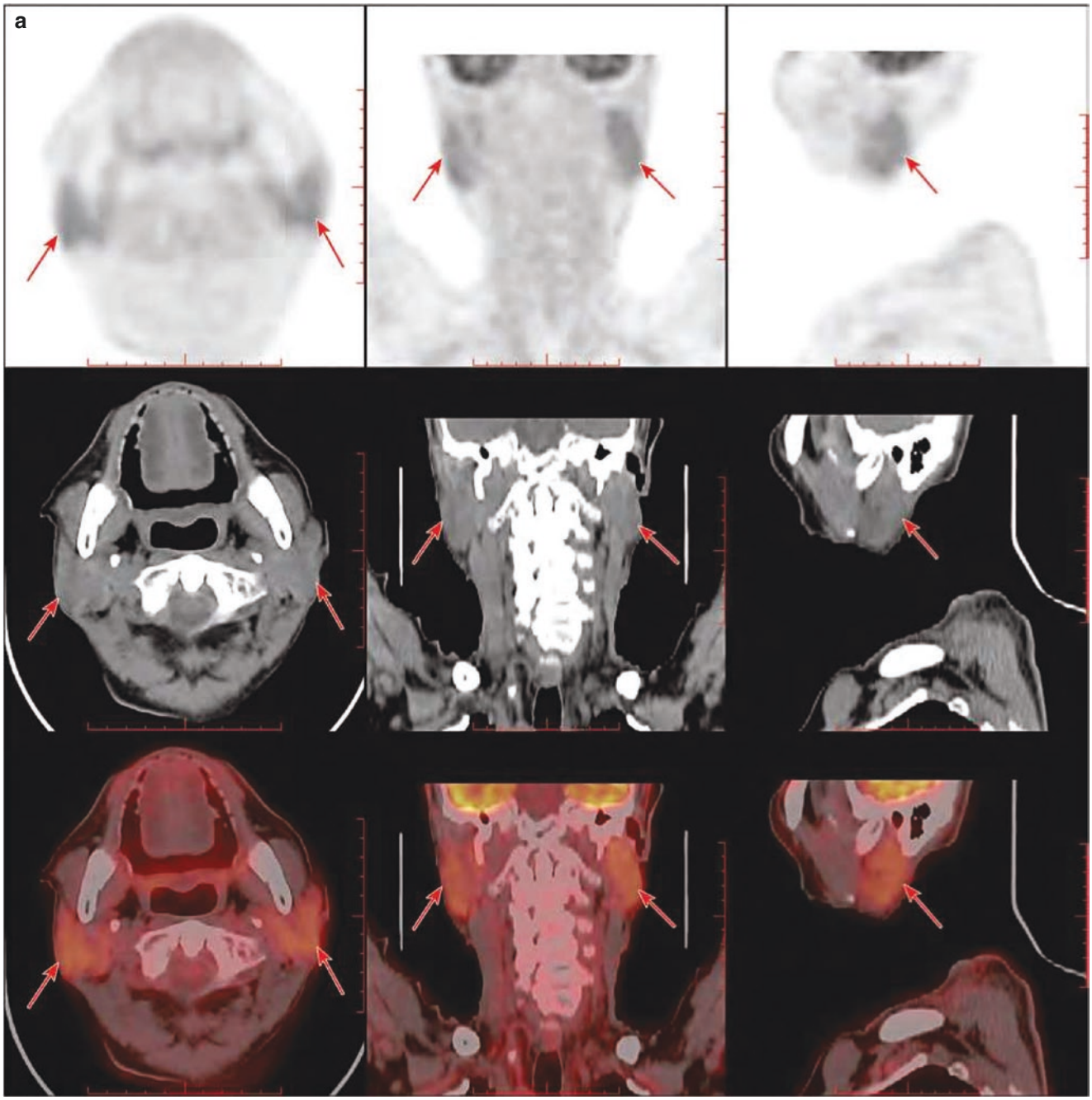


Fig. 19.6 ^{18}F-FDG PET/CT images of bilateral parotid gland inflammation. A 73-year-old male patient with gastric cancer was reexamined in the hospital after operation: (**a**) PET/CT image of diffuse elevated metabolism of bilateral parotid glands; (**b**) PET/CT image of diffuse elevated metabolism of bilateral parotid glands. PET/CT showed bilateral parotid gland enlargement with inhomogeneous increases density, and radioactive distribution increased diffusely. SUVmax was about 5.2

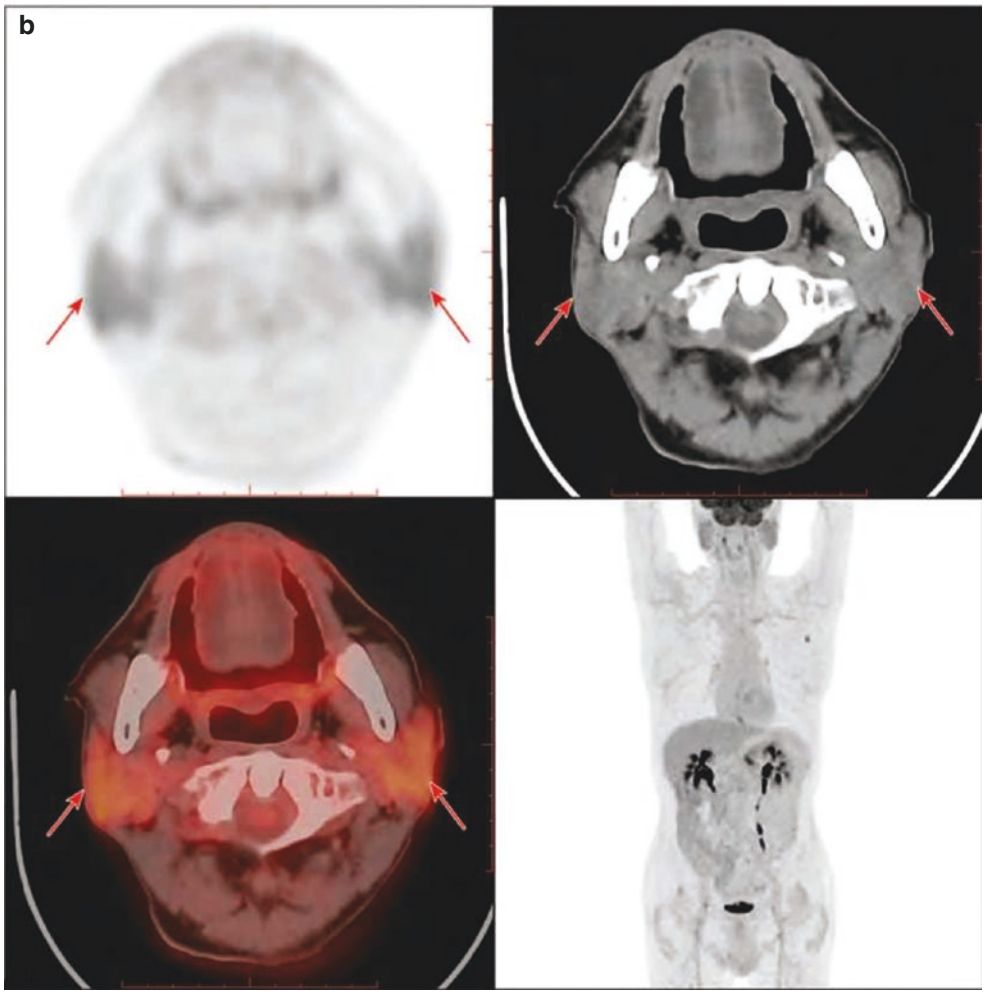


Fig. 19.6 (continued)

2 Common Benign Tumors of the Salivary Gland

2.1 Pleomorphic Adenoma

2.1.1 Clinical Overview

Pleomorphic adenomas of the salivary gland, including pleomorphic adenoma of the parotid gland (also known as mixed tumor of parotid gland), pleomorphic adenoma of the submandibular gland, and pleomorphic adenoma of the minor salivary gland. There are different opinions on histology: Some studies believe that the tumor originates from two germinal layers, so it is named mixed tumor. Later, most scholars believe that the so-called mixed tumor actually originates from the epithelium, including the myoepithelium, glandular epithelium, and tumor matrix, so the name pleomorphic adenoma is more suitable, but most are still used to call it mixed tumor.

Pleomorphic adenoma of the parotid gland is the most common benign tumor of the parotid gland. Pathologically, pleomorphic adenoma of the parotid gland is round or oval with complete envelope. The cross-section of the tumor is solid, off-white, or light yellow. Its main components are light blue cartilage-like tissue and translucent jelly-like mucinous tissue, occasionally bleeding or cystic necrosis, that is, the tumorous epithelial tissue is mixed with mucinous tissue, cartilage-like tissue, and collagen fibers. Under the microscope, the cells are arranged in a cord or sheet shape, which can form cysts of varying sizes, including fibrous tissue, mucinous tissue, and cartilage-like tissue. The mucous-like tissue is the most prominent, and sometimes calcification can be seen. About 25% can be associated with cancer. If the tumor suddenly grows faster and some signs of malignant tumor appear, the possibility of malignant transformation should be considered.

The histopathological characteristics of pleomorphic adenoma of the submandibular gland and minor salivary gland in the oral cavity are similar to that of the parotid gland. Pleomorphic adenoma of the submandibular gland often presents as a painless mass in one side of the subman-

dibular region with clear boundary and slow growth. Pleomorphic adenoma of the minor salivary gland in the oral cavity usually starts from the oral submucous or vagal minor salivary gland and can occur in any part of the oral mucosa, most commonly in the posterior part of the hard palate, followed by the junction of the posterior hard palate and the soft hard palate on one side, and rarely in the midline and anterior part of the hard palate. Clinically, pleomorphic adenoma of the palate usually presents as a semicircular, oval, or nodular painless mass with smooth mucosal surface, which is often found by accident. Pathologically, pleomorphic adenomas of the submandibular gland and minor salivary gland in the oral cavity with a diameter of less than 3 cm have a smooth surface, and the larger ones may be lobulated, with fibrous tissue envelopes of varying thickness, which are easy to separate from the surrounding tissues. Most of the sections are solid, and cystic degeneration areas can be seen in larger sections. Under the light microscope, it shows the pleomorphism of the tissue structure rather than the cell itself. It is often mixed with mucus-like or cartilage-like tissue between the epithelial and mutated myoepithelial cell components.

2.1.2 PET/CT Diagnostic Points

Pleomorphic adenoma of the parotid gland usually occurs in the superficial lobe of the parotid gland and often involves the parapharyngeal space in the deep lobe. Most of the lesions are round or oval with clear edge. PET/CT scan without contrast agents shows equal or slightly high density, and sometimes low-density cystic necrosis or punctate calcification can be seen. The FDG uptake of the solid part of the tumor is increased or slightly higher, which may be inhomogeneous. Salivary gland angiography shows that the salivary duct is compressed and bent, presenting a "ball-holding sign," which was a characteristic manifestation.

Polymorphic adenomas of the submandibular gland are mostly masses with uniform density on PET/CT scan without contrast agents, which can be lobulated, and the density can be higher than that of the surrounding glandular tissues. The boundary is clear. The larger ones have inhomogeneous density. Sometimes, punctate calcification can be seen. The FDG uptake of the solid part of the tumor is increased or slightly higher, which may be inhomogeneous. The FDG uptake of the small ones may not be increased.

The PET/CT scan without contrast agents shows polymorphic adenoma of the minor salivary gland in the oral cavity is round, oval, or lobulated soft tissue mass similar to or slightly less than the adjacent muscles in density, with clear boundary and uniform density. Some of them show cystic degeneration, necrosis, compression, and absorption of adjacent bone, and they may penetrate the hard palate and invade the nasal cavity or completely locate in the maxilla. Sclerotic margin is often seen in adjacent bone. FDG uptake is increased or slightly higher, which may be inhomogeneous, or there may be no significant increase in metabolism.

2.1.3 Typical Cases

A 70-year-old male patient with PET/CT reexamination after lung cancer surgery. Pathology: (right parotid gland) pleomorphic adenoma (Fig. 19.7)

2.1.4 Differential Diagnosis

This disease mainly needs to be differentiated from adenolymphoma (also known as lymphopapillary cystadenoma, Warthin tumor), parapharyngeal space tumor, parotid lymphadenitis, eosinophilic granuloma, retromandibular mandibular vein, parotid malignant tumor, etc. The smaller pleomorphic adenomas are not characteristic and cannot be differentiated from other benign salivary gland tumors or low-grade malignant salivary gland tumors. If a large lobulated soft tissue mass in the parotid or submandibular gland area is found, pleomorphic adenoma should be considered first.

Adenocarcinoma is a common benign parotid tumor in the second position, which is often multiple. It can involve bilateral parotid glands or there are multiple lesions in one side of the gland. There are often cystic areas of varying sizes, and ^{18}F-FDG uptake is increased. The differential diagnosis between small single adenolymphoma and pleomorphic adenoma is difficult, and the diagnosis mainly depends on the incidence. Adenolymphoma is more common in male, but it can be multiple and small in size. The mass is soft and often has a history of growth and decline. Usually, there is cyst in the mass, which can be as a sign for identification.

Parotid gland lymphadenitis and small mixed tumor of eosinophilic granuloma are not easy to differentiate from parotid gland lymphadenitis and eosinophilic granuloma, which should be analyzed in combination with medical history.

Parapharyngeal space tumors often cause the fat in the parapharyngeal space to move outward, while tumors in the deep lobe of the parotid gland often cause the fat tissue in the parapharyngeal space to move inward. Parapharyngeal space tumors can be neuronal tumors or ectopic minor salivary gland tumors. Neurolemmoma usually occurs in the space of the carotid sheath and is prone to cystic degeneration, and the edge of the cystic lesion area is clear. The malignant tumors of the parotid gland have mixed density, irregular edge, unclear boundary, and blurred fat space, the metabolism of ^{18}F-FDG is abnormally increased, and sometimes the destruction of mastoidale or styloid process bone or cervical enlarged lymph nodes can be seen.

Pleomorphic adenoma of the oral small salivary gland should be differentiated from other benign tumors in the palate, including myoepithelioma, papilloma, and fibroma. The abovementioned tumors are difficult to differentiate from pleomorphic

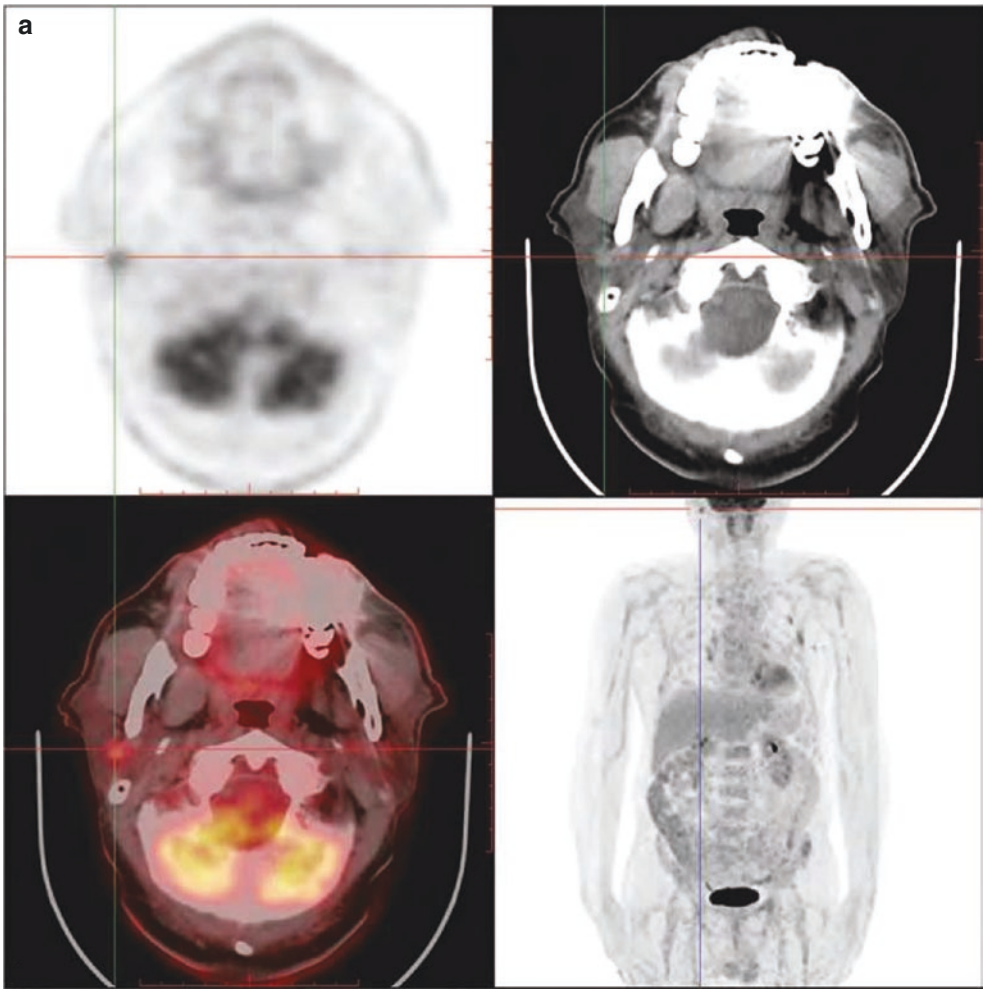


Fig. 19.7 ^{18}F-FDG PET/CT images of pleomorphic adenoma of the right parotid gland. (**a**) PET/CT image of hypermetabolic nodules of the right parotid gland; (**b**) PET/CT image of hypermetabolic nodules of the right parotid gland. PET/CT showed a round slightly high-density nodule shadow in the superficial lobe of the right parotid gland, with clear edge and a diameter of about 0.9 cm, the radioactivity distribution increased, and the SUVmax was about 5.7. Pathology: (right parotid gland) pleomorphic adenoma

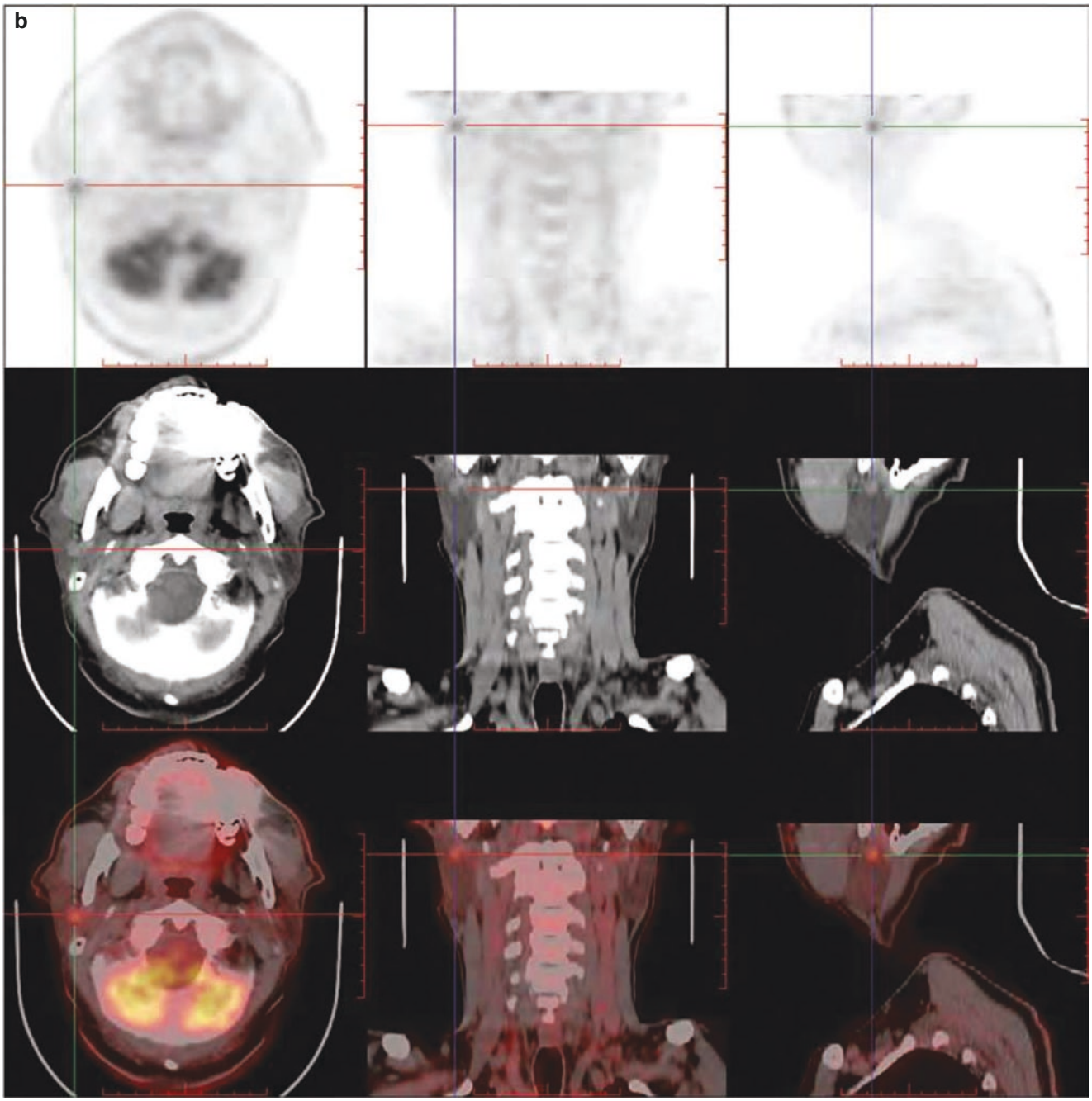


Fig. 19.7 (continued)

adenomas by imaging examination alone, but their incidence is significantly lower than that of pleomorphic adenoma. Malignant tumors are often accompanied by local pain, the surface of the lesion is not smooth, and there may be ulcers. Most of the lesions show infiltrative growth, with unclear boundary; cystic degeneration, necrosis, and hemorrhage are common; and metastatic enlarged cervical lymph nodes can be seen.

2.1.5 Summary

Most pleomorphic adenomas have high ^{18}F-FDG uptake, but this is not specific. The occasional high uptake of ^{18}F-FDG in the parotid gland is common in metastases, physiological uptake, and infectious diseases. In the reports on the application of ^{18}F-FDG PET/CT in the differential diagnosis of parotid benign and malignant lesions, most studies believe that SUV cannot effectively differentiate between benign and malignant parotid lesions. Pleomorphic adenomas, Warthin tumors, large eosinophilic tumors, and other benign tumors can also show high uptake of ^{18}F-FDG. Therefore, differential diagnosis is difficult at times, and the differential diagnosis from other parotid benign tumors mainly depends on the incidence.

2.2 Adenolymphoma

2.2.1 Clinical Overview

Adenolymphoma, also known as papillary cystadenoma lymphomatosum (PCL) or Warthin tumor, is a benign tumor of the parotid gland second only to pleomorphic adenoma, accounting for 15.3% of parotid epithelial tumors and 20.6% of benign tumors. Adenolymphoma of the salivary gland is derived from the salivary gland itself or the salivary gland tissue enclosed in the lymph nodes, and it mainly occurs in one side of the parotid gland, but rarely in the submandibular gland. It is common in the lower pole of the parotid gland and mandibular area and rare in the preauricular area; the location is shallow, the growth is slow, the tumor is generally small, and the diameter is rarely more than 3 cm, with soft, smooth texture and mild activity; after anti-infection treatment, there is no obvious reduction in size, which can be distinguished from inflammation. The occurrence of adenolymphoma may be the result of multiple factors such as gender, region, heredity, age, tobacco, infection, and immunity. Smoking is closely related to the occurrence of adenolymphoma. The disease is a kind of ectopic adenoma and benign epithelial tumor which mainly occurs in the parotid gland, so it is considered to be a disease specific to the parotid gland area. Although adenolymphoma has a benign histological morphology, it has the characteristics of multicentric growth and is accompanied by other types of tumors, which can occur simultaneously on both sides. Clinically, for elderly patients with long-term smoking history, when a soft mass with a diameter of about 3 cm is found in the parotid gland, the possibility of Warthin tumor of the parotid gland should be highly suspected. The history of mass growth and decline is one of the prominent clinical features of Warthin tumor. A cold or upper respiratory tract infection can induce tumor enlargement. The disease rarely has malignant transformation, and the epithelial component can become squamous cell carcinoma or mucoepidermoid carcinoma; the interstitial component mostly becomes mucosal-associated lymphoma.

2.2.2 PET/CT Diagnostic Points

Adenolymphoma usually occurs in the superficial lobe of the parotid gland. It can be multiple in one side or concurrently involves bilateral parotid glands. It is the most common tumor of bilateral glands. PET/CT scan without contrast agents shows round or oval shape with clear edge, mostly less than 2 cm in diameter, and the density can be uniform, comparable to the muscle density at the same level. The low-density area of tumor-associated cyst can be seen. The metabolism of ^{18}F-FDG is slightly or moderately increased.

2.2.3 Typical Cases

Case 1: Male patient, 66 years old. PET/CT was performed to evaluate the general condition after lung cancer surgery. Pathology: (left parotid gland) a large number of eosinophilic epithelial cells; Warthin tumor should be considered (Fig. 19.8).

Case 2: A 66-year-old male patient with a history of non-Hodgkin's lymphoma. PET/CT was performed to evaluate the general condition. Pathology: (left parotid gland) scattered inflammatory cells, tissue cells, eosinophilic ductal epithelial cells; Warthin tumor should be first considered (Fig. 19.9).

2.2.4 Differential Diagnosis

Pleomorphic adenoma: a small unilateral single Warthin tumor is difficult to differentiate from it on imaging. The diagnosis mainly depends on the incidence and pathological results. Large single Warthin tumor usually has a relatively large glandular cavity or bad void cavity, and ^{18}F-FDG uptake can be slightly increased. MRI shows that it is characterized by hyperintensity nodules on T1WI images and T_2WI signal can be hypointensity, isointensity, or hyperintensity. The signal intensity was closely related to the histological components, which can assist the diagnosis.

Sjogren's syndrome (SS) is considered to be an autoimmune disease, which is more common in middle-aged and elderly women. It is characterized by diffuse enlargement of unilateral or bilateral parotid glands, and the submandibular or sublingual glands can also be enlarged at the same time. Clinically, dry eyes, dry mouth, rheumatoid arthritis history, and bilateral lacrimal gland enlargement contribute to the diagnosis of the disease.

Malignant lymphoma may involve bilateral parotid glands, mostly extranodal type. Nodules in parotid gland lymphoma often complicate with enlarged lymph nodes in the neck space, and the enlarged lymph nodes often fuse into blocks, grow fast, and have a short medical history.

2.2.5 Summary

Adenolymphoma of the salivary gland has no specific clinical manifestations. Adenolymphoma is often found accidentally in the PET/CT diagnosis of other diseases. Patients with cystic solid mass are easily misdiagnosed as mixed tumor of the salivary gland, lymphadenitis, or cyst. Therefore, imaging examinations cannot be used as the only basis for diagnosis, and the diagnosis must be made in combination with medical history and clinical manifestations. When the middle-aged and elderly male patients with long-term smoking history have a round soft tissue mass in the posterior lower pole of the parotid gland, with clear edge; solid or cystic solid, bilateral or multifocal; and increased ^{18}F-FDG uptake, Warthin tumor of the parotid gland is suggested.

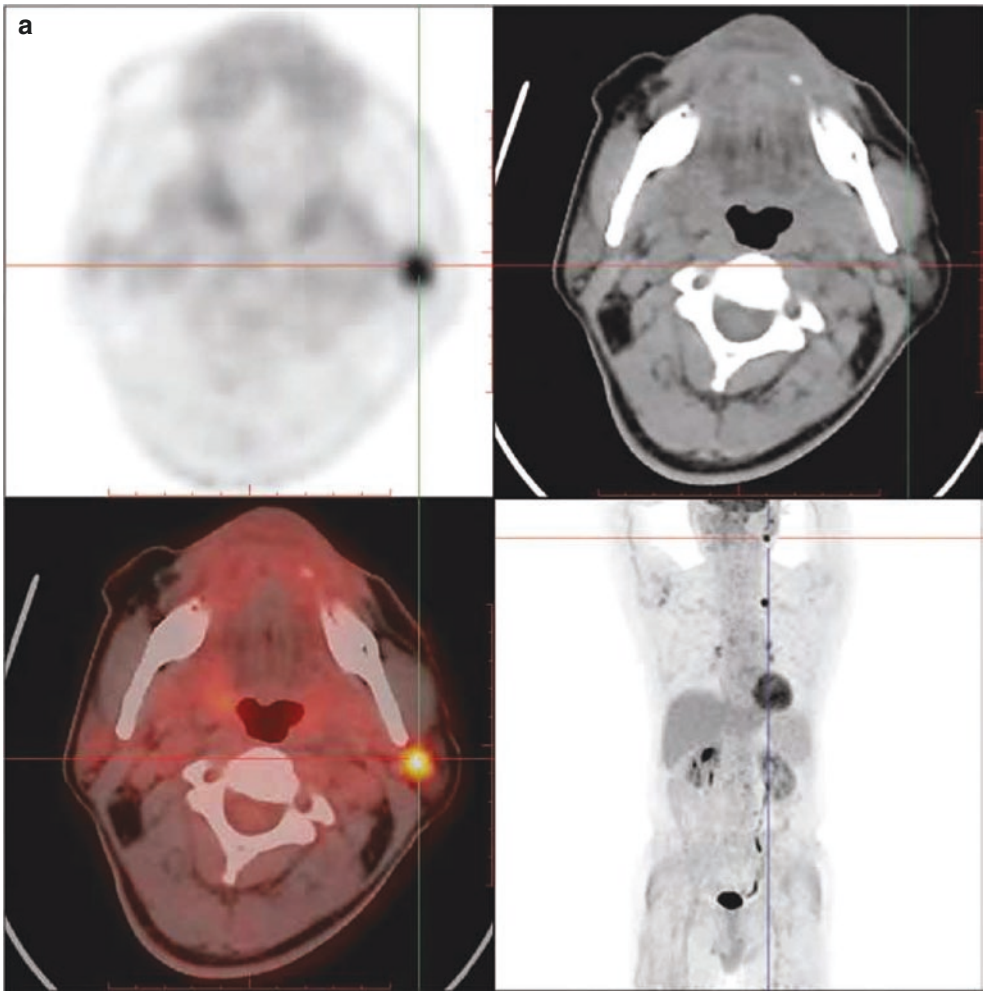


Fig. 19.8 ^{18}F-FDG PET/CT images of Warthin tumor of the left parotid gland. (**a–c**) PET/CT images of hypermetabolic nodules in the left parotid gland. PET/CT showed that there was a round, slightly high-density, small nodule shadow in the lower pole of the left parotid gland, with clear edges and a size of about 1.0 cm × 0.9 cm. The density was uniform, comparable to the muscle density at the same level. The radioactive distribution was abnormally concentrated, and the SUVmax was about 15.6

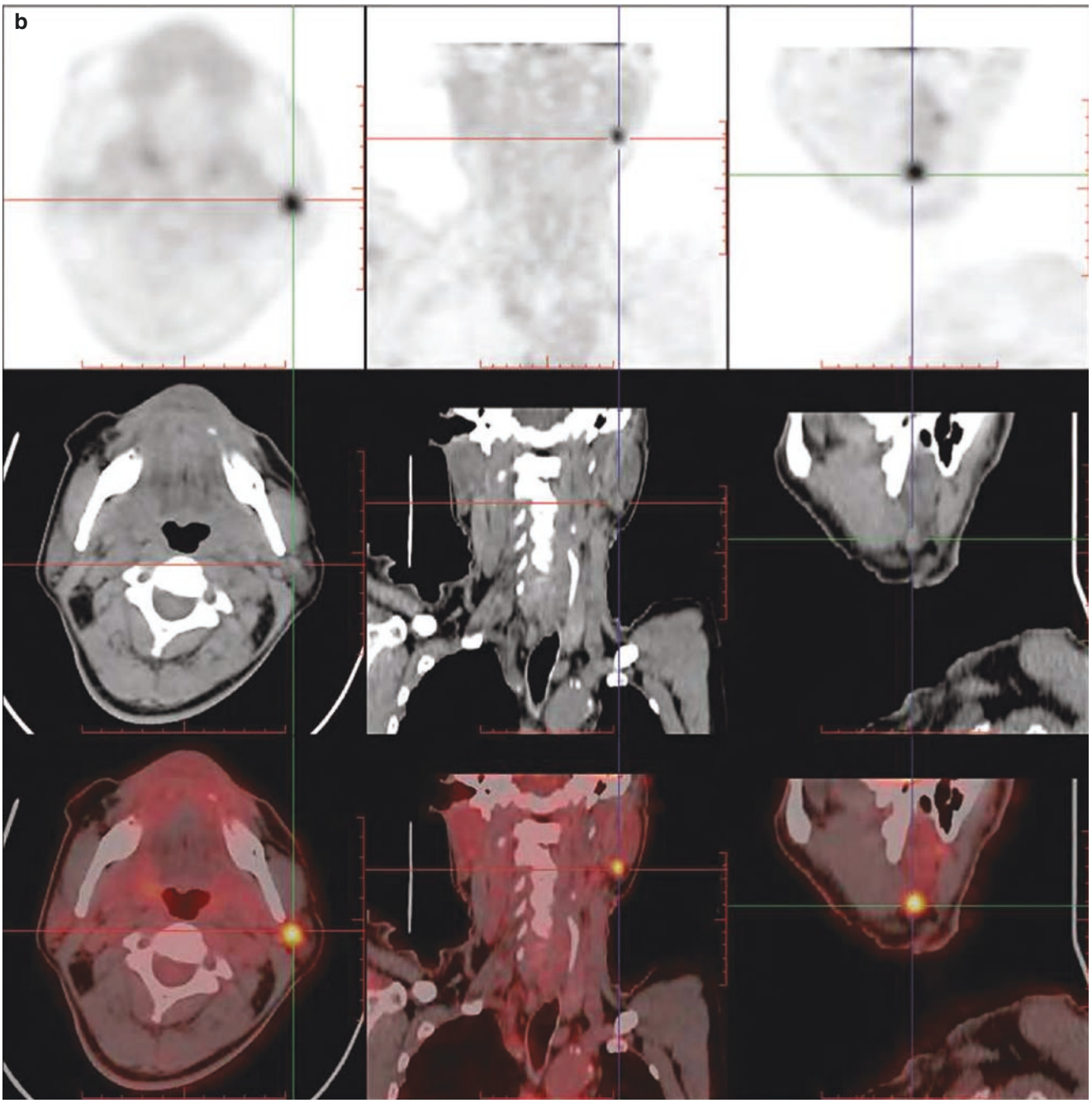
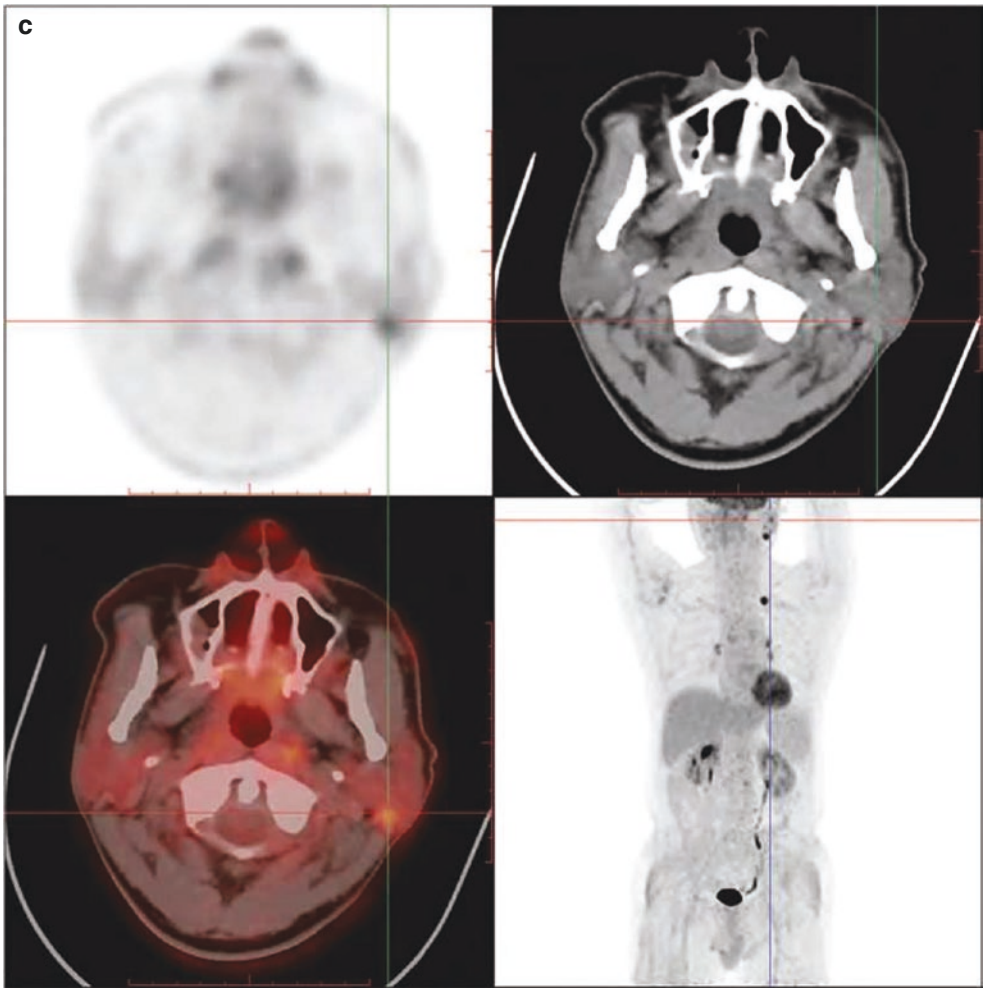


Fig. 19.8 (continued)



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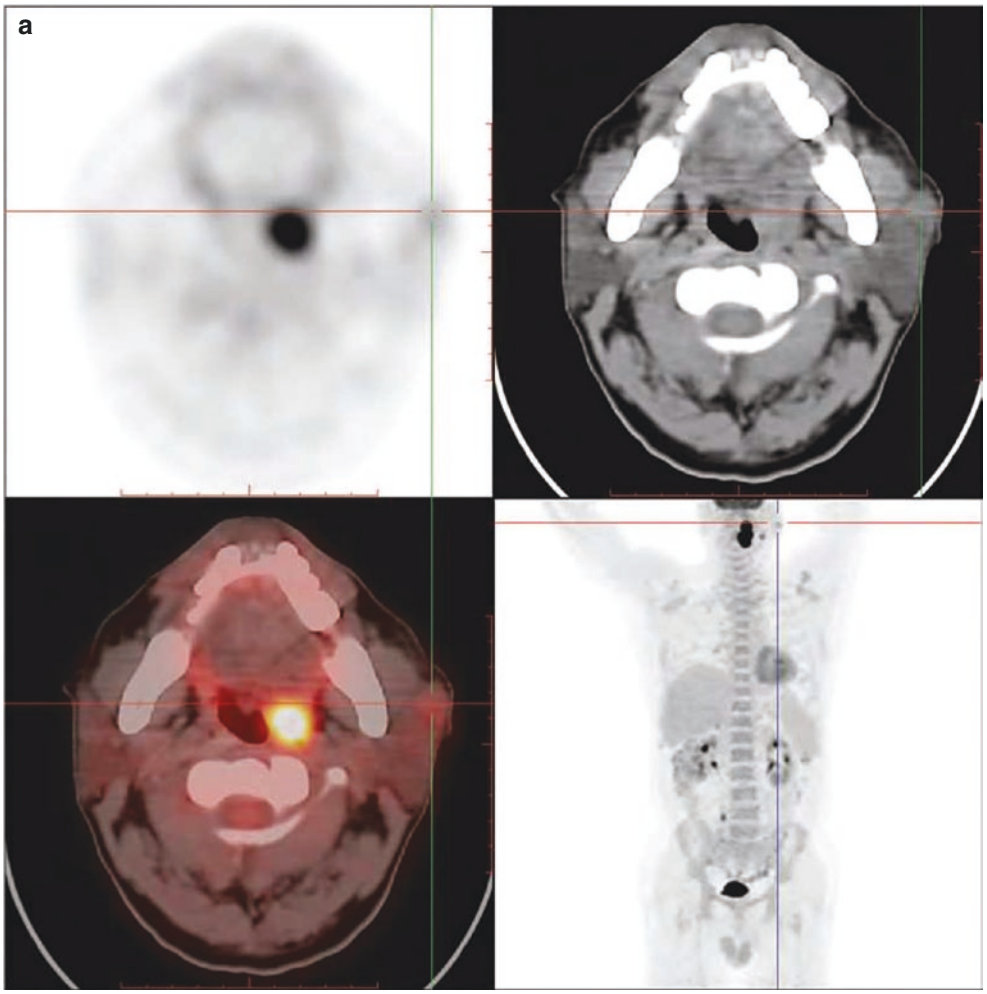

Fig. 19.9 ^{18}F-FDG PET/CT images of non-Hodgkin's lymphoma with Warthin tumor. (**a**) PET/CT image of a slightly hypermetabolic nodule on the anterior outer edge of the left parotid gland (before treatment), with clear edge, about 1.0 cm in diameter, with uniform density and slightly increased FDG uptake (SUVmax 2.3). (**b**) PET/CT image of a slightly hypermetabolic nodule in the left parotid gland (after treatment). The patient underwent PET/CT reexamination after 4 months of treatment. The nodule size did not change significantly. The radioactivity distribution was slightly higher than before, and SUVmax was about 2.5

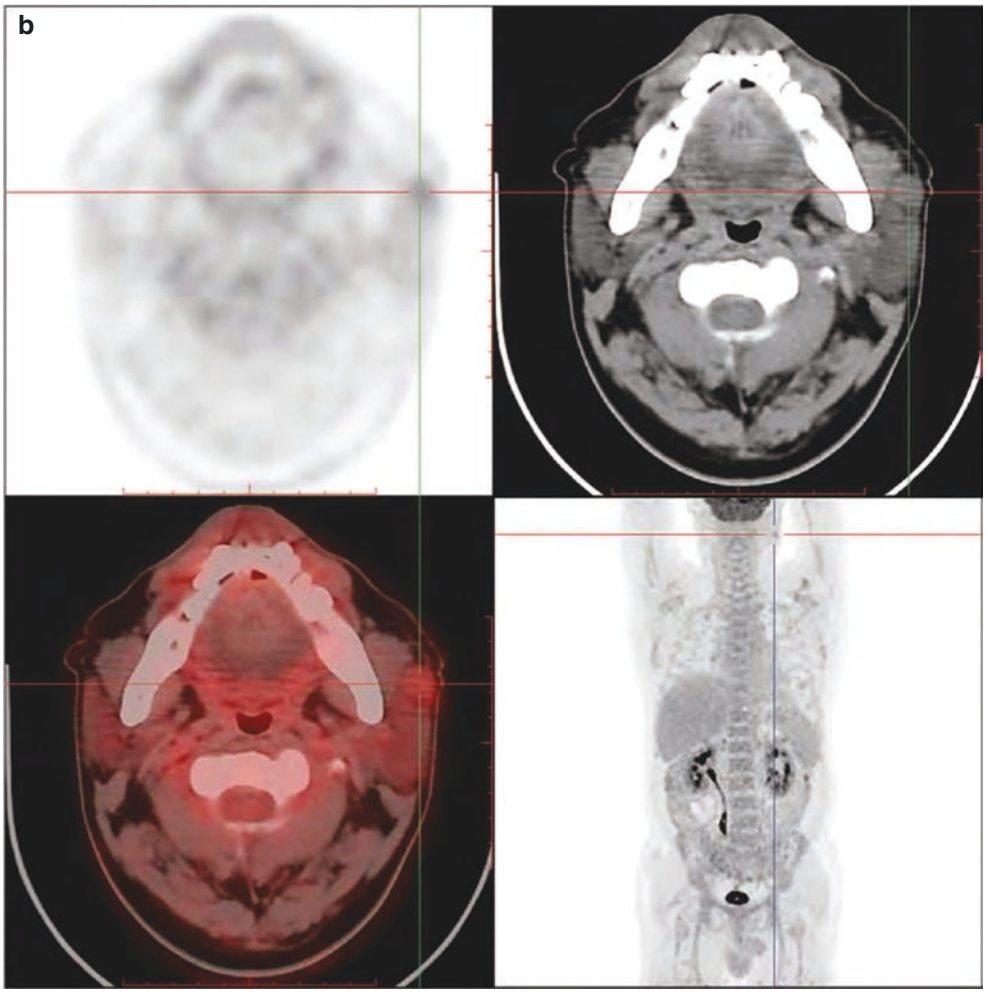

Fig. 19.9 (continued)

Further Reading

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