Tumors of the pharyngomaxillary space

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A bulging of the soft palate should alert one to the possibility of a mass in the pharyngomaxillary space. Work-up includes CT scan or MRI and possible needle aspiration. Open biopsy should be avoided. Benign, mixed tumors are most commonly encountered. Surgical excision by external approach is generally advocated.

Tumors within the pharyngomaxillary (parapharyngeal) space present challenges in diagnostic assessment and surgical technique. Because of the anatomic complexity of this space, determining the exact tumor location and extent of involvement is difficult. Pharyngomaxillary masses range from benign salivary gland tumors to lesions of neurogenic and vascular origin.

In this paper, the anatomy, pathogenesis, clinical presentation, radiographic analysis, and surgical approaches to this tumor are reviewed. Also, a report of a typical case is presented.

Report of case

A 27-year-old woman complained of a painless bulging of her left soft palate of several months' duration. She denied having dysphagia, epistaxis, nasal congestion, or ear pain. She had undergone tonsillectomy one year earlier.

Physical examination revealed a definite bulging of the soft palate on the left side and lateral pharyngeal wall in the left tonsillar fossa area. There was no grossly visible lesion. The oral airway was adequate. Examination of the superficial lobe of the parotid gland disclosed no abnormalities. No thyroid enlargement or cervical adenopathy was palpated. Tympanic membranes were normal, and there was no evidence of serous fluid. Nasopharyngoscopy revealed fullness of the left nasopharynx.

Skinny-needle biopsy was performed with a 20-gauge needle in the soft palate region. Aspiration cytology revealed only inflammatory cells. Contrast computed tomography (CT) showed a 10 × 6 cm, nonenhancing mass of the left parapharyngeal space. A fat plane between

the deep lobe of the parotid gland and the mass could not be identified clearly, and magnetic resonance imaging (MRI) was performed to help ascertain its presence (Figs 1-5).

Open incisional biopsy of the soft palate was performed. The yellow lymphoid tissue was replaced by white, gritty tissue as dissection was carried deeper into the substance of the soft palate. The pathologic diagnosis was pleomorphic adenoma.

Resection of the deep-lobe parotid gland tumor was performed two weeks after initial diagnosis. An external approach was used for easy access and to ensure preservation of the facial nerve. A 7 × 4 × 5 cm, well-encapsulated tumor of the deep lobe of the parotid gland was resected. The patient had an uneventful postoperative course, and her facial nerve function remained intact. Two months later, resection of the soft palate biopsy site was performed to prevent recurrence from tumor seeding. No tumor cells were identified on microscopic examination of the resected specimen.

Discussion

Anatomy

A space between the lateral wall of the nasopharynx and the ramus of the mandible and pterygoid muscle, the pharyngomaxillary space is divided into the prestyloid and retrostyloid compartments by the styloid process and stylomandibular ligament. The retrostyloid compartment contains the contents of the carotid sheath and the glossopharyngeal, accessory, hypoglossal, and sympathetic nerves.^{1,2} Infections that reach the prestyloid compartment may extend to the base of the skull, which forms the space's superior boundary. Inferiorly, the space reaches the level of the hyoid bone.

The stylomandibular ligament, which attaches the styloid process to the angle of the mandible, forms a narrow tunnel, through which deep-lobe parotid tumors may extend into the parapharyngeal space. Because this tunnel is fairly rigid, the tumor that forms has a typical dumbbell shape, with wide lateral and medial portions and a narrow neck.^{3,4}

Fig 1. CT with contrast showing large left pharyngomaxillary mass. There does not seem to be a fat plane between the mass and the parotid gland posterior to the mandibular ramus.

Fig 2. CT axial view.

Fig 3. T_2 -weighted MRI of pharyngomaxillary space mass. If present, a fat plane would appear as a 'bright' signal in these views.

This space communicates with other deep neck spaces, including the retropharyngeal space and the submandibular space. Therefore, infections in this area may spread into other regions of the neck or into the superior mediastinum. Tumors originating here tend to grow into the area of least resistance, which is the relatively pliable medial boundary (lateral pharyngeal wall). Thus, medial displacement of the soft palate, the lateral nasopharynx, and the lateral pharyngeal wall is characteristic of pharyngomaxillary space masses.⁵

Pathogenesis

These tumors usually are benign. Work and Hybels⁵ retrospective study of 40 patients with pharyngomaxillary space tumors revealed that 82% of the masses were benign; 48% were lesions of the salivary gland, and 32% were neurogenic tumors. Similar findings were reported by McIlrath and associates.⁶

Benign, mixed tumors are the most common form of salivary gland tumors, although adenocarcinomas and adenoid cystic and mucoepidermoid carcinomas may be encountered. Of neurogenic tumors, schwannomas occur most frequently, followed by chemodectomas and neurofibromas.⁵ Miscellaneous tumors that may invade this area include glomus lesions, arteriovenous malformations, internal carotid artery aneurysms, lymphomas, rhabdomyosarcomas, and leiomyomas (Table I).

The most common tumor type, pleomorphic adenoma, can arise from the deep lobe of the parotid gland or accessory parotid gland tissue, or it can be of minor salivary gland origin. Although there have been attempts to differentiate the site of origin using CT⁷ or combined CT-sialography,⁸ this may be difficult, or even impossible, to achieve.

Clinical presentation and diagnosis

A patient who has a mass in the pharyngomaxillary space has few symptoms. Sore throat, vague discomfort with swallowing, and otalgia may be present. Rarely, neurogenic tumors may present with symptoms related to the affected nerve. For example, a tumor originating in the sympathetic nerve may result in Horner's syndrome, while a vagus nerve lesion may cause loss of sensation in the ipsilateral pharynx along with unilateral vocal cord paralysis. Accessory nerve lesions may produce motor disturbances of the trapezius muscle.⁹

The most common physical findings are medial bulging of the lateral pharyngeal wall and tonsillar fossa, as well as downward displacement of the soft palate. Unilateral serous otitis media also may

Fig 4. MRI axial view.

Fig 5. MRI cross-sectional view.

exist. Erosion of the mucous membrane may represent a malignant neoplasm, and biopsy of the area should be performed. In general, biopsy of the soft palate is not recommended because of the possibility of tumor seeding. Skinny-needle aspiration may be used, because there has been no reported seeding with this modality. If malignancy is suspected, incisional biopsy may be performed from either an external or intraoral approach. In these cases, the surgeon should be prepared for complete surgical excision.

Radiographic analysis is the next step in diagnosis. The major goals are to determine whether the mass is of parotid or extraparotid origin and whether it is benign or malignant. To distinguish parotid from extraparotid lesions, Som and coworkers⁸ used sialography in combination with CT. However, with the improvement in resolution of CT scanners and the advent of MRI, sialography may not be needed to make an accurate assessment.

The single most useful finding in nonenhancing masses is the presence of a fat plane between the mass and the deep lobe of the parotid gland. The fat plane may be obliterated in cases of intraparotid lesions, while most extraparotid masses will allow its delineation. Large pharyngomaxillary tumors may cause enough compression to obliterate the fat plane, however. Therefore, a nonvisible fat plane correctly identifies an intraparotid tumor in only 80% of cases.¹⁰

MRI may be of even greater help in delineating the size, location, and extent of a tumor accurately, and it allows easier recognition of the fat plane in difficult cases. Irregular or poorly defined margins on CT scans may suggest malignancy.⁷ For an enhancing (on CT scan), extraparotid mass, angiography is used to delineate glomus tumors, aneurysms, and other vascular lesions.

Treatment

Generally, the best surgical approach to tumors of the pharyngomaxillary space is an external one. This allows for better visualization and control of bleeding, as well as easier identification of the major nerves and vessels in the operative field. External approaches include submandibular (cervical) approach, parotid approach, and cervical-transpharyngeal approach with midline mandibulotomy. The first two approaches can be combined with a mandibulotomy if greater access and exposure are needed.^{3,11-15}

The cervical approach should be reserved for small extraparotid tumors that lie deep to the deep lobe of the parotid gland. The classic parotid incision is used most widely for deep-lobe parotid and

TABLE 1: TYPES OF PHARYNGOMAXILLARY TUMORS.

<i>Salivary gland tumors</i>
Pleomorphic adenoma
Adenoid cystic carcinoma
Adenocarcinoma
Mucoepidermoid carcinoma
<i>Neurogenic tumor</i>
Schwannoma
Neurofibroma
Chemodectoma
Neuroma
<i>Vascular tumors</i>
Arteriovenous malformation
Hemangioma
Aneurysm
Glomus lesion
<i>Miscellaneous tumors</i>
Teratoma
Leiomyoma
Rhabdomyosarcoma
Hibernoma
Lymphoma
Desmoid

dumbbell-shaped tumors. This approach allows for precise anatomic dissection and preservation of the facial nerve.

If the tumor is very large, mandibulotomy is performed in a step-wise fashion at the angle of the mandible. The cervical-transpharyngeal approach with midline mandibulotomy is reserved for large extraparotid tumors. A tracheostomy is recommended in conjunction with this approach because of the tongue and floor of mouth edema that develops following extensive submucosal dissection.

Only in cases of small tumors that arise from the palate or lateral pharyngeal wall should an internal or peroral approach be used. This procedure carries a greater risk of vessel and nerve injury, primarily because of lack of exposure.

Conclusions

Tumors of the pharyngomaxillary space usually present as painless bulging of the lateral pharyngeal wall. The overwhelming majority of tumors will be benign and of either salivary gland or neurogenic origin. However, differential diagnosis should include glomus tumors and other vascular lesions, as well as malignant tumors.

Combined CT-sialography as an initial radiographic tool has given way to the newer generation of CT scanners. MRI provides a more detailed radiographic analysis than CT, and it may be used in difficult cases in which further delineation of the mass is needed. Angiography is now reserved for highly vascular tumors that have been evaluated by contrast CT.

Although open biopsy was performed in our case, this technique generally is discouraged. When an

accurate tissue sample can be obtained, skinny-needle aspiration biopsy has the theoretic advantage of no tumor seeding.

A classic external parotid surgical approach is generally the best because of visualization and ease in preserving vital structures. When the tumor is massive, this approach combined with mandibulotomy provides an extremely wide operative field. Peroral excisions are reserved for small lesions of the soft palate or lateral pharyngeal wall.

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GLUCOTROL® (glipizide) Tablets

Brief Summary of Prescribing Information

INDICATIONS AND USAGE: GLUCOTROL is indicated as an adjunct to diet for the control of hyperglycemia in patients with non-insulin-dependent diabetes mellitus (NIDDM, type II) after an adequate trial of dietary therapy has proved unsatisfactory.

CONTRAINDICATIONS: GLUCOTROL is contraindicated in patients with known hypersensitivity to the drug or with diabetic ketoacidosis, with or without coma, which should be treated with insulin.

SPECIAL WARNING ON INCREASED RISK OF CARDIOVASCULAR MORTALITY: The administration of oral hypoglycemic drugs has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin. This warning is based on the study conducted by the University Group Diabetes Program (UGDP), a long-term prospective clinical trial designed to evaluate the effectiveness of glucose-lowering drugs in preventing or delaying vascular complications in patients with non-insulin-dependent diabetes. The study involved 823 patients who were randomly assigned to one of four treatment groups (*Diabetes*, 19, supp. 2:747-830, 1970). UGDP reported that patients treated for 5 to 8 years with diet plus a fixed dose of tolbutamide (1.5 grams per day) had a rate of cardiovascular mortality approximately 2-1/2 times that of patients treated with diet alone. A significant increase in total mortality was not observed, but the use of tolbutamide was discontinued based on the increase in cardiovascular mortality, thus limiting the opportunity for the study to show an increase in overall mortality. Despite controversy regarding the interpretation of these results, the findings of the UGDP study provide an adequate basis for this warning. The patient should be informed of the potential risks and advantages of GLUCOTROL and of alternative modes of therapy.

Although only one drug in the sulfonylurea class (tolbutamide) was included in this study, it is prudent from a safety standpoint to consider that this warning may also apply to other oral hypoglycemic drugs in this class, in view of their close similarities in mode of action and chemical structure.

PRECAUTIONS: Renal and Hepatic Disease: The metabolism and excretion of GLUCOTROL may be slowed in patients with impaired renal and/or hepatic function. Hypoglycemia may be prolonged in such patients should it occur. **Hypoglycemia:** All sulfonylureas are capable of producing severe hypoglycemia. Proper patient selection, dosage, and instructions are important to avoid hypoglycemia. Renal or hepatic insufficiency may increase the risk of hypoglycemic reactions. Elderly, debilitated or malnourished patients and those with adrenal or pituitary insufficiency are particularly susceptible to the hypoglycemic action of glucose-lowering drugs. Hypoglycemia may be difficult to recognize in the elderly or people taking beta-adrenergic blocking drugs. Hypoglycemia is more likely to occur when caloric intake is deficient, after severe or prolonged exercise, when alcohol is ingested, or when more than one glucose-lowering drug is used.

Loss of Control of Blood Glucose: A loss of control may occur in diabetic patients exposed to stress such as fever, trauma, infection or surgery. It may then be necessary to discontinue GLUCOTROL and administer insulin.

Laboratory Tests: Blood and urine glucose should be monitored periodically. Measurement of glycosylated hemoglobin may be useful.

Information for Patients: Patients should be informed of the potential risks and advantages of GLUCOTROL, of alternative modes of therapy, as well as the importance of adhering to dietary instructions, of a regular exercise program, and of regular testing of urine and/or blood glucose. The risks of hypoglycemia, its symptoms and treatment, and conditions that predispose to its development should be explained to patients and responsible family members. Primary and secondary failure should also be explained.

Drug Interactions: The hypoglycemic action of sulfonylureas may be potentiated by certain drugs including nonsteroidal anti-inflammatory agents and other drugs that are highly protein bound, salicylates, sulfonamides, chloramphenicol, probenecid, coumarins, monoamine oxidase inhibitors, and beta-adrenergic blocking agents. *In vitro* studies indicate that GLUCOTROL binds differently than tolbutamide and does not interact with salicylate or dicumarol. However, caution must be exercised in extrapolating these findings to a clinical situation. Certain drugs tend to produce hypoglycemia and may lead to loss of control, including the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid. A potential interaction between oral miconazole and oral hypoglycemic agents leading to severe hypoglycemia has been reported. Whether this interaction also occurs with the intravenous, topical, or vaginal preparations of miconazole is not known.

Carcinogenesis, Mutagenesis, Impairment of Fertility: A 20-month study in rats and an 18-month study in mice at doses up to 75 times the maximum human dose revealed no evidence of drug-related carcinogenicity. Bacterial and *in vivo* mutagenicity tests were uniformly negative. Studies in rats of both sexes at doses up to 75 times the human dose showed no effects on fertility.

Pregnancy: Pregnancy Category C. GLUCOTROL (glipizide) was found to be mildly fetotoxic in rat reproductive studies at all dose levels (5-50 mg/kg). This fetotoxicity has been similarly noted with other sulfonylureas, such as tolbutamide and tolazamide. The effect is perinatal and believed to be directly related to the pharmacologic (hypoglycemic) action of GLUCOTROL. In studies in rats and rabbits no teratogenic effects were found. There are no adequate and well-controlled studies in pregnant women. GLUCOTROL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Because recent information suggests that abnormal blood glucose levels during pregnancy are associated with a higher incidence of congenital abnormalities, many experts recommend that insulin be used during pregnancy to maintain blood glucose levels as close to normal as possible.

Nonteratogenic Effects: Prolonged severe hypoglycemia has been reported in neonates born to mothers who were receiving a sulfonylurea drug at the time of delivery. This has been reported more frequently with the use of agents with prolonged half-lives. GLUCOTROL should be discontinued at least one month before the expected delivery date.

Nursing Mothers: Since some sulfonylurea drugs are known to be excreted in human milk, insulin therapy should be considered if nursing is to be continued.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: In controlled studies, the frequency of serious adverse reactions reported was very low. Of 702 patients, 11.8% reported adverse reactions and in only 1.5% was GLUCOTROL discontinued.

Hypoglycemia: See PRECAUTIONS and OVERDOSAGE sections.

Gastrointestinal: Gastrointestinal disturbances, the most common, were reported with the following approximate incidence: nausea and diarrhea, one in 70; constipation and gastralgia, one in 100. They appear to be dose-related and may disappear on division or reduction of dosage. Cholestatic jaundice may occur rarely with sulfonylureas. GLUCOTROL should be discontinued if this occurs.

Dermatologic: Allergic skin reactions including erythema, morbilliform or maculopapular eruptions, urticaria, pruritus, and eczema have been reported in about one in 70 patients. These may be transient and may disappear despite continued use of GLUCOTROL; if skin reactions persist, the drug should be discontinued. Porphyrin cutanea tarda and photosensitivity reactions have been reported with sulfonylureas.

Hematologic: Leukopenia, agranulocytosis, thrombocytopenia, hemolytic anemia, aplastic anemia, and pancytopenia have been reported with sulfonylureas.

Metabolic: Hepatic porphyria and disulfiram-like alcohol reactions have been reported with sulfonylureas. Clinical experience to date has shown that GLUCOTROL has an extremely low incidence of disulfiram-like reactions.

Endocrine Reactions: Cases of hyponatremia and the syndrome of inappropriate antidiuretic hormone (SIADH) secretion have been reported with this and other sulfonylureas.

Miscellaneous: Dizziness, drowsiness, and headache have each been reported in about one in fifty patients treated with GLUCOTROL. They are usually transient and seldom require discontinuance of therapy.

OVERDOSAGE: Overdosage of sulfonylureas including GLUCOTROL can produce hypoglycemia. If hypoglycemic coma is diagnosed or suspected, the patient should be given a rapid intravenous injection of concentrated (50%) glucose solution. This should be followed by a continuous infusion of a more dilute (10%) glucose solution at a rate that will maintain the blood glucose at a level above 100 mg/dL. Patients should be closely monitored for a minimum of 24 to 48 hours since hypoglycemia may recur after apparent clinical recovery. Clearance of GLUCOTROL from plasma would be prolonged in persons with liver disease. Because of the extensive protein binding of GLUCOTROL, dialysis is unlikely to be of benefit.

DOSEAGE AND ADMINISTRATION: There is no fixed dosage regimen for the management of diabetes mellitus with GLUCOTROL. In general, it should be given approximately 30 minutes before a meal to achieve the greatest reduction in postprandial hyperglycemia.

Initial Dose: The recommended starting dose is 5 mg before breakfast. Geriatric patients or those with liver disease may be started on 2.5 mg. Dosage adjustments should ordinarily be in increments of 2.5-5 mg, as determined by blood glucose response. At least several days should elapse between titration steps.

Maximum Dose: The maximum recommended total daily dose is 40 mg.

Maintenance: Some patients may be effectively controlled on a once-a-day regimen, while others show better response with divided dosing. Total daily doses above 15 mg should ordinarily be divided.

HOW SUPPLIED: GLUCOTROL is available as white, dye-free, scored, diamond-shaped tablets imprinted as follows: 5 mg tablet—Pfizer 411 (NDC 5 mg 0049-4110-66) Bottles of 100; 10 mg tablet—Pfizer 412 (NDC 10 mg 0049-4120-66) Bottles of 100.

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