CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 14-2025: A 29-Year-Old Woman with Peritonsillar Swelling and Bleeding

Rahmatullah Wais Rahmati, M.D., M.P.H.,[1-3] Katherine L. Reinshagen, M.D.,[4-6] Rosh K.V. Sethi, M.D., M.P.H.,[3,7,8] David S. Shulman, M.D.,[9,10] and Emily M. Hartsough, M.D.[11,12]

Author affiliations are listed at the end of the article.

N Engl J Med 2025;392:1954-64.
DOI: 10.1056/NEJMcpc2300972

CME

PRESENTATION OF CASE

Dr. Margaret B. Mitchell (Otolaryngology): A 29-year-old woman was admitted to this hospital because of sore throat and peritonsillar swelling and bleeding.

The patient had been well until 7 weeks before the current admission, when sore throat developed. When the soreness did not abate after 1 week, she sought evaluation at a primary care clinic of another hospital. Screening tests of a nasopharyngeal swab for severe acute respiratory syndrome coronavirus 2 RNA and streptococcal antigen were negative. The patient was instructed to rest and drink fluids.

During the next 4 days, the throat soreness increased in severity to the point that the patient was unable to sleep through the night. She returned to the primary care clinic, and azithromycin was prescribed. During the subsequent 5 days, she took the prescribed antibiotic, but the throat soreness did not abate. She called the primary care clinic and was instructed to go to the emergency department of the other hospital.

On evaluation in the emergency department, 31 days before the current admission, the patient described pain and swelling on the right side of the throat and noted that when she swallowed food, it felt as though the food became "stuck." She reported fatigue but no fever, headache, shortness of breath, cough, nausea, vomiting, abdominal pain, diarrhea, or rash.

On examination, the temporal temperature was 36.9°C, the blood pressure 105/77 mm Hg, the heart rate 74 beats per minute, and the oxygen saturation 99% while the patient was breathing ambient air. She appeared well and had a normal voice without hoarseness or stridor. The mucous membranes were moist. Edema and fluctuance were seen in the right peritonsillar area of the soft palate. The right tonsil had no erythema, swelling, or exudate. The uvula deviated to the left. No trismus was noted. The lungs were clear on auscultation. There was no palpable lymphadenopathy and no rash. The white-cell count was 6700 per microliter (reference range, 4000 to 11,000). Other laboratory test results are shown in Table 1.

Table 1. Laboratory Data.

Variable	Reference Range, Other Hospital	On Initial Presentation, Other Hospital	Reference Range, Adults, This Hospital*	On Admission, This Hospital
White-cell count (per μl)	4000–11,000	6700	4500–11,000	13,470
Differential count (per μl)				
Neutrophils	1600–8300	4400	1800–7700	8970
Lymphocytes	600–5900	1800	1000–4800	2750
Monocytes	200–1400	500	200–1200	1420
Eosinophils	0–800	0	0–900	200
Basophils	0–100	0	0–300	70
Hemoglobin (g/dl)	11.2–15.7	13.9	12.0–16.0	15.1
Hematocrit (%)	34.1–44.9	41.5	36.0–46.0	44.9
Platelet count (per μl)	150,000–400,000	261,000	150,000–400,000	339,000
Prothrombin time (sec)	—	—	11.5–14.5	12.5
Prothrombin-time international normalized ratio	—	—	0.9–1.1	0.9
Activated partial-thromboplastin time (sec)	—	—	22.0–36.0	28.5

* Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Massachusetts General Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

Dr. Katherine L. Reinshagen: Computed tomography (CT) of the neck, performed after the intravenous administration of contrast material, revealed a hypodense lesion in the right peritonsillar region of the oropharynx that measured 2.6 cm by 2.1 cm by 3.8 cm (Fig. 1). There was minimal peripheral enhancement. The presence of the lesion resulted in mild effacement of the oropharynx. Minimal fat stranding was present in the right parapharyngeal fat. No edema was noted in the right medial pterygoid muscle. A right jugulodigastric lymph node had a normal appearance.

Dr. Mitchell: The patient was discharged home with a prescription for amoxicillin–clavulanate and was advised to schedule a follow-up visit at the otolaryngology clinic of the other hospital.

Twenty-six days before the current admission, the patient was evaluated at the otolaryngology clinic of the other hospital. The right peritonsillar lesion was incised, and 3 ml of sanguineous fluid was drained. The next day, the patient returned to the otolaryngology clinic because of increased pain and swelling on the right side of the throat and bleeding from the incision site. On examination, the right peritonsillar area was more edematous than it had been the previous day, and ecchymosis, friable mucosa, and some necrotic granulation tissue were noted. The incision site was partially open with oozing of bloody fluid. A repeat drainage of fluid at this site was attempted, and a hematoma was evacuated with suction. Bleeding was treated with silver nitrate and oxidized regenerated cellulose; however, oozing at the site continued. The patient was taken to the operating room urgently.

On examination while the patient was under anesthesia, there was oozing of bloody fluid from multiple sites in the right peritonsillar area. Oxymetazoline-soaked gauze and a human gelatin–thrombin matrix sealant were used to achieve hemostasis. The patient was admitted to the other hospital. Dexamethasone and ampicillin–sulbactam were administered, and an infusion of lactated Ringer's solution was initiated. On the second hospital day, after confirmation that bleeding had stopped, she was discharged home with instructions to resume treatment with amoxicillin–clavulanate and to take acetaminophen and oxycodone as needed for pain.

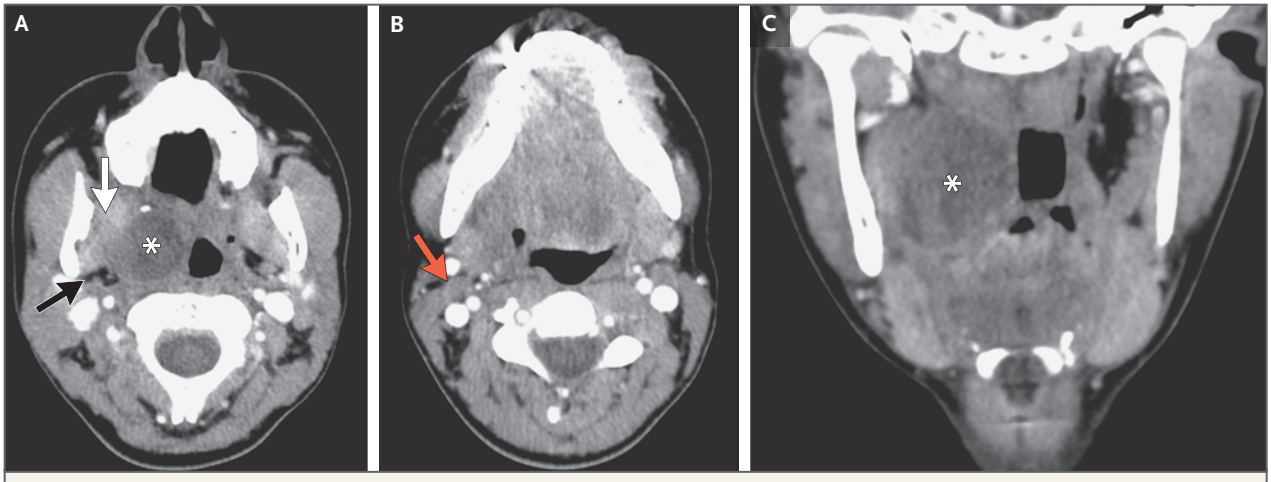

Figure 1. Initial CT Scans of the Neck.

Contrast-enhanced CT of the neck was performed on initial presentation to the other hospital. Axial (Panels A and B) and coronal (Panel C) images at the level of the oropharynx show a hypodense lesion (Panels A and C, asterisks) with no substantial rim enhancement centered in the right peritonsillar region of the oropharynx. The presence of the mass has resulted in mild effacement of the oropharynx. There is minimal, if any, fat stranding in the right parapharyngeal fat (Panel A, black arrow). The right medial pterygoid muscle (Panel A, white arrow) and right jugulodigastric lymph node (Panel B, red arrow) have a normal appearance.

During the next 2 weeks, the pain and swelling on the right side of the throat decreased. However, 8 days before the current admission, the patient noticed that her voice sounded "froggy." She returned to the otolaryngology clinic of the other hospital, and treatment with clindamycin and methylprednisolone was started. During the subsequent 4 days, the patient noticed intermittent bleeding on the right side of the throat. She was referred to the otolaryngology clinic of a second hospital. Four days before the current admission, aspiration of the swollen area of the right peritonsillar region reportedly yielded dark blood.

On the morning of the current admission, the patient awoke with increased pain and swelling on the right side of the throat. Several hours later, she felt a "pop" and noticed bleeding on the right side of the throat. She presented to the otolaryngology clinic of the second hospital, where she received oral vitamin K and aminocaproic acid. She was advised to seek evaluation in the emergency department of this hospital.

On evaluation, the patient described a "froggy" voice and difficulty speaking because of the pain and swelling in her throat. She also had difficulty swallowing, including swallowing oral secretions, and she had limited her diet to very soft foods and liquids. A review of systems was notable for fatigue, easy bruising, and heavy periods. She had no fever, headache, shortness of breath, cough, nausea, vomiting, abdominal pain, diarrhea, or rash.

The patient had previously been healthy. She took clindamycin, vitamin K, and aminocaproic acid, and she used a levonorgestrel-releasing intrauterine device. There were no known drug allergies. She lived alone in an urban area of New England. She did not smoke tobacco, drink alcohol, or use illicit drugs. Her mother had endometriosis, her maternal grandmother had Alzheimer's disease, her maternal grandfather had pancreatic cancer, and her paternal grandfather had heart disease.

On examination, the temporal temperature was 36.4°C, the blood pressure 111/66 mm Hg, the heart rate 82 beats per minute, and the oxygen saturation 100% while the patient was breathing ambient air. She appeared well and had mild muffled dysphonia. There was no stridor or stertor. A bulging mass that was erythematous, ecchymotic, edematous, firm, and compressible was present in the right peritonsillar area. There was a surgical defect in this area with a large, dark clot that extended almost to the left tonsil, nearly obstructing the airway. Gentle palpation of the right peritonsillar area elicited bleeding from around the clot. Examination with

the use of a fiberoptic bronchoscope did not reveal other abnormalities in the nasal cavity, nasopharynx, oropharynx, hypopharynx, or larynx. No palpable cervical lymphadenopathy was noted. The white-cell count was 13,470 per microliter (reference range, 4500 to 11,000); the platelet count was normal. Blood levels of hemoglobin, electrolytes, and calcium were normal, as were results of coagulation and kidney-function tests. Other laboratory test results are shown in Table 1.

Dr. Reinshagen: CT angiography of the neck, performed after the intravenous administration of contrast material, revealed that the size of the hypodense right peritonsillar lesion had increased to 3.4 cm by 3.6 cm by 4.6 cm, with mildly complex attenuation (Fig. 2). The lesion involved the soft palate and extended into the submucosal nasopharynx. Minimal rim enhancement and mild fat stranding in the right parapharyngeal fat were unchanged from the previous imaging study. The lesion was inseparable from the right medial pterygoid muscle, which was not enlarged or edematous. No extravasation of contrast material was seen.

Dr. Mitchell: Treatment with ampicillin–sulbactam was started. Vitamin K and aminocaproic acid therapy were stopped. Intravenous hydromorphone, acetaminophen, and ondansetron were administered. The patient was admitted to the surgical intensive care unit.

A diagnostic procedure was performed.

DIFFERENTIAL DIAGNOSIS

Dr. Rahmatullah Wais Rahmati: I was involved in the care of this patient, and I am aware of the final diagnosis. This previously healthy 29-year-old woman presented with almost 2 months of progressive throat pain, along with a tonsillar mass. Key points regarding the patient's presenting illness include the presence of progressive throat pain despite multiple courses of antibacterial therapy; the absence of fever, trismus, and lymphadenopathy; the presence of bleeding, with no purulent material aspirated during multiple drainage attempts; and imaging studies showing minimal fat stranding of the parapharyngeal fat, no muscle or bone invasion, and no evidence of lymphadenopathy.

To develop a differential diagnosis, it is important to consider the anatomy of the deep neck spaces and their associated tissues. In this patient, the peritonsillar and pharyngeal mucosal

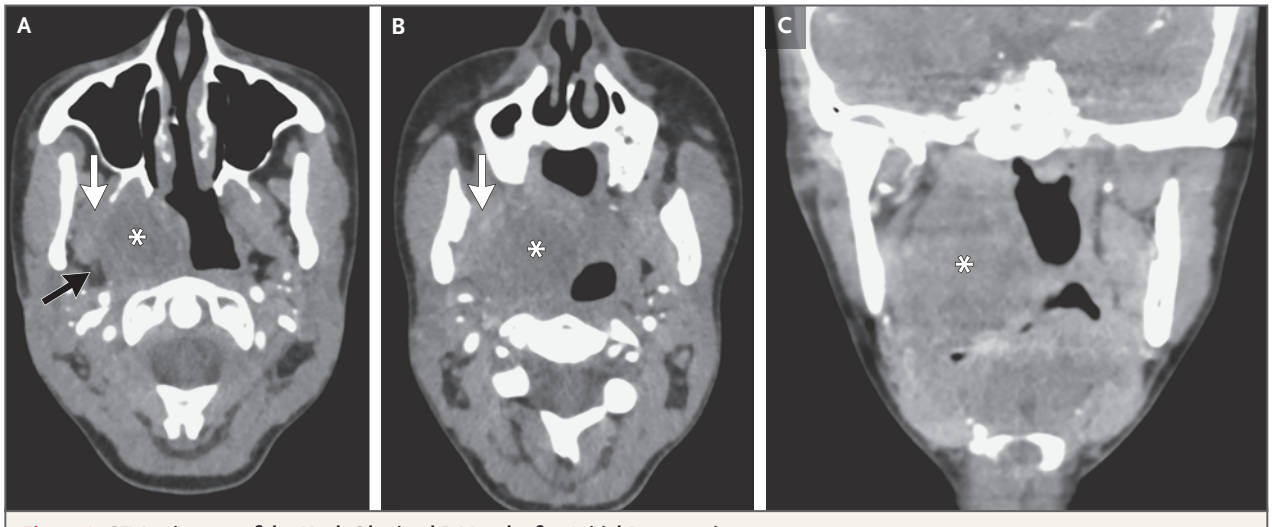

Figure 2. CT Angiogram of the Neck Obtained 1 Month after Initial Presentation.

Contrast-enhanced CT angiography of the neck was performed 1 month after the patient's initial presentation to the first hospital. Axial (Panels A and B) and coronal (Panel C) images show enlargement of the right peritonsillar lesion (asterisks), which now extends above the soft palate and into the submucosal nasopharynx. Although the lesion is inseparable from the right medial pterygoid muscle, no enlargement or edema is present within the muscle (Panels A and B, white arrows). Minimal fat stranding is seen in the right parapharyngeal fat (Panel A, black arrow).

spaces are relevant, and within these spaces lie the palatine tonsils, mucosa, minor salivary glands, muscle, and connective tissue. The broad categories of infectious, inflammatory, and neoplastic diseases involving the tissues of the peritonsillar and pharyngeal mucosal spaces must be considered. A disease process involving these spaces may extend into adjacent areas, which include the parapharyngeal, carotid, masticator, and retropharyngeal spaces, and could cause radiographic and clinical findings of displacement of the parapharyngeal fat, displacement of the great vessels, trismus, and neck stiffness, respectively, owing to involvement of those spaces.

PERITONSILLAR ABSCESS

This patient initially presented for a consultation with an otolaryngologist after a 3-week history of pain on the right side of the throat, dysphagia, peritonsillar edema, and identification of a 3.8-cm hypodense lesion within the peritonsillar space on CT. These findings are highly suggestive of a peritonsillar abscess. However, certain characteristic clinical and radiographic features of a peritonsillar abscess are not present in this patient, including fever, trismus, lymphadenopathy, normal-appearing tonsils, and a CT scan showing minimal fat stranding of the parapharyngeal fat. In particular, the absence of trismus is not consistent with the diagnosis of peritonsillar abscess, since in my experience, trismus is an almost universal finding in patients with a lesion of this size.

The patient underwent an incision and drainage procedure, which yielded only a small amount of sanguineous fluid without any purulence. This finding does not completely rule out a peritonsillar infection, since she may be in a phlegmonous stage of the disease process. However, nearly 3 weeks of symptoms — in addition to the absence of findings characteristic of an abscess on physical examination and CT — makes tonsillar infection or abscess an unlikely diagnosis in this patient.

After approximately 4 weeks of symptoms, the patient's illness was transitioning from an acute process to a subacute condition. Therefore, we should expand the differential diagnosis to include autoimmune conditions such as systemic lupus erythematosus and mixed connective-tissue disease, vasculitic diseases such as granulomatosis with polyangiitis, granulomatous conditions such as sarcoidosis, infiltrative diseases such as amyloidosis, and neoplastic processes.

These conditions in particular have the potential to cause mucosal lesions, masses, and ulceration in the pharynx and thus could explain this patient's throat pain and dysphagia. The brief period of abatement of symptoms, possibly in response to glucocorticoid therapy, may also support the possibility of these conditions, since most are responsive to glucocorticoid therapy. Although these conditions are under consideration, the absence of fever and systemic organ involvement, as well as the unremarkable results of routine laboratory tests, make these diagnoses unlikely. At this stage, an additional laboratory workup, magnetic resonance imaging, and biopsy would be helpful in refining the differential diagnosis.

Unfortunately, worsening pain, voice change (a new symptom), and recurrent bleeding developed in the patient. Of greater concern is the development of the tonsillar mass, which leads to a key question: Which conditions can cause rapid growth of a tonsillar mass? Figure 3 shows the tonsillar mass and its effects on the surrounding tissues.

BENIGN NEOPLASM

At this point, a neoplastic process rises to the top of the differential diagnosis. A number of benign neoplasms (papillomas, fibromas, muscle and connective-tissue tumors, vascular tumors, and salivary-gland tumors) are related to the tissue types located in the peritonsillar and pharyngeal mucosal spaces of the oropharynx. Most of these lesions are small and either do not involve recurrent bleeding or, in the case of a hemangioma or vascular malformation, are associated with profuse bleeding. A benign tumor in the salivary gland, such as a pleomorphic adenoma, can develop within this space and can result in swelling of the soft palate and peritonsillar region. However, the rapid time course of tumor growth in this patient makes this diagnosis unlikely.

MALIGNANT NEOPLASM

Malignant neoplasms that warrant consideration in this patient are squamous-cell carcinoma, lymphoma, salivary-gland cancer, and sarcoma.

Squamous-Cell Carcinoma

Squamous-cell carcinoma is the most common cancer that involves the tonsils. Although squamous-cell carcinoma of the tonsils has historically been caused primarily by tobacco-related and alcohol-related carcinogenesis, it is now more commonly associated with human papillomavirus types 16 and 18. Patients typically present with a neck mass resulting from metastatic involvement of the cervical lymph nodes. Tumors at the primary site tend to be small, yet nodal disease may be extensive.[1] However, squamous-cell carcinoma is unlikely in this patient, given the absence of local muscle invasion and cervical lymphadenopathy, both of which would be expected in association with a tumor of the size seen in this case.

Lymphoma

When a rapidly growing tonsillar mass is encountered in a young patient, it is important to consider lymphoma. Extranodal non-Hodgkin's lymphoma of the head and neck region usually develops within the lymphoid tissues of Waldeyer's ring; the palatine tonsils are the most common site of involvement.[2] Patients may present with odynophagia, dysphagia, or a submucosal mass.

Salivary-Gland Cancer

Minor salivary-gland cancers, which account for less than 3% of head and neck cancers, may develop within the soft tissues surrounding the tonsils and inside the soft palate.[3] Low-grade tumors may lack the clinical and radiographic

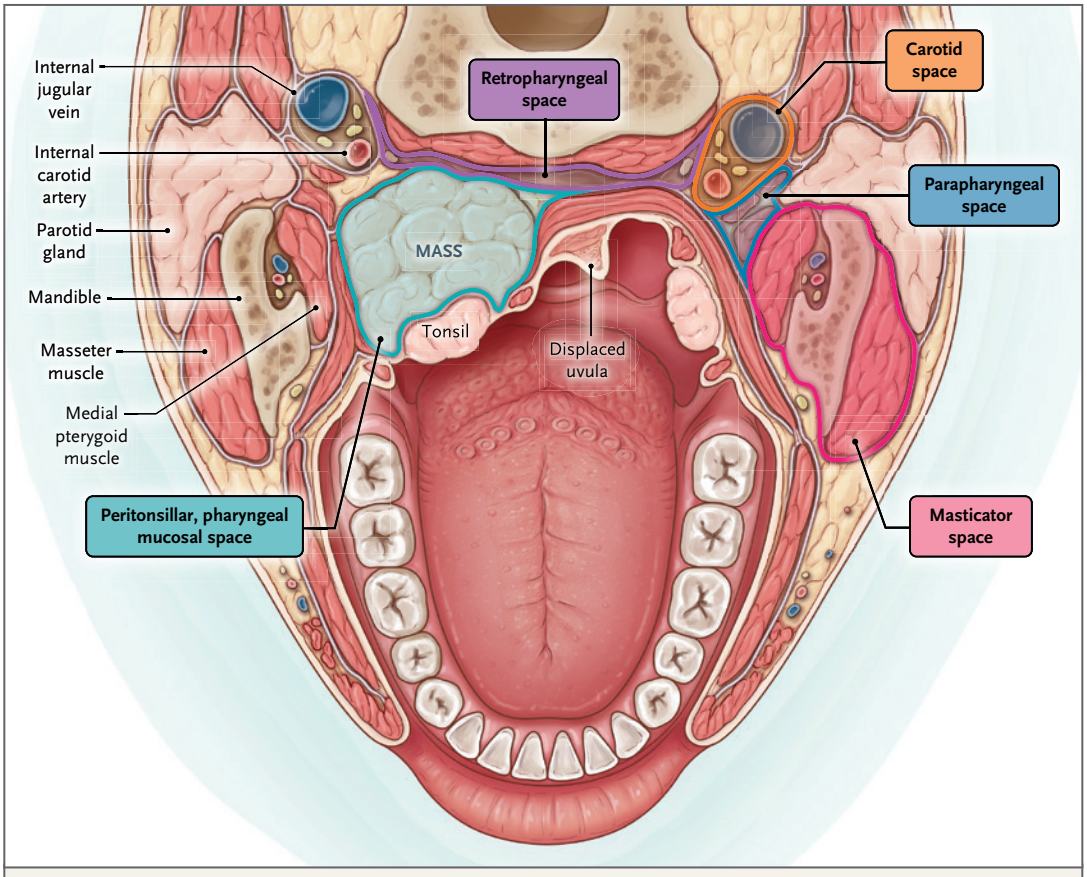

Figure 3. Deep Neck Spaces and Their Associated Tissues.

Shown is the location of the patient's mass (approximately 4 cm in diameter) in the right peritonsillar, pharyngeal mucosal space with medial displacement of the palatine tonsil. The mass does not invade the pterygoid muscles in the masticator space. The parapharyngeal fat is displaced posterolaterally, without fat stranding that would have suggested inflammation. The neurovascular structures within the carotid space are intact and displaced posteriorly. There is no extension into the retropharyngeal space.

evidence of local invasion and lymphadenopathy, as in this patient, but would also have a slow rate of growth. Meanwhile, a high-grade tumor may have rapid growth but is also likely to act aggressively, with local tissue invasion and lymphadenopathy.

Sarcoma

Sarcomas are rare tumors that may arise from the musculoskeletal and connective tissues of the neck. Nearly 200 different subtypes have been reported in adults. These tumors may appear as a painless mass without lymph-node involvement.[4]

When I evaluated this patient, I thought that the most likely diagnosis was a malignant neoplasm — possibly minor salivary-gland cancer, lymphoma, or sarcoma — but it is not possible to distinguish among these cancers without first obtaining tissue for pathological evaluation. Given this patient's presentation involving bleeding from a large oropharyngeal mass and concerns about airway complications, examination and biopsy while the patient was under anesthesia was recommended.

DR. RAHMATULLAH WAIS RAHMATI'S DIAGNOSIS

Malignant neoplasm consistent with minor salivary-gland cancer, lymphoma, or sarcoma.

PATHOLOGICAL DISCUSSION

Dr. Emily M. Hartsough: A biopsy specimen obtained from the right side of the oropharynx was submitted for pathological evaluation. Hematoxylin and eosin staining of sections of the tissue specimen showed overlying tonsil with ulceration and reactive changes from the previous surgical intervention, along with an infiltrative round-cell tumor deep in the tonsil tissue (Fig. 4A). The tumor was characterized by alternating areas of hypocellularity with myxoid stroma and hypercellularity with foci of tumor-cell condensation (Fig. 4B). Coagulative necrosis and hemorrhage were present. The round-to-oval tumor cells contained dispersed-to-hyperchromatic chromatin and occasional prominent nucleoli with sparse, amphophilic cytoplasm. Numerous mitotic figures and apoptotic bodies were present (Fig. 4C). Rhabdomyoblasts were not readily identified, and anaplasia was absent.

Immunohistochemical staining showed that the tumor cells were diffusely positive for desmin and myoD1 and multifocally positive for myogenin (Fig. 4D, 4E, and 4F). These immunohistochemical findings confirmed the presence of skeletal muscle differentiation of the tumor cells, with the focal myogenin staining pattern favoring a diagnosis of embryonal rhabdomyosarcoma.

A representative formalin-fixed, paraffin-embedded tissue specimen containing tumor cells was sent for molecular testing. Fluorescence in situ hybridization, performed with break-apart probes to the *FOXO1* locus, did not detect the presence of *FOXO1* rearrangements, which effectively ruled out a diagnosis of alveolar rhabdomyosarcoma.[5] Next-generation sequencing revealed variants in the RAS pathway, including single-nucleotide variants in *HRAS* and *GNAS* and copy-number variants in *HRAS*. Somatic driver mutations involving the RAS pathway have been identified in genomic studies of embryonal rhabdomyosarcoma.[6,7] Cytogenetic analysis of fresh tumor tissue obtained from this patient revealed a complex karyotype, including trisomy 8. Although not specific, trisomy 8 is a recurrent aberration observed in patients with rhabdomyosarcoma.[8]

PATHOLOGICAL DIAGNOSIS

Embryonal rhabdomyosarcoma.

DISCUSSION OF ONCOLOGIC MANAGEMENT

Dr. David S. Shulman: Rhabdomyosarcoma is a soft-tissue sarcoma that primarily affects children, yet approximately 40% of affected patients present in the adult years.[9] Embryonal rhabdomyosarcoma is the most common histologic subtype, typically arising in the head and neck or genitourinary system.[10] Molecular characterization has become increasingly important in the workup of rhabdomyosarcoma with the recognition that gene translocations and mutations in genes such as *MYOD1* are prognostic.[11] Clinical trial data in adults with rhabdomyosarcoma are lacking — a common challenge in managing this disease in adolescents and young adults. Data from registry studies have shown that adults with rhabdomyosarcoma have outcomes

that are inferior to those in children. Specifically, among patients with localized disease, the 5-year overall survival is 47% among adults as compared with 82% among children.[9] Some data suggest that adults who are treated according to treatment guidelines for children have better

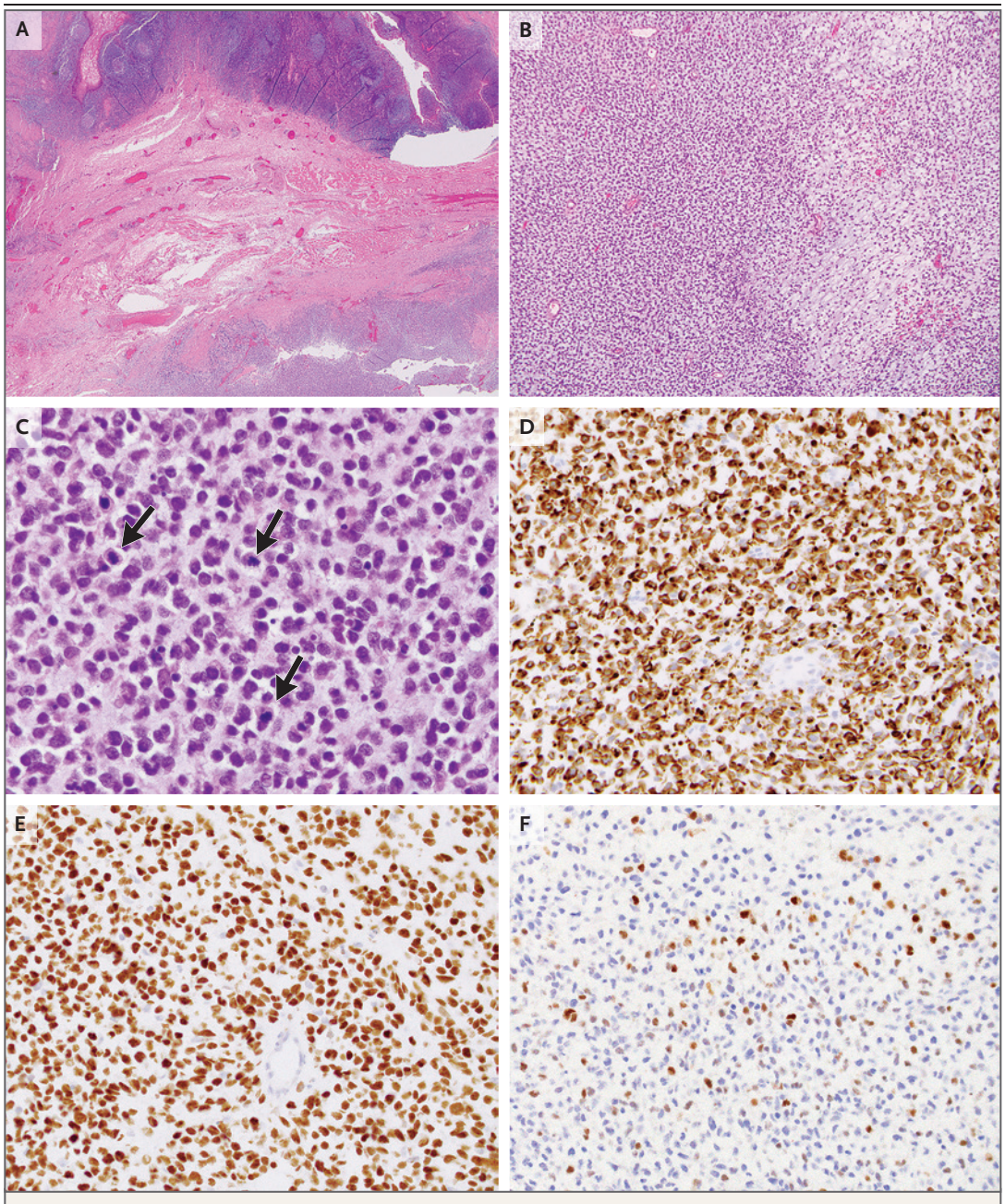

Figure 4. Biopsy Specimen of the Oropharyngeal Mass.

Hematoxylin and eosin staining of the oropharyngeal tissue specimen (Panel A) shows an infiltrative round-cell neoplasm deep in the tonsil tissue. At higher magnification, an alternating hypocellular and hypercellular pattern of growth is seen in a myxoid background (Panel B), and round-to-oval cells with a high nuclear-to-cytoplasmic ratio, scant amphophilic cytoplasm, and numerous mitoses are noted (Panel C, arrows). Immunohistochemical staining shows that the tumor cells are diffusely positive for desmin (Panel D) and myoD1 (Panel E) and multifocally positive for myogenin (Panel F).

outcomes than those who are not treated according to such guidelines.[12]

Treatment of rhabdomyosarcoma includes chemotherapy, surgery when feasible, and radiation therapy for control of local residual disease. Vincristine, dactinomycin, and cyclophosphamide are commonly used chemotherapeutic agents for the treatment of pediatric rhabdomyosarcoma and are used in a risk-adapted fashion.[13-16] The standard of care for pediatric patients is evolving, and it is important that the specific treatment approach for any given patient is informed by a pediatric oncologist with expertise in soft-tissue sarcomas.

This patient had nonparameningeal head and neck primary rhabdomyosarcoma arising from a favorable (operable) site of disease (stage 1, clinical group III). The degree to which the stage and clinical groupings in children can be applied to adults is unknown, and an optimal chemotherapy regimen for adults with rhabdomyosarcoma has not been established. Exposure to cardiotoxic agents and radiation therapy is less of a concern in adults than in children, and intensive regimens are often selected for adult patients, given their historically poor outcomes.

In the case of this patient, owing to the risk of impending airway obstruction by the tumor, a combination of vincristine, doxorubicin, and cyclophosphamide was selected as the initial treatment. After the patient received the first cycle of chemotherapy, there was evidence of early progression; therefore, treatment with ifosfamide and etoposide was administered, along with radiation therapy, in cycle 2. After completion of radiation therapy for local control, the patient went on to complete a total of 14 cycles of alternating treatment with the combination of vincristine, doxorubicin, and cyclophosphamide and the combination of ifosfamide and etoposide. This regimen is commonly used in North America and Europe to treat Ewing's sarcoma.[17]

DISCUSSION OF SURGICAL MANAGEMENT

Dr. Rosh K.V. Sethi: Surgery has an important role in the locoregional management of soft-tissue sarcomas. In patients with nonparameningeal head and neck rhabdomyosarcoma, surgical management always warrants consideration. En bloc resection is the favored approach, with the goal of achieving wide negative margins.[18] The treating surgeon carefully examines the patient to determine the extent of disease, obtains appropriate axial imaging to assess the proximity of critical structures, and counsels the patient about the potential effect of surgery on function and cosmesis. Although regional spread of disease is rare, surgical management of the neck may be considered in cases in which worrisome tumor features or confirmed nodal metastases are present.

In this case, the patient underwent diagnostic tonsillectomy. She was noted to have centrally necrotic and friable tonsillar tissue, along with induration, on the right side and dishwater-gray fluid in the peritonsillar space. Imaging was notable for evidence of extensive local disease with involvement of the pterygoid muscles, soft palate, retromolar trigone, and buccinator. If surgery were to be pursued, the procedure would involve radical right tonsillectomy with partial pharyngectomy, soft-palate resection, and possible marginal mandibulectomy with the use of a transoral approach that might also lead to lip-split mandibulotomy (an incision through the lower lip and mandible to gain access to the posterior oral cavity and oropharynx) for better access and visualization. One would anticipate clinically significant complications with severe swallowing dysfunction, including possible dependence on a gastrostomy feeding tube for nutritional support. Given the functional implications of surgery in this patient, along with low confidence in clearing the surgical margins, surgery was not offered; instead, systemic treatment was initiated.

FOLLOW-UP

Dr. Shulman: The patient's treatment course was complicated by multiple acute side effects of chemotherapy and radiation therapy, including fever, neutropenia, mucositis, and pain. These toxic effects are common with rhabdomyosarcoma therapies, particularly in cases in which radiation therapy to the head and neck is used. This patient's treatment carries the risk of long-term complications associated with chemotherapy and radiation therapy, including cardiomyopathy, infertility, secondary cancer, and toxic effects specifically related to treatment of head and neck rhabdomyosarcoma.[12,13]

The results of successive pediatric cooperative-group trials have led to the availability of treatment involving reduced exposure to anthracycline agents that can cause late cardiac toxic effects as well as reduced exposure to radiation, which can increase the risk of secondary cancers. Attempts to reduce exposure to alkylating agents that can cause infertility have been less successful, and the appropriate cumulative dose of such agents in children with rhabdomyosarcoma remains controversial.[11,14] This type of risk-adapted therapy has not been studied in adults.

Given the short- and long-term toxic effects of these therapies, initiation of survivorship care beginning on the first day of diagnosis is essential when measures for fertility preservation and cardioprotection can be considered. The psychosocial effect of a cancer diagnosis and intensive treatment during this transitional phase of life should not be underestimated, and a psychosocial needs assessment should be part of treatment and follow-up care.

PATIENT PERSPECTIVE

The Patient: My first symptom was a sore throat that never went away. As the swelling and list of unusual symptoms grew, my confidence that it was nothing shrank. It was confusing and exhausting. Dr. Rahmati was the sixth physician I sought out for an opinion.

Self-advocacy is often imagined as tenacity, but it was just how I was channeling my frustration. Frustration at my body for being so mysterious and stumping a competent medical community. Frustration at not having answers. Looking for a diagnosis felt like being underwater and seeing the reflection of the sun, trying to swim to the surface but realizing you're too far below and running out of air. I firmly believe that if patients speak up in these moments and physicians use stories like mine to inform how they approach the unusual, maybe one fewer person will experience what I did.

FINAL DIAGNOSIS

Embryonal rhabdomyosarcoma of the pharynx.

This case was presented at Department of Otolaryngology–Head and Neck Surgery Grand Rounds at Mass Eye and Ear.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank Dr. Kathy M. Tran for organizing the case conference and Drs. Mark Varvares and Ivan Chebib for providing assistance with the preparation of an earlier version of the manuscript.

AUTHOR INFORMATION

[1] Department of Otolaryngology, Head and Neck Surgery, Mass Eye and Ear, Boston; [2] Department of Otolaryngology, Head and Neck Surgery, Massachusetts General Hospital, Boston; [3] Department of Otolaryngology, Head and Neck Surgery, Harvard Medical School, Boston; [4] Department of Radiology, Mass Eye and Ear, Boston; [5] Department of Radiology, Massachusetts General Hospital, Boston; [6] Department of Radiology, Harvard Medical School, Boston; [7] Department of Surgical Oncology, Dana–Farber Cancer Institute, Boston; [8] Department of Surgery, Brigham and Women's Hospital, Boston; [9] Department of Pediatrics, Dana–Farber Cancer Institute, Boston; [10] Department of Pediatrics, Boston Children's Hospital, Boston; [11] Department of Pathology, Massachusetts General Hospital, Boston; [12] Department of Pathology, Harvard Medical School, Boston.

REFERENCES

1. O'Sullivan B, Huang SH, Su J, et al. Development and validation of a staging system for HPV-related oropharyngeal cancer by the International Collaboration on Oropharyngeal cancer Network for Staging (ICON-S): a multicentre cohort study. Lancet Oncol 2016;17:440-51.
2. Rayess HM, Nissan M, Gupta A, Carron MA, Raza SN, Fribley AM. Oropharyngeal lymphoma: a US population based analysis. Oral Oncol 2017;73:147-51.
3. Goel AN, Badran KW, Braun APG, Garrett AM, Long JL. Minor salivary gland carcinoma of the oropharynx: a population-based analysis of 1426 patients. Otolaryngol Head Neck Surg 2018;158:287-94.
4. Pellitteri PK, Ferlito A, Bradley PJ, Shaha AR, Rinaldo A. Management of sarcomas of the head and neck in adults. Oral Oncol 2003;39:2-12.
5. Davicioni E, Anderson MJ, Finckenstein FG, et al. Molecular classification of rhabdomyosarcoma — genotypic and phenotypic determinants of diagnosis: a report from the Children's Oncology Group. Am J Pathol 2009;174:550-64.
6. Shern JF, Chen L, Chmielecki J, et al. Comprehensive genomic analysis of rhabdomyosarcoma reveals a landscape of alterations affecting a common genetic axis in fusion-positive and fusion-negative tumors. Cancer Discov 2014;4:216-31.
7. Skapek SX, Ferrari A, Gupta AA, et al. Rhabdomyosarcoma. Nat Rev Dis Primers 2019;5:1.
8. Nishimura R, Takita J, Sato-Otsubo A, et al. Characterization of genetic lesions in rhabdomyosarcoma using a high-density single nucleotide polymorphism array. Cancer Sci 2013;104:856-64.
9. Sultan I, Qaddoumi I, Yaser S, Rodriguez-Galindo C, Ferrari A. Comparing adult and pediatric rhabdomyosarcoma in the surveillance, epidemiology and end results program, 1973 to 2005: an analysis of 2,600 patients. J Clin Oncol 2009;27:3391-7.
10. Crist WM, Garnsey L, Beltangady MS, et al. Prognosis in children with rhabdomyosarcoma: a report of the intergroup rhabdomyosarcoma studies I and II. J Clin Oncol 1990;8:443-52.
11. Shern JF, Selfe J, Izquierdo E, et al. Genomic classification and clinical outcome in rhabdomyosarcoma: a report from an international consortium. J Clin Oncol 2021;39:2859-71.
12. Ferrari A, Dileo P, Casanova M, et al.

Rhabdomyosarcoma in adults: a retrospective analysis of 171 patients treated at a single institution. Cancer 2003;98:571-80.
13. Raney RB, Walterhouse DO, Meza JL, et al. Results of the Intergroup Rhabdomyosarcoma Study Group D9602 protocol, using vincristine and dactinomycin with or without cyclophosphamide and radiation therapy, for newly diagnosed patients with low-risk embryonal rhabdomyosarcoma: a report from the Soft Tissue Sarcoma Committee of the Children's Oncology Group. J Clin Oncol 2011;29:1312-8.
14. Walterhouse DO, Pappo AS, Meza JL, et al. Reduction of cyclophosphamide dose for patients with subset 2 low-risk rhabdomyosarcoma is associated with an increased risk of recurrence: a report from the Soft Tissue Sarcoma Committee of the Children's Oncology Group. Cancer 2017;123:2368-75.
15. Arndt CAS, Stoner JA, Hawkins DS, et al. Vincristine, actinomycin, and cyclophosphamide compared with vincristine, actinomycin, and cyclophosphamide alternating with vincristine, topotecan, and cyclophosphamide for intermediate-risk rhabdomyosarcoma: Children's Oncology Group Study D9803. J Clin Oncol 2009;27:5182-8.
16. Hawkins DS, Chi Y-Y, Anderson JR, et al. Addition of vincristine and irinotecan to vincristine, dactinomycin, and cyclophosphamide does not improve outcome for intermediate-risk rhabdomyosarcoma: a report from the Children's Oncology Group. J Clin Oncol 2018;36:2770-7.
17. Grier HE, Krailo MD, Tarbell NJ, et al. Addition of ifosfamide and etoposide to standard chemotherapy for Ewing's sarcoma and primitive neuroectodermal tumor of bone. N Engl J Med 2003;348:694-701.
18. Eilber FR, Eckardt J. Surgical management of soft tissue sarcomas. Semin Oncol 1997;24:526-33.