Pediatric Surgical Pathology of the Larynx and Trachea

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Congenital Cysts: Saccular and Vallecular Cysts

Congenital cysts of the larynx are rare but potentially serious causes of airway obstruction in infants. According to De Santo and colleagues, congenital laryngeal cysts can be broadly classified as either saccular or ductal types [1]. "Ductal" cysts are far more common than "saccular" cysts and are caused by obstruction of the ducts of mucous glands [2]. "Saccular" cysts, on the other hand, are mucous distensions of the laryngeal saccule thought to be caused by atresia of the opening of the laryngeal ventricle.

Vallecular Cysts

Definition

A vallecular cyst is defined as a benign, unilocular cystic mass of variable size that arises from the lingual surface of the epiglottis and contains clear and noninfected fluid [3]. Other terms reported in the literature to describe vallecular cysts include mucous retention cyst, epiglottic cyst, base of tongue cyst, and ductal cyst.

Vallecular cysts are rare and have a reported incidence between 3.49 and 5.3 cases per 100,000 live births [4]. Histologically, the lining of the cyst may contain squamous and respiratory epithelium with mucous glands. As such, vallecular cysts are considered to be caused by either a ductal obstruction of a mucous gland or as a result of an embryological malformation.

Clinical Presentation

Vallecular cysts may be incidentally diagnosed during an antenatal ultrasound or MRI scan. Asymptomatic incidental cysts are also found in older children and adults, typically during intubation for unrelated surgical interventions. On the other hand, the most common clinical presentation in newborns and young infants includes a combination of stridor, respiratory distress, dysphonia, cyanotic episodes, cough, feeding difficulty, and failure to thrive. Stridor is the most common presenting symptom of a vallecular cyst. If unrecognized, cysts may enlarge or become infected resulting in severe airway compromise and death.

Definitive diagnosis is obtained with direct laryngoscopy by flexible endoscopy in the awake state or with rigid instrumentation under general anesthesia. As the cyst enlarges, it may cause prolapse of the epiglottis resulting in secondary laryngomalacia.

Differential Diagnosis

Lingual thyroid, thyroid remnant cyst, thyroglossal duct cyst, lymphatic malformation, cystic teratoma, dermoid cyst, hemangioma, and hamartoma.

Radiological Features

If a vallecular cyst is detected on antenatal ultrasound, a fetal MRI should be considered to further delineate the size and location of the lesion and the risk of airway obstruction at birth. In severe cases, an elective EXIT procedure or other perinatal intervention should be considered.

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A lateral neck soft tissue radiograph may reveal a soft tissue mass that alters the airway contour.

US—nonvascular, homogeneous, hypoechoic mass. Imperceptible wall. If infected may show septations and a thickened wall.

CT—a low-density, unilocular cystic lesion, thin wall, no enhancement post contrast.

MRI—Hypointense on T1; hyperintense on T2; no enhancement with gadolinium.

As the differential diagnosis includes a lingual thyroid, some clinicians recommend thyroid screening and a thyroid scan to clarify the diagnosis and avoid the risk of hypothyroidism after excision of the cyst.

It should be emphasized that if there are signs or symptoms of airway compromise, an infant should not be sent for cross-sectional imaging if sedation is required. An alternative approach would be to assess and secure the airway in the operating theatre first, then proceeding with the imaging study.

Management

Surgical management of the vallecular cyst can be achieved at the same time as a diagnostic procedure if performed under general anesthesia. Trans-oral, endoscopic excision or marsupialization is usually sufficient to relieve the obstruction. Simple aspiration of the cyst, however, is associated with a high rate of recurrence.

Marsupialization remains the most common surgical approach. This can be achieved with several modalities including CO_2 laser, microdebrider, electrocautery, coblation, and microlaryngeal instruments.

Clinical Examples

A 9-year-old female was undergoing a surgical procedure and at the time of intubation, an incidental vallecular lesion was identified. The patient did not have any airway compromise but complained of dysphagia. A suspension microlaryngoscopy revealed the lesion shown below in Fig. 11.1a. It was excised with a CO_2 laser (Fig. 11.1b). Histology is shown in Fig. 11.1c–f.

Saccular Cysts

Definition (Classification/Subtypes, Epidemiology, Genetics, etc.)

Saccular cysts represent distensions of the laryngeal saccule caused by obstruction at the ventricular orifice. The obstruction leads to the gradual accumulation of mucous secretions within the saccule that eventually leads to airway distortion and compromise. In the United Kingdom, the incidence has been conservatively estimated to be 1.40 per 100,000 live births [2].

Saccular cysts have been classified according to the direction of their extension and their histological origin [1, 5]. The classification system proposed by Forte and colleagues: [5] 1. applies to all congenital laryngeal cysts, including saccular cysts; 2. categorizes the extension and histological components of the cysts; and 3. predicates a recommended treatment (see Table 11.1).

Clinical Presentation

Saccular cysts have a similar clinical presentation as vallecular cysts. However, it has been reported that saccular cysts have a tendency to present earlier, often with significant stridor, relative to ductal cysts.

Differential Diagnosis

Thyroid remnant cyst, thyroglossal duct cyst, lymphatic malformation, cystic teratoma, hemangioma, and hamartoma.

Radiological Features

The radiological appearance on ultrasound, computed tomography, and MRI is similar to that seen for vallecular cysts. However, there may be intralaryngeal, paraglottic, and extralaryngeal extension (Fig. 11.2a–c). Cross-sectional imaging is strongly recommended to assess the extent of the lesion which may inform the most appropriate surgical approach.

Management

Similar to vallecular cysts, several reports recommend transoral endoscopic marsupialization at the time of diagnostic suspension laryngoscopy. However, if there is evidence of extralaryngeal extension, an open approach may be required to prevent recurrence, airway complications, and need for tracheostomy [5]. Open approaches described include laryngofissure, midline thyroidotomy, and a trans-thyrohyoid membrane approach.

Clinical Examples

A 4-year-old male presented with stridor, hoarseness, and dysphagia. Endoscopic assessment revealed a mass within

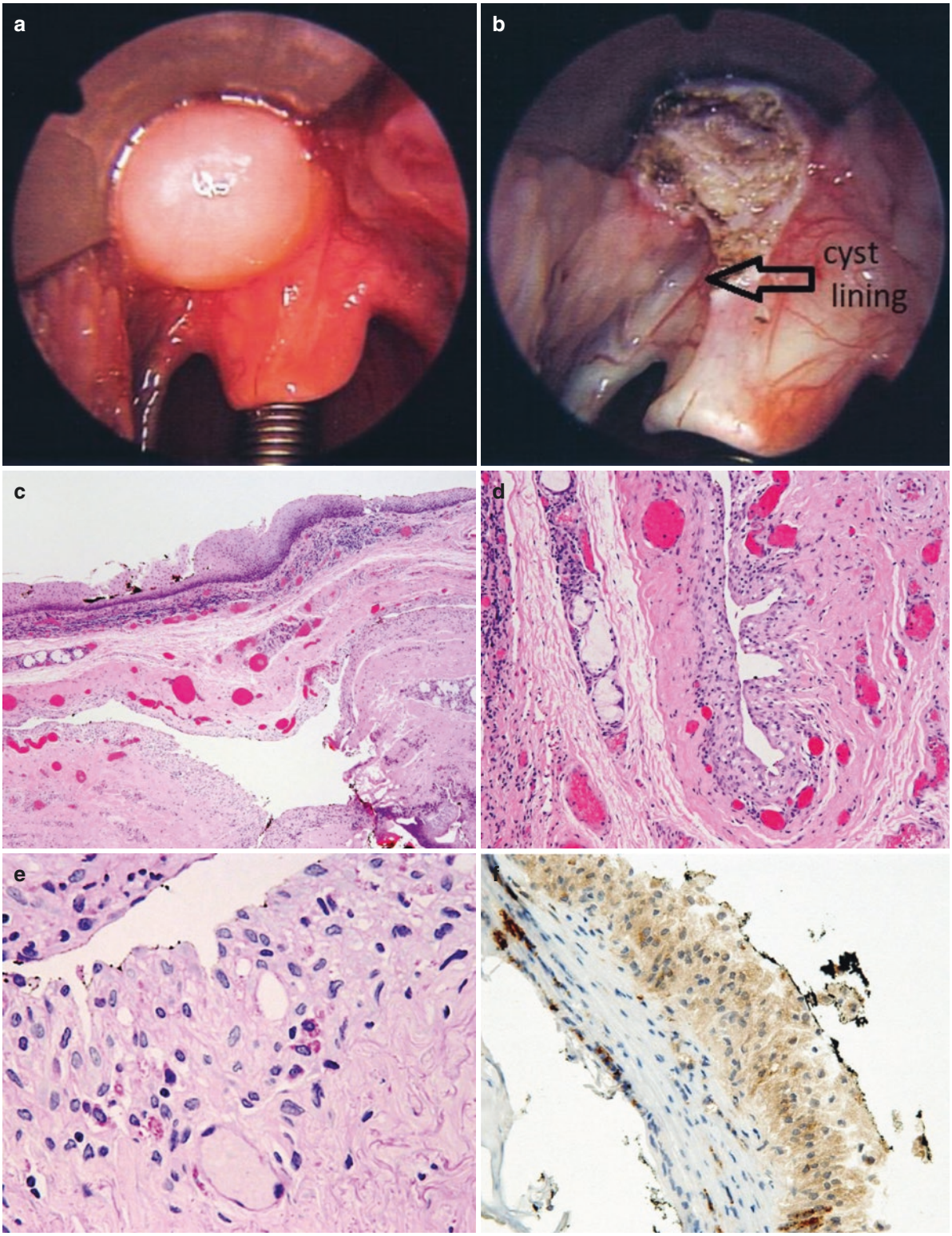

Fig. 11.1 (**a**) Endoscopic view of a vallecular cyst. (**b**) Cyst dissected and removed with CO2 laser. (**c**) Section shows a collapsed and empty cystic space deep to the surface. Most part of its inner lining, with the exception of a focal area, is denuded and is shown in (**d**). (**d**) The cyst wall is lined by nonkeratinizing stratified squamous epithelium. Adjacent to it is mucinous glandular tissues. (**e**) PASD stain shows that in the partially denuded areas there are infiltrates of macrophages. Some of them contain granules in their cytoplasm that stain red. This finding demonstrates the presence of mucin phagocytosed by these macrophages. (**f**) Immunostain with CD68, a macrophage marker. This demonstrates the presence of large numbers of chronic inflammatory macrophages (stained brown) in the denuded portion of the cyst lining

the left supraglottis (Fig. 11.3). Imaging suggested that this represented a Type 1 saccular cyst. The cyst was marsupialized with microlaryngoscopy and CO_2 laser as shown in Fig. 11.3 below.

Table 11.1 Classification system of laryngeal cysts proposed by Forte et al. [5]

Type I—Intralaryngeal	Cyst remains within the confines of larynx (Endodermal elements only)
Type II—Extralaryngeal Extension	Cyst extends beyond the larynx
	IIa—Endodermal elements only
	IIb—Endodermal and mesodermal elements

Vocal Fold Granuloma

Definition (Classification/Subtypes, Epidemiology, Genetics, etc.)

Vocal fold granulomas are unilateral or bilateral round lesions emanating from the vocal process of the arytenoid cartilages. They are usually caused by trauma and aggravated by extraesophageal reflux [6]. As such, a vocal fold granuloma is a reactive and reparative process resulting in the deposition of granulation tissue and fibrosis. The most common forms of trauma include endotracheal intubation, voice misuse and overuse, and external laryngeal blunt trauma. Endotracheal intubation, especially if prolonged, traumatic, inappropriately sized, and subject to repeated

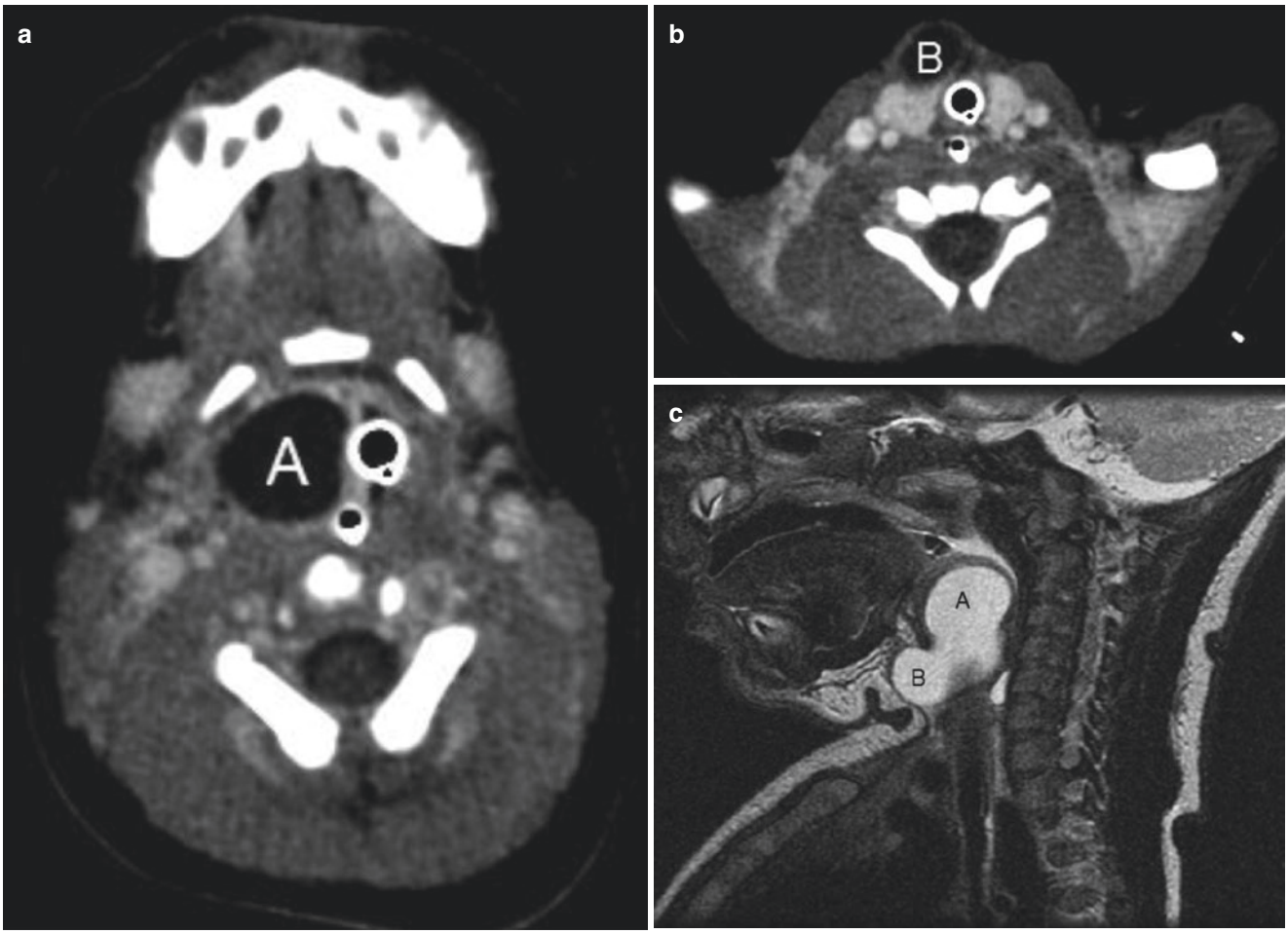

Fig. 11.2 (**a**) Axial contrast enhanced CT of a newborn with a large obstructive laryngeal cyst taken at the level of the hyoid bone. The intralaryngeal component is labeled (A). (**b**) Axial CT of same newborn at the level of the thyroid gland showing the extralaryngeal component labelled (B). (**c**) Sagittal T2 MRI showing both the intralaryngeal (A) and the extralaryngeal (B) components of the cyst. Surgical excision was performed through an external approach given these findings on imaging

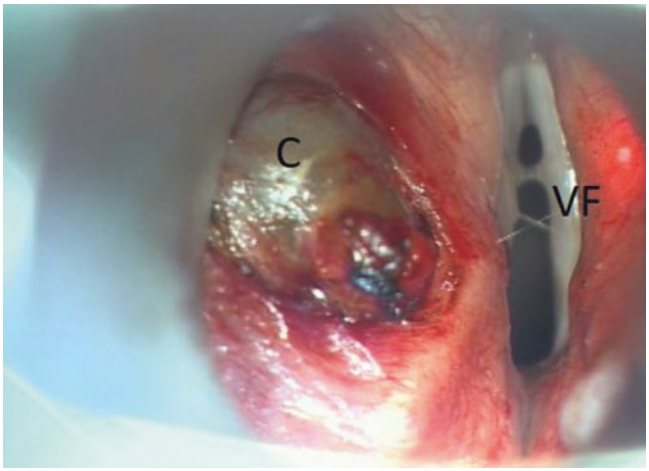

Fig. 11.3 Microlaryngoscopy shows cyst (C) in left supraglottic area was marsupialized using CO_2 laser. The right vocal fold is labeled VF

movement, is the most common inciting cause of granulation tissue formation. Inherent patient characteristics may also predispose to granuloma formation as some patients develop lesions even after short, uneventful intubations. In adult patients, unilateral granulomas may indicate the presence of a carcinoma, especially if the patient has other important risk factors for developing malignancy.

Clinical Presentation

Patients may present with dysphonia, dry cough, foreign body sensation, and pain with speaking and swallowing. If the lesion continues to increase in size, the young patient may present with airway obstructive symptoms requiring immediate surgical intervention.

Diagnosis is established with either awake flexible endoscopy or direct laryngoscopy under general anesthesia.

Differential Diagnosis

Granulomatous diseases of the larynx (e.g., tuberculosis), amyloidosis, dysplasia, and squamous cell carcinoma.

Radiological Features

The condition is not typically investigated with imaging in children.

Management

The management of vocal fold granulomas includes minimizing ongoing trauma to the vocal folds, speech therapy, and medical management in the form of inhaled or systemic steroids, and proton pump inhibitors. Recurrences may be treated with local injection of steroids or botulinum toxin into the thyroarytenoid muscle to decrease the impact against the opposite vocal fold during phonation. If there are symptoms of airway obstruction, surgical excision of the granuloma with microlaryngeal instruments may be required. If surgery is required, adjuvant treatment with steroids or botulinum toxin is advised [7].

Clinical Examples

A 15-month-old male was intubated for 24 h postrepair of a ventricular septal defect. He was extubated uneventfully and was discharged home with no airway symptoms. After two months, he returned to hospital with stridor and increased work of breathing. Endoscopy revealed the presence of a vocal fold granuloma emanating from the left arytenoid area causing near total obstruction of the glottic lumen. The lesion was excised with CO_2 laser as shown below (Fig. 11.4a, b). Histology revealed a granuloma (Fig. 11.4c–e).

Vocal Fold Nodules

Definition

Vocal fold nodules (VFNs) are bilateral, focal thickenings of the epithelium and lamina propria, typically at the junction of the anterior 1/3 and posterior 2/3 of the vocal folds [8]. This location is common as this is the point of maximal contact between the two vocal folds during phonation. Vocal abuse results in repetitive trauma at this contact point which in turn causes an inflammatory reaction and damage to the superficial layer of the lamina propria [9].

Clinical Presentation

VFNs are the most common cause of dysphonia in children [10]. VFNs are identified in 35–78% of children with dysphonia [11–15]. They are more predominant in males (2:1) in the preadolescent age group [11, 16]. However, after the onset of puberty, persistence of symptoms and nodules is more likely in females [12]. Predisposing factors for the development of VFNs include an extroverted, communicative personality, recurrent upper respiratory tract infections, mouth breathing, laryngopharyngeal reflux, velopharyngeal insufficiency, and hearing impairment [17–21].

Commonly, children present with a history of voice misuse and overuse. The hoarseness is typically worse at the end of the day or after activities that require exertion of the voice (sports, singing, socializing, etc.). In severe cases, children may be aphonic.

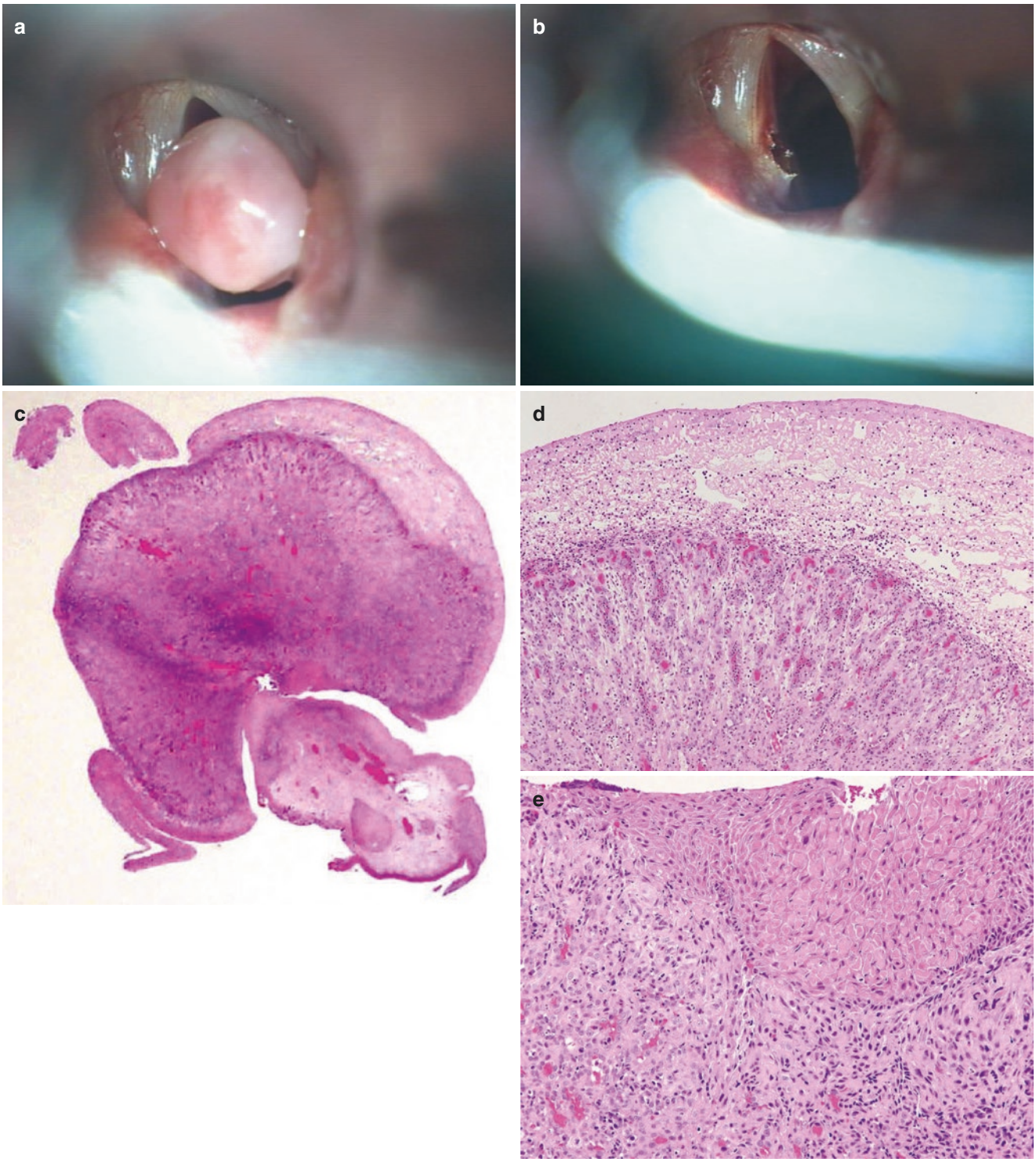

Fig. 11.4 (**a**) Microlaryngoscopy showing obstructive granuloma of larynx. (**b**) Microlaryngoscopy showing obstructive granuloma of larynx after removal. The lesion was based from the left vocal process. (**c**) H&E stain of granulation polyp. Although the term granuloma is applied to these lesions, histological section shows this mucosal polypoid nodule comprises nongranulomatous fibroinflammatory granulation tissues that is ulcerated (left side of the surface of the nodule shown) and covered by a fibrinous exudate (right side of the surface of this nodule shown). Granulomatous inflammation characterized by the presence of multinucleated giant cell infiltrates are absent. (**d**) H&E. Surface of the mucosal polypoid tissue is covered by a friable fibrinous exudate with infiltrates of chronic inflammatory cells. The matrix of the polypoid tissue comprises compact proliferations of small blood vessels within mildly fibrotic stroma. (**e**) H&E. Surface of the nonulcerated portion of the mucosal polypoid tissue shows a lining of squamous cell epithelium that has undergone reactive hyperplasia. The mucosa beneath is replaced by a mildly fibrotic granulation tissue

When examined endoscopically, VFNs appear as discrete, bilateral, symmetrical nodules. During phonation, the nodules prevent full closure of the glottis resulting in an "hourglass" shaped glottic opening with a gap anterior and posterior to the location of the nodules. These gaps result in turbulent airflow and inefficient vocal fold vibration which is perceived by the listener as hoarseness.

Differential Diagnosis

Vocal fold cysts, polyps, and vocal fold edema.

Radiological Features

The condition is not typically investigated with imaging in children.

Management

Any child presenting with persistent hoarseness should be referred for further assessment, preferably to a center with a voice clinic that has expertise with pediatric voice disorders. A comprehensive evaluation includes perceptual-auditory vocal analysis by an experienced speech-language pathologist using validated tools, objective computer assisted voice analysis, application of validated voice-related quality of life tools, and direct or indirect visualization of the vocal folds. Flexible nasolaryngoscopy or rigid laryngoscopy is preferably performed in the clinic. In the very uncooperative child, this may need to be completed in the operating theatre.

The primary goals of treatment are the curtailing of the vocal behaviors that caused the repetitive injury to the vocal folds, the adoption of vocal hygiene strategies, and the introduction of voice therapy. In the compliant patient, voice therapy has been shown to be effective in treating VFNs [22]. Surgical excision should only be considered in a patient who has demonstrated high compliance with nonsurgical treatment but remains with a very dysfunctional voice, or if a more concerning diagnosis is suspected.

Clinical Example

A 6-year-old male presents with worsening hoarseness and a history of chronic voice overuse and shouting. Figure 11.5 demonstrates the typical appearance of vocal fold nodules.

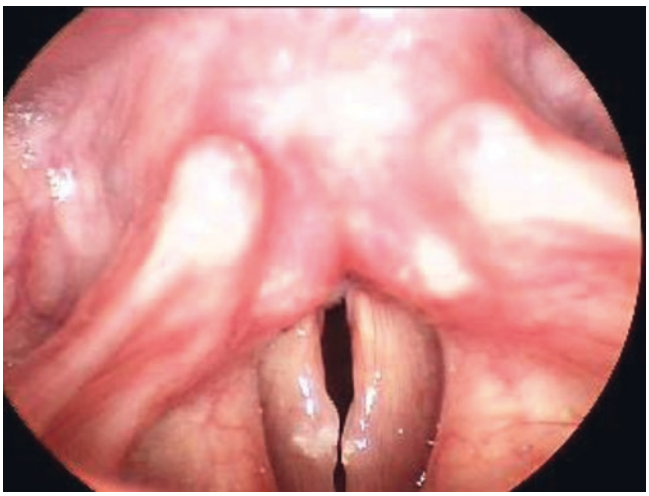

Fig. 11.5 Bilateral vocal fold nodules as seen on rigid laryngoscopy performed in the clinic setting. The vocal fold nodules come into contact during phonation resulting in an hourglass shaped opening of the glottis. Thick, white mucus commonly collects over the nodules

Recurrent Respiratory Papillomatosis (Fig. 11.5)

Definition

Juvenile-onset recurrent respiratory papillomatosis (JoRRP) is the most common benign neoplasm of the larynx in children. It is a rare condition with a reported incidence between 0.24 and 4.3 per 100,000 North American children under the age of 14 years [23, 24]. It is caused by the human papillomavirus (HPV), subtypes HPV 6 and 11. Several risk factors for the acquisition of JoRRP have been identified and include young maternal age, first born child, active maternal genital warts during pregnancy, prolonged delivery duration greater than 10 h, and genetic and immune response factors [25]. The most common staging system for JoRRP is the Derkay–Coltrera score which summarizes the location and size of the lesions in the airway [26]. The score, however, does not necessarily capture the clinical aggressiveness of the disease. A consensus definition of aggressive disease is a patient that requires more than 3–4 debulking procedures per year.

Clinical Presentation

Children with JoRRP present with a history of progressive hoarseness, cough, stridor, and increased work of breathing. With advanced disease, they may present with apnea and respiratory distress. Children typically present before the age of 4 years, but may present at any age. In the initial stages of the disease, children may be misdiagnosed as having vocal fold nodules or asthma. Any child with persistent voice symptoms or airway symptoms (especially if the mother has any of the risk factors for JoRRP acquisition listed above) should be referred to an otolaryngologist for an urgent evaluation.

Awake flexible nasolaryngoscopy should be performed in children with suspected JoRRP. The typical finding would be the presence of multiple wart-like lesion in the glottic and supraglottic area. HPV has a tropism for transitional epithelium and as such, papillomas are usually located on the vocal folds and anterior commissure. Lesions, however, have also been found in the nasopharynx, laryngeal surface of the epiglottis, arytenoids, subglottis, trachea, and bronchi. Patients with JoRRP should be evaluated with direct laryngoscopy and bronchoscopy in the operating theatre for biopsy, staging, and removal of the lesions. Typically the lesions recur and patients require multiple debriding procedures to manage their disease.

The majority (60%) of patients experience an improvement in the severity of their disease over time [27]. However, some may have worsening with rapid regrowth of the lesions, extension to the distal airway, pulmonary disease, or malignant transformation.

Differential Diagnosis

Vocal fold nodules, vocal fold granuloma, vocal fold polyp, glottic or subglottic stenosis, granulomatous disease, and Gorlin–Goltz syndrome.

Radiological Features

Plain radiographs of the chest are usually negative unless the papillomas have spread to the trachea, bronchi, or lung parenchyma. With distal airway involvement, radiographs may reveal intratracheal or mainstem bronchi lesions, atelectasis, and solid or cavitated pulmonary nodules. If suspicious lesions are identified, further imaging with helical CT of the chest is strongly recommended.

Management

Children with laryngeal papillomas require suspension microlaryngoscopy and bronchoscopy in the operating theatre for staging and removal of the lesions. These procedures present anesthetic challenges and should only be performed in centers with experience performing microlaryngoscopy in children.

Several techniques have been used to remove the papillomas including cold instrumentation, microdebrider, laser, and coblator, depending on surgeon preference. A tracheotomy should be avoided as it predisposes the patient to distal airway spread of the disease.

Severe cases may require adjuvant therapy in the form of either intralesional (cidofovir, bevacizumab, etc.) or systemic (interferon, indole-3-carbinol, bevacizumab, HPV vaccination, etc.) treatments.

All patients should be monitored for regrowth of the lesions with surveillance endoscopies performed at regular intervals.

Clinical Examples

Case 1

A 14-year-old female presents with recurrent dysphonia and stridor after repeated surgical resection of wart-like lesions on the vocal folds. She requires surgery every 4 months and has been subjected to 22 surgical procedures since presenting at 6 years of age. Surgical resections were performed with a microdebrider as shown in Fig. 11.6a below. A biopsy of the respiratory papillomas demonstrated a characteristic histological appearance and stained positive for the human papillomavirus with in situ hybridization techniques (Fig. 11.6b–e).

Case 2

A 15-year-old female with Gorlin-Goltz syndrome presented with dysphonia and globus sensation. Endoscopic examination revealed “papilloma-like” lesions on the epiglottis and right glossoepiglottic fold (Fig. 11.7a). The lesions were biopsied and revealed the following histopathological appearances with prominent lymphoid follicular hyperplasia (Fig. 11.7b–d).

Laryngeal Malignancy

Definition

Laryngeal malignancies are extremely rare in childhood. A recent review of The National Cancer Database in the USA identified 22 cases of squamous cell carcinoma of the larynx in children 0–19 years of age from 2004 to 2013 [28]. A systematic review of the English literature (up until 2016) identified only 16 cases of laryngeal squamous cell carcinoma in children 0–20 years of age [29]. Nonepithelial malignancies of the larynx (synovial cell sarcoma, chondrosarcoma, rhabdomyosarcoma, etc.) are rarely reported. Laryngeal malignancies, regardless of age are staged according to the TNM staging system.

Clinical Presentation

Patients presenting with laryngeal malignancies present with dysphonia, stridor, cough, hemoptysis, dysphagia, and increased work of breathing. All children presenting with these symptoms should be examined with flexible nasolaryngoscopy or direct laryngoscopy and bronchoscopy in the operating theatre for staging and biopsy.

Children with laryngeal malignancies may have a medical condition that increases the risk of developing a malignancy.

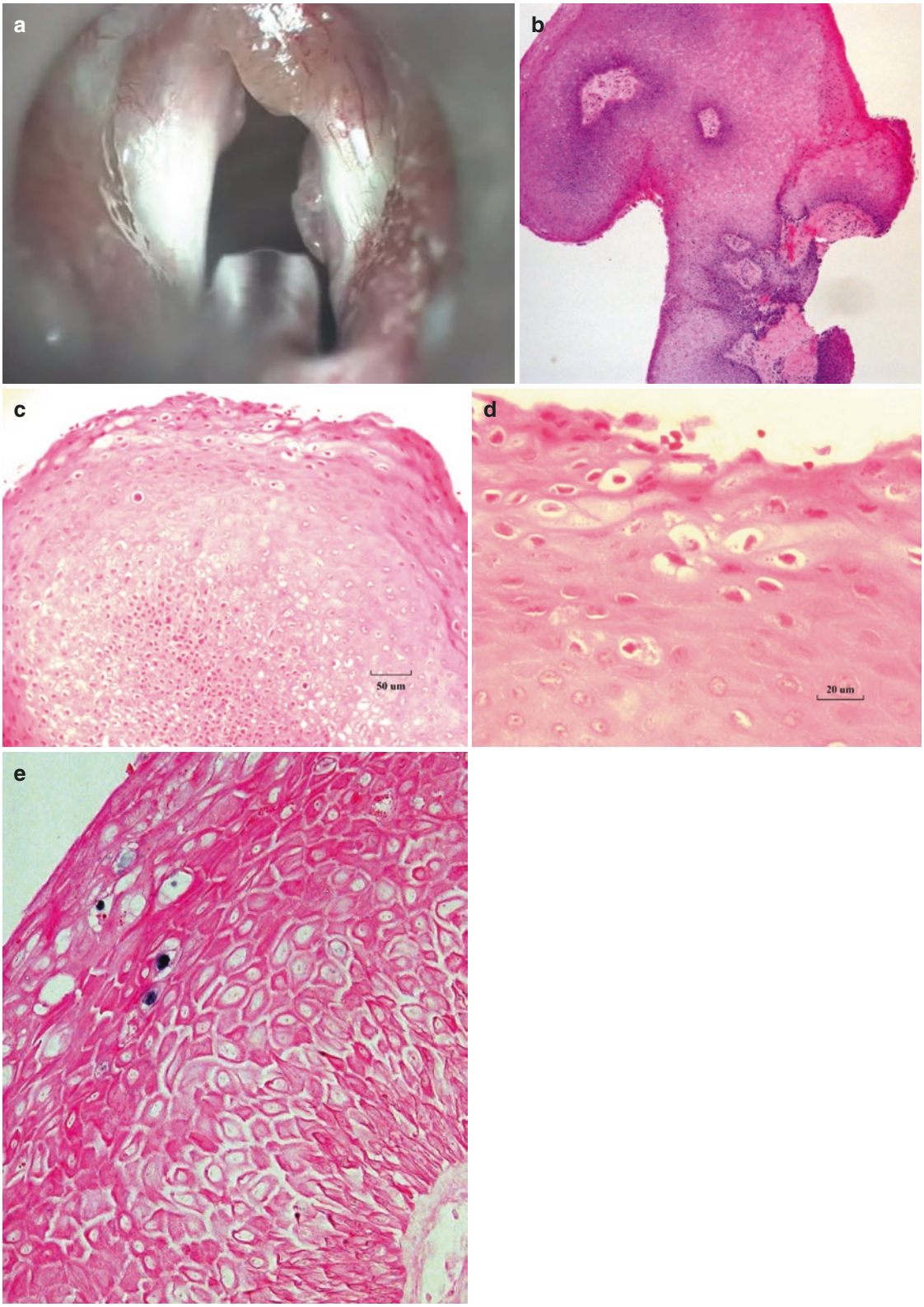

Fig. 11.6 (**a**) Microlaryngoscopy showing multiple papillomata. (**b**) H&E stain of this papillomatous tissue shows marked squamous hyperplasia. (**c**) H&E. Higher magnification of the hyperplastic squamous epithelium shows that the squamous cells retain a bland cytological appearance and maintain polarity and normal maturation features as they ascended to the surface. (**d**) H&E. Some of the squamous cells in the superficial regions of the squamous epithelium have koilocytic changes which are characterized by cytoplasmic clearing with a dark shrunken nucleus with hyperchromasia. (**e**) In situ hybridization (ISH) for HPV 6/11 show the presence of infected squamous cells (blue color stained nuclei) within the population of keratinocytes that have koilocyte appearances

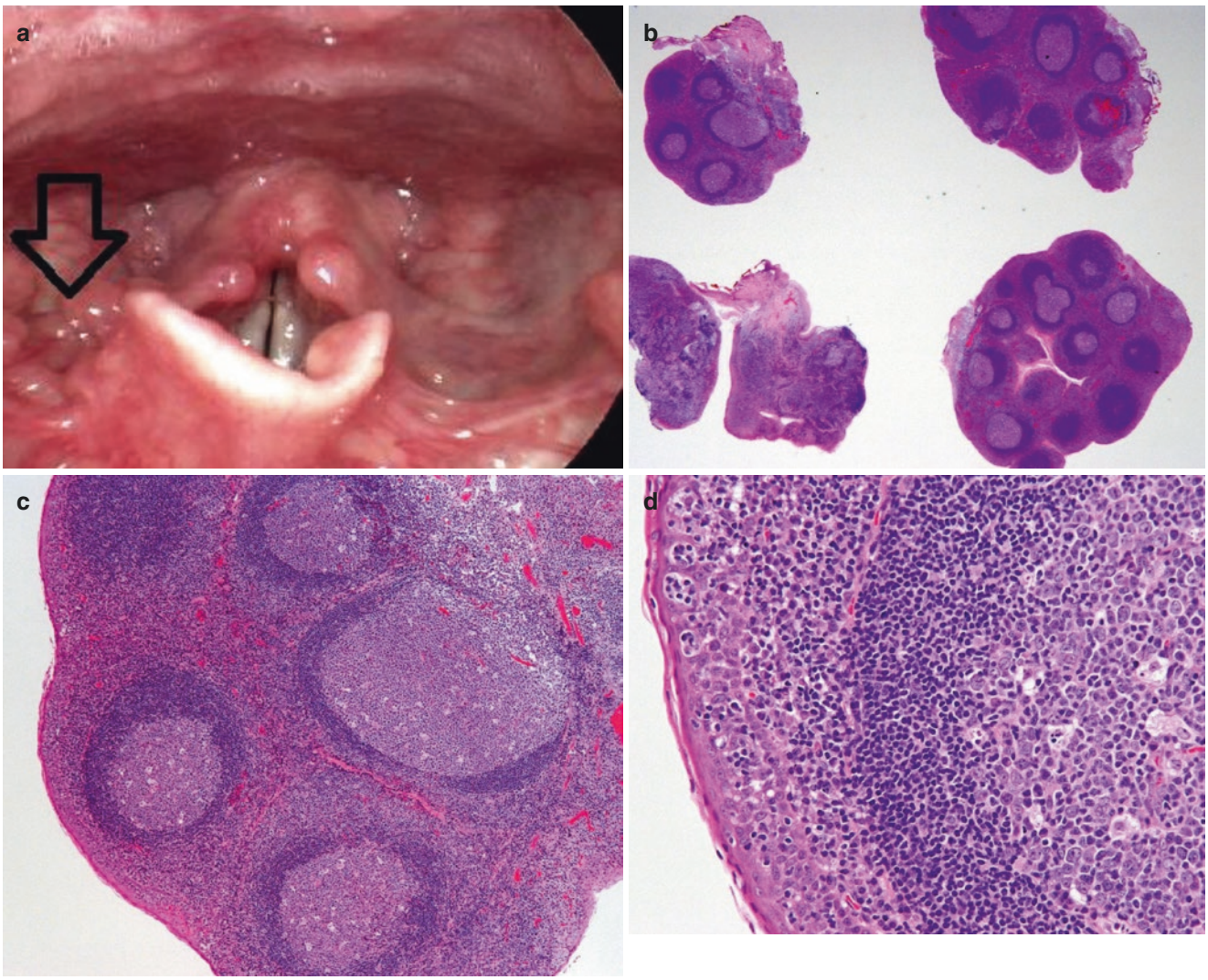

Fig. 11.7 (**a**) Papilloma-like lesions on the epiglottis and right glossoepiglottic fold area (*arrow*). (**b**) H&E stain of the mucosal tissue contains normal reactive lymphoid follicles. (**c**) The secondary lymphoid follicles are well formed, widely spaced apart, separated by a mildly reactive interfollicular T-cell zone (**d**). The squamous epithelium overlying the reactive germinal centers are normal, with increased infiltrates of reactive mucosa associated lymphocytes

Conditions that predispose children to malignancies include Li-Fraumeni syndrome, Fanconi anemia, immunosuppression, previous radiotherapy, HIV infection, HPV infection with high risk HPV subtypes (HPV 16, 18).

Differential Diagnosis

Hemangioma, vascular malformation, granular cell tumor, chondroma, schwannoma, and laryngeal papilloma.

Radiological Features

Children with laryngeal malignancies require cross-sectional imaging of the neck with computed tomography and magnetic resonance to determine the extent of the tumor and identify metastatic adenopathy.

Management

Laryngeal malignancies require multimodality therapy that may include surgery (endoscopic, partial laryngectomy, and total laryngectomy), chemotherapy, and/or radiotherapy. The specific treatment will depend on the histopathology, stage of the disease, and patient-specific factors. The treatment regimen should be decided by consensus at a formal Tumor Board.

Children presenting with severe airway compromise may require a tracheostomy to secure the airway during treatment.

Clinical Examples

An 8-year-old male presented to the emergency department with progressive stridor, aphonia, and weight loss. Cross-sectional imaging demonstrated a very large mass involving the thyroid and cricoid cartilages (Fig. 11.8a, b). Endoscopic examination revealed a large necrotic mass involving the supraglottis and lateral pharyngeal wall with almost complete obstruction of the airway (Fig. 11.8c). An emergency tracheostomy was performed to stabilize the airway. Once the airway was established, a biopsy of the lesion was performed which revealed a synovial cell sarcoma (Fig. 11.8d–h).

Given the size and extent of the tumor, neoadjuvant chemotherapy and radiotherapy were administered to decrease the size of the primary tumor and facilitate surgical resection. The tumor responded to treatment as demonstrated in the following computed tomography images 6 weeks after initiating treatment.

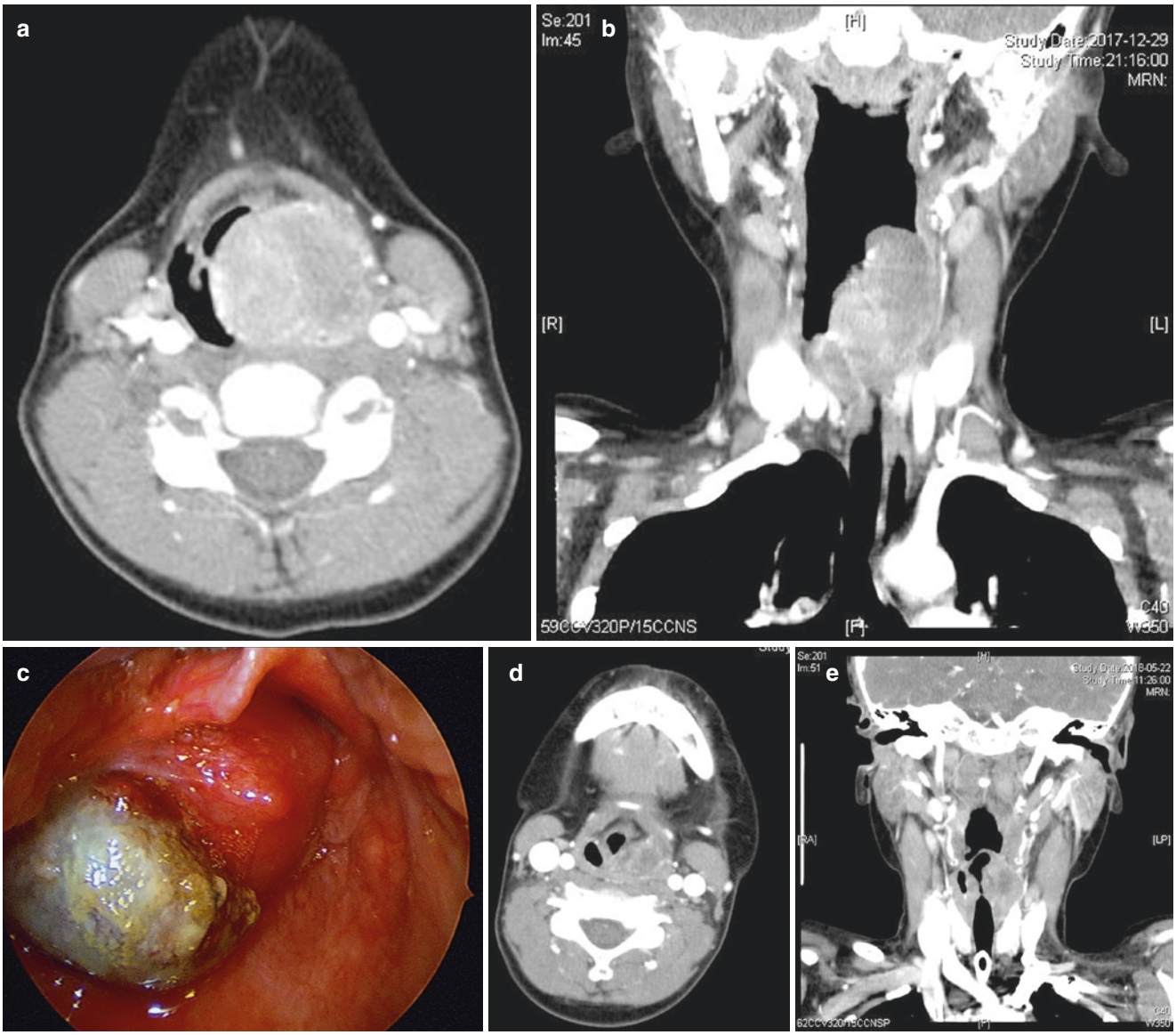

Fig. 11.8 (**a**) Axial CT with contrast shows large obstructive mass. (**b**) Coronal CT with contrast shows a heterogeneous enhancement of the mass. (**c**) Photo taken after performing emergency tracheotomy shows large mass obstructing the airway. (**d**) Axial CT showing good tumor response after neoadjuvant chemotherapy and radiotherapy. (**e**) Coronal CT showing good tumor response after neoadjuvant chemotherapy and radiotherapy. (**f**) Gross appearance of resected tumor. (**g**) H&E. Left Pharyngeal mass biopsy shows a solid monophasic spindle cell growth formed by interlacing short fascicles. (**h**) H&E. These tumor cell fascicles are made up of spindle cells with oval, elongated, and frequent pleomorphic hyperchromatic nuclei and inconspicuous nucleoli. They have eosinophilic fibrillar cytoplasm fibrils. Mitotic figures are present (left edge, at 10 o'clock position). Cytogenetic analysis was positive for *SS18(SYT)* gene rearrangement that is typical of synovial sarcoma (not shown)

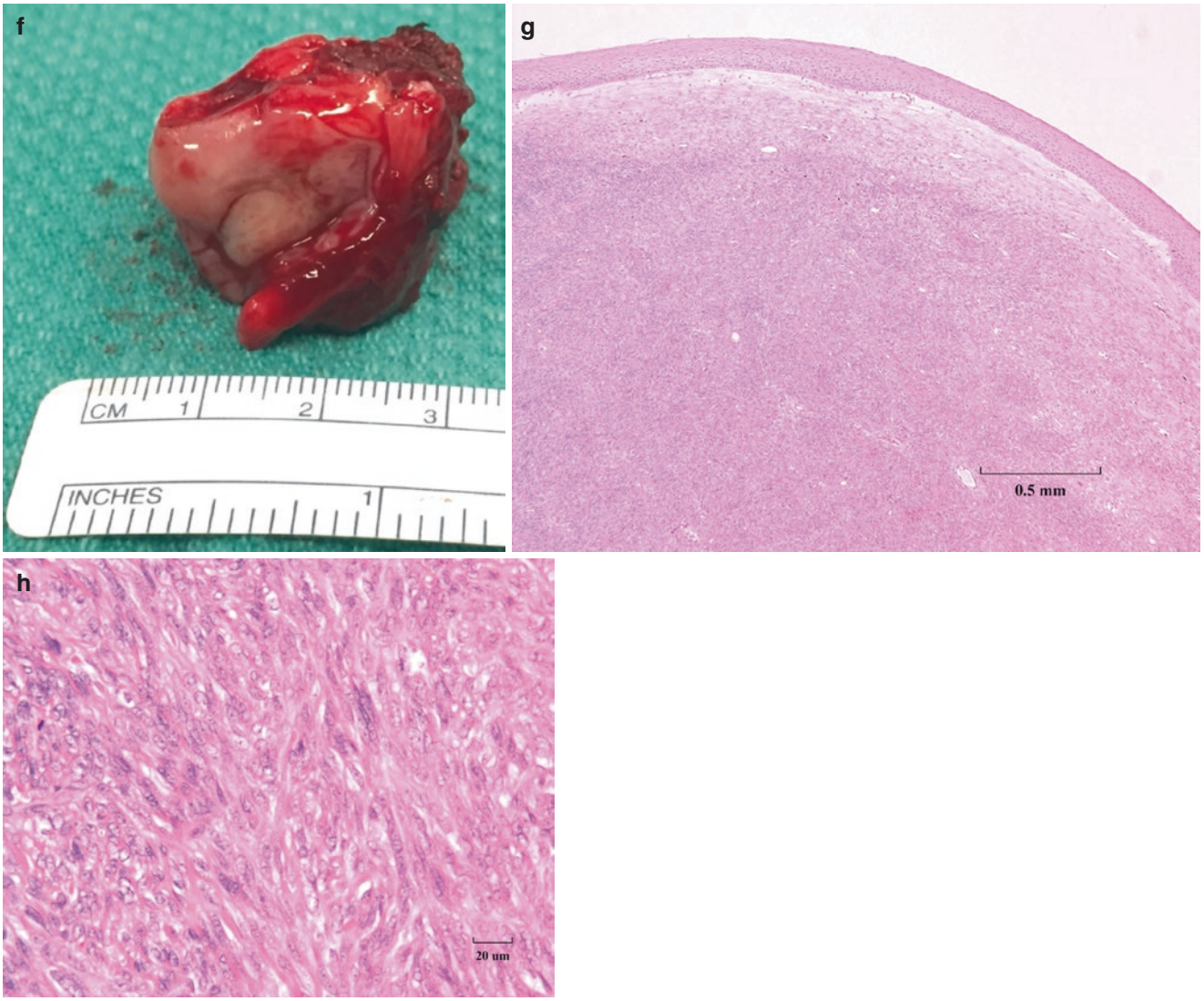

Fig. 11.8 (continued)

The tumor decreased in size to the point where it was possible to excise the lesion with a left supra-cricoid vertical hemilaryngo-pharyngectomy. The hemi-larynx was reconstructed with a radial forearm free flap. A comprehensive level I-V neck dissection was also performed. The surgical margins were clear and the neck nodes negative.

Subglottic Cyst

Definition

Subglottic cysts are mucous containing cysts predominantly identified in infants with a history of prematurity and neonatal intubation [30, 31]. They are caused by the retention of mucus from native mucous glands as a result of subepithelial fibrosis induced by local trauma. The most common traumatic injury is endotracheal intubation. The role of the number and duration of intubations on the risk of developing a subglottic cyst is not known. However, it has been suggested that laryngopharyngeal reflux may contribute to the development of a subglottic cyst [32].

The estimated incidence has been reported at 1.9 per 100,000 live births and between 0.05% and 0.69% of live premature births (between 24 and 27 weeks) [33, 34].

Clinical Presentation

Infants may present with biphasic stridor, recurrent atypical croup, dysphonia, dyspnea, dysphagia, and failure to thrive. If there is a history of prematurity and/or intubation in the neonatal period, subglottic cyst should be considered as the cause of the respiratory compromise.

Subglottic cysts may not be visualized with flexible nasolaryngoscopy. However, a soft tissue radiograph of the neck

in the anterior-posterior plane (croup series) may reveal an asymmetric subglottic narrowing. A definitive diagnosis is achieved in the operating theatre with direct laryngoscopy and bronchoscopy.

Differential Diagnosis

Subglottic stenosis, laryngomalacia, vocal fold insufficiency, subglottic hemangioma, croup, and foreign body aspiration.

Radiological Features

As described above, a croup series may reveal an asymmetric subglottic narrowing suggestive of subglottic pathology including a cyst or hemangioma. Cross-sectional imaging is not required or advised if the patient has a significantly compromised airway.

Management

Definitive management of subglottic cysts is achieved with microlaryngoscopy and marsupialization of the cyst [35]. This can be achieved with cold instruments, laser, and microdebrider. Postoperative intubation may be required in medically complex patients, and in patients with a persistently compromised airway after marsupialization. If possible, recovery without intubation is desirable.

It should be noted that recurrence of subglottic cysts is common, occurring in 25–70% of infants [36]. As such, ongoing monitoring is strongly advised which includes interval bronchoscopies in the operating theatre.

Clinical Examples

The following endoscopic images (Figs. 11.9, 11.10 and 11.11) were obtained from infants that were born premature and have a history of neonatal endotracheal intubation. The subglottic cysts can be single, multiple, small, or significantly obstructing the airway.

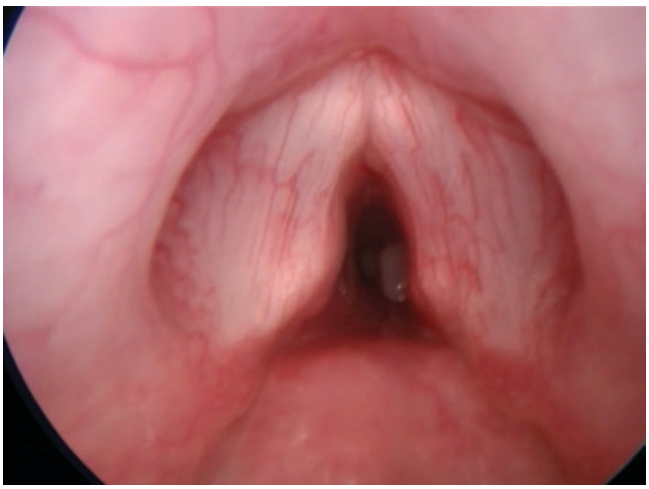

Fig. 11.9 Endoscopic view of the glottis demonstrates the presence of a cyst emanating from the right lateral aspect of the subglottis

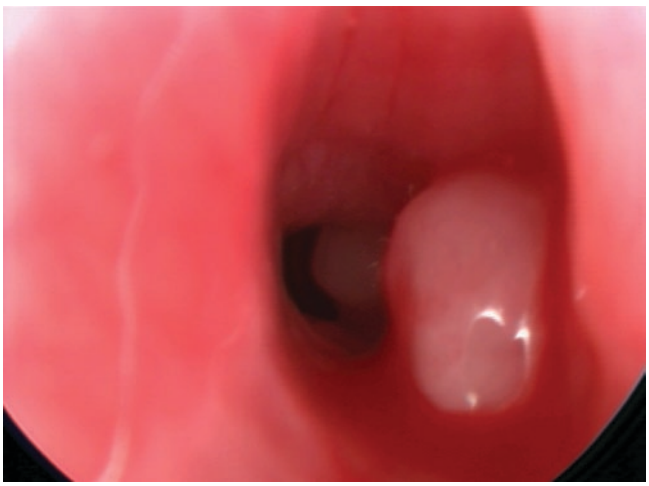

Fig. 11.10 A closer endoscopic view reveals the presence of a second subglottic cyst

Infantile (Subglottic) Hemangioma

Definition

Infantile hemangiomas comprise the most common benign head and neck tumors in children [37]. Infantile hemangiomas may arise in the subglottic lumen (subglottic hemangioma) in isolation or contemporaneously in other locations. The presence of any cutaneous hemangioma, especially in the beard distribution (chin, anterior neck, lower lip) and the onset of airway symptoms greatly increases the odds of having a subglottic hemangioma [38].

According to the International Society for the Study of Vascular Anomalies (ISSVA), infantile hemangiomas are classified as *focal*, *segmental*, or *indeterminate*. Within the larynx, they can be classified as left-sided, right-sided, bilateral, or circumferential [39]. Left-sided subglottic hemangiomas are the most common presenting location.

Clinical Presentation

Infantile hemangiomas are not apparent at birth. Rather, they become clinically evident in the first 1–3 months of life as the lesions undergo a period of rapid proliferation. The onset of biphasic stridor, croup-like cough, apnea, and "dying

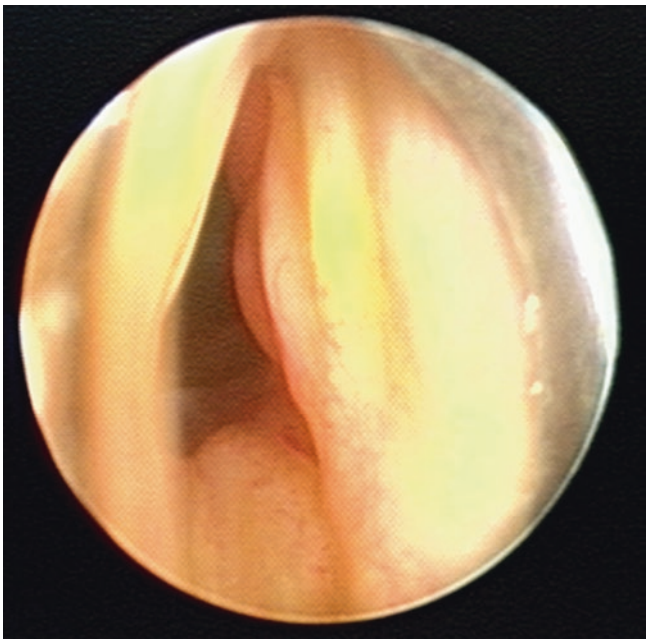

Fig. 11.11 Endoscopic examination of the larynx reveals multiple, sessile subglottic cysts

spells" at 2–3 months of age in a previously asymptomatic infant should strongly raise the suspicion of a subglottic hemangioma. This is particularly true if one or more cutaneous hemangiomas are present.

The untreated infantile hemangioma continues to proliferate in the first year of life, although at a lower rate of growth. As such, the worsening of signs and symptoms of airway compromise should be anticipated. Infantile hemangiomas then undergo involution in the subsequent years with 50% completely involuted by 5 years and 90% by 9 years of age [40].

Infants may present to the emergency department with worsening of airway symptoms during an upper respiratory tract infection leading to a presumed diagnosis of croup. A temporary response to nebulized epinephrine and oral steroids may further mislead the treating physician to the wrong diagnosis of croup.

Subglottic hemangiomas may be visualized during awake flexible nasolaryngoscopy. However, confirmation of diagnosis and staging of severity typically requires direct laryngoscopy and bronchoscopy. A biopsy is avoided due to the risk of hemorrhage.

Differential Diagnosis

Congenital hemangioma, kaposiform hemangioendothelioma, vascular malformation, subglottic stenosis, subglottic cyst, croup, and vocal fold insufficiency.

Radiological Features

Soft tissue radiographs of the neck and chest (croup series) will demonstrate subglottic narrowing. Asymmetric narrowing arising from the left side strongly suggests the presence of a subglottic hemangioma.

Cross-sectional imaging with computed tomography or magnetic resonance may be required if the hemangioma extends beyond the larynx or if the differential diagnosis includes a vascular malformation or other vascular tumor.

Management

The management of subglottic hemangiomas has evolved greatly over the past 20 years. Traditional treatment modalities have included systemic corticosteroids, intralesional steroids, endoscopic resection with CO_2 laser, open surgical resection via laryngofissure and tracheostomy. Treatment with steroids was typically prolonged and children developed serious side-effects including immune compromise, hypertension, insulin resistance, adrenal suppression, and Cushingoid body changes. Excision with laser was limited to smaller, focal lesions to avoid complications such as subglottic scarring and stenosis.

In 2008, the first report of rapid regression of infantile hemangiomas following the administration of the nonselective beta-blocker propranolol was published [41]. This report has transformed the management of subglottic hemangioma and all new diagnoses are now treated medically with beta-blocker therapy. Most institutions follow established protocols for the introduction of beta-blocker therapy to infants to avoid serious complications such as bradycardia, hypotension, bronchospasm, and the masking of signs of hypoglycemia.

Clinical Examples

A 2-month-old female presented with recurrent croup-like symptoms without evidence of an upper respiratory tract infection. The symptoms improved with systemic steroids but the stridor would return when the medications were discontinued.

A soft tissue radiograph of the neck revealed an asymmetrical subglottic narrowing with soft tissue arising from the left side of the subglottis (Fig. 11.12a). The diagnosis of subglottic hemangioma was confirmed on endoscopy (Fig. 11.12b). The patient was treated with systemic beta-blocker medication but required intubation at the end of the rigid bronchoscopy. The final image demonstrates the

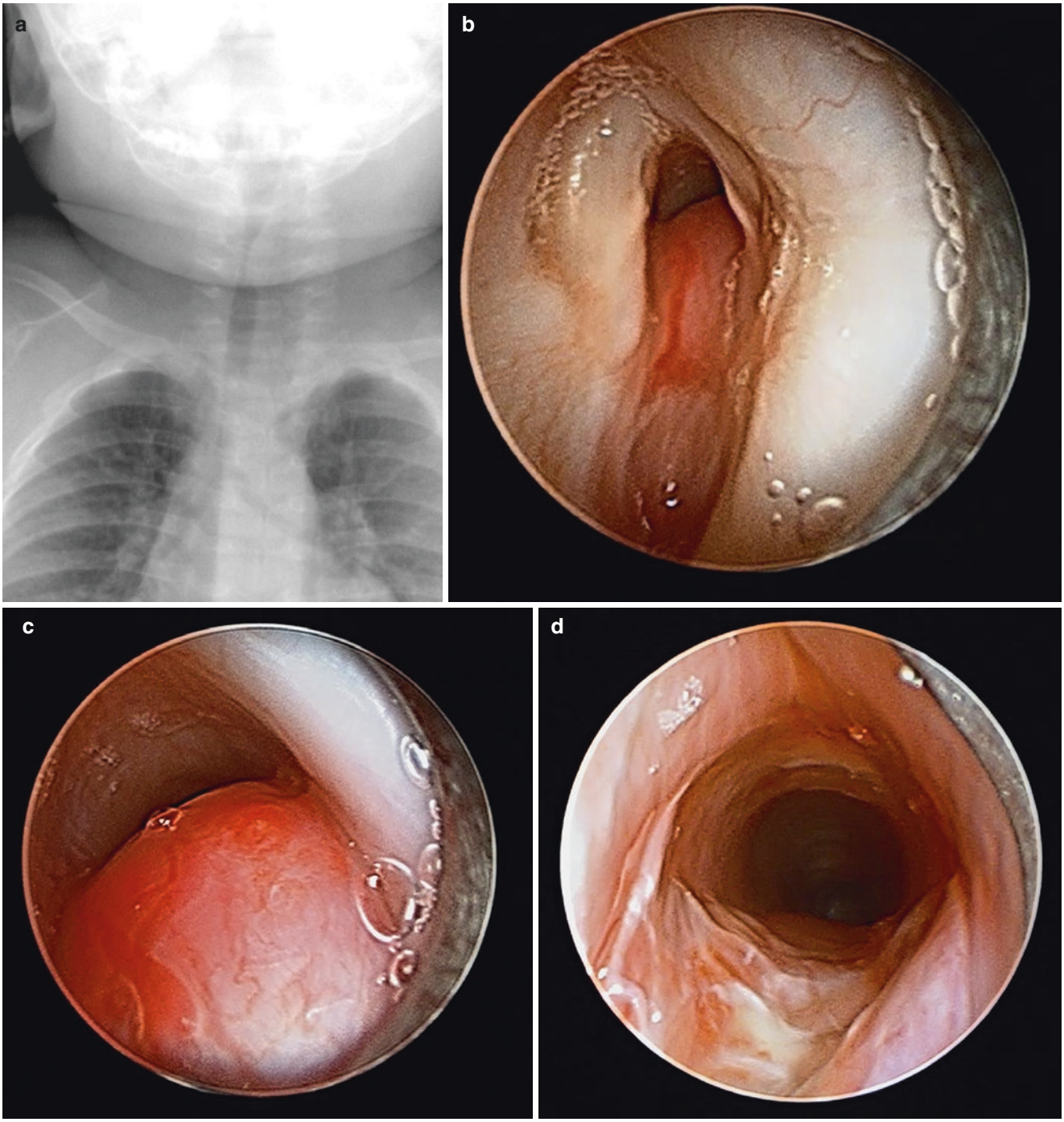

Fig. 11.12 (**a**) Soft tissue radiograph of the neck shows an asymmetrical subglottic narrowing with soft tissue arising from the left side of the subglottis. (**b**) Subglottic hemangioma at presentation. (**c**) Subglottic hemangioma close-up photo at presentation. (**d**) Subglottic hemangioma at extubation after 7 days of beta blocker treatment

appearance of the subglottis immediately after extubation following 7 days of treatment with beta-blockers (Fig. 11.12c and d).

Bronchogenic Cyst

Definition

Bronchogenic cyst is a congenital lesion arising from the aberrant budding of the ventral aspect of the primitive foregut (future tracheobronchial tree) [42, 43]. As such, they are also referred to as foregut duplication cysts. These rare lesions are usually located in the mediastinum or lung parenchyma. However, they may migrate to an ectopic location in the neck, abdomen, or subcutaneous sites. A classification system based on site of origin was described by Maier in 1948 [44].

Bronchogenic cysts are four times more common in males and have a reported prevalence of 1 in 42,000 to 1 in 68,000 individuals [45, 46]. The diagnosis is confirmed histologically and requires the presence of respiratory epithelium, islands of hyaline cartilage in the wall of the cyst, seromucinous glands, and smooth muscle.

Clinical Presentation

Patients typically present in childhood with a neck mass (when extra-thoracic), chronic cough, dysphagia, and stridor. Upper mediastinal cysts may migrate above the sternum with inspiratory or Valsalva maneuvers rendering them more clinically apparent [47].

Differential Diagnosis

Lymphatic malformation, thymic cyst, branchial cleft cyst, thyroglossal duct cyst, thyroid cyst, and teratoma.

Radiological Features

A neck and chest radiograph may reveal a mediastinal mass with displacement of trachea. However, cross-sectional imaging is essential prior to surgical intervention to define the origin, contents and relation to neighboring structures. Patients with airway compromise that do not tolerate a supine position for prolonged periods of time are preferentially imaged with computed tomography as images can be acquired in a more timely fashion compared with magnetic resonance imaging. Symptomatic children should not be sedated without a secure airway.

Management

Surgical excision is advocated for bronchogenic cysts to relieve symptoms and eliminate the risk of future infection, hemorrhage or malignant transformation [48, 49]. A combined cervical and thoracic approach may be required to safely remove the lesion. The cysts may be intimately attached to the trachea, bronchi, or esophagus. The surgeon must anticipate the possibility that the airway or esophagus may require surgical repair if entered.

Clinical Examples

A 7-month-old male was referred to clinic with a 5 month history of stridor which was presumed to be caused by laryngomalacia. The stridor, however, was biphasic and the patient was failing to thrive. A chest radiograph revealed the presence of a mediastinal mass with significant tracheal compression and deviation (Fig. 11.13a). Cross-sectional imaging confirmed the presence of a cystic mass within the upper mediastinum, adjacent to the left tracheal wall (Fig. 11.13b). The mass was excised through a low neck incision that included a partial sternotomy. The mass was adherent to the left tracheal wall and when excised, a tracheal defect remained that required primary repair (Fig. 11.13c and d). Histopathology revealed the presence of cartilage, smooth muscle, and respiratory epithelium consistent with bronchogenic cyst (Fig. 11.13e–g).

Tracheal Hamartoma

Definition

A hamartoma has been defined by Albrecht as a focal tumor or malformation consisting of the abnormal arrangement of the tissue elements of the organ in which it is found [50]. For the trachea, hamartoma components include cartilage, smooth muscle, adipose, fibrous, and epithelial tissue. Primary tracheal hamartomas are extremely rare in children with only a handful of reports published in the literature [51, 52]. Hamartomas of the trachea can be intra- or extraluminal.

Clinical Presentation

Infants and children with hamartomas present with airway obstructive symptoms either due to intraluminal tumors or tracheal compression from extraluminal masses.

Rigid bronchoscopy is used to confirm the presence of a tracheal mass and perform a diagnostic biopsy.

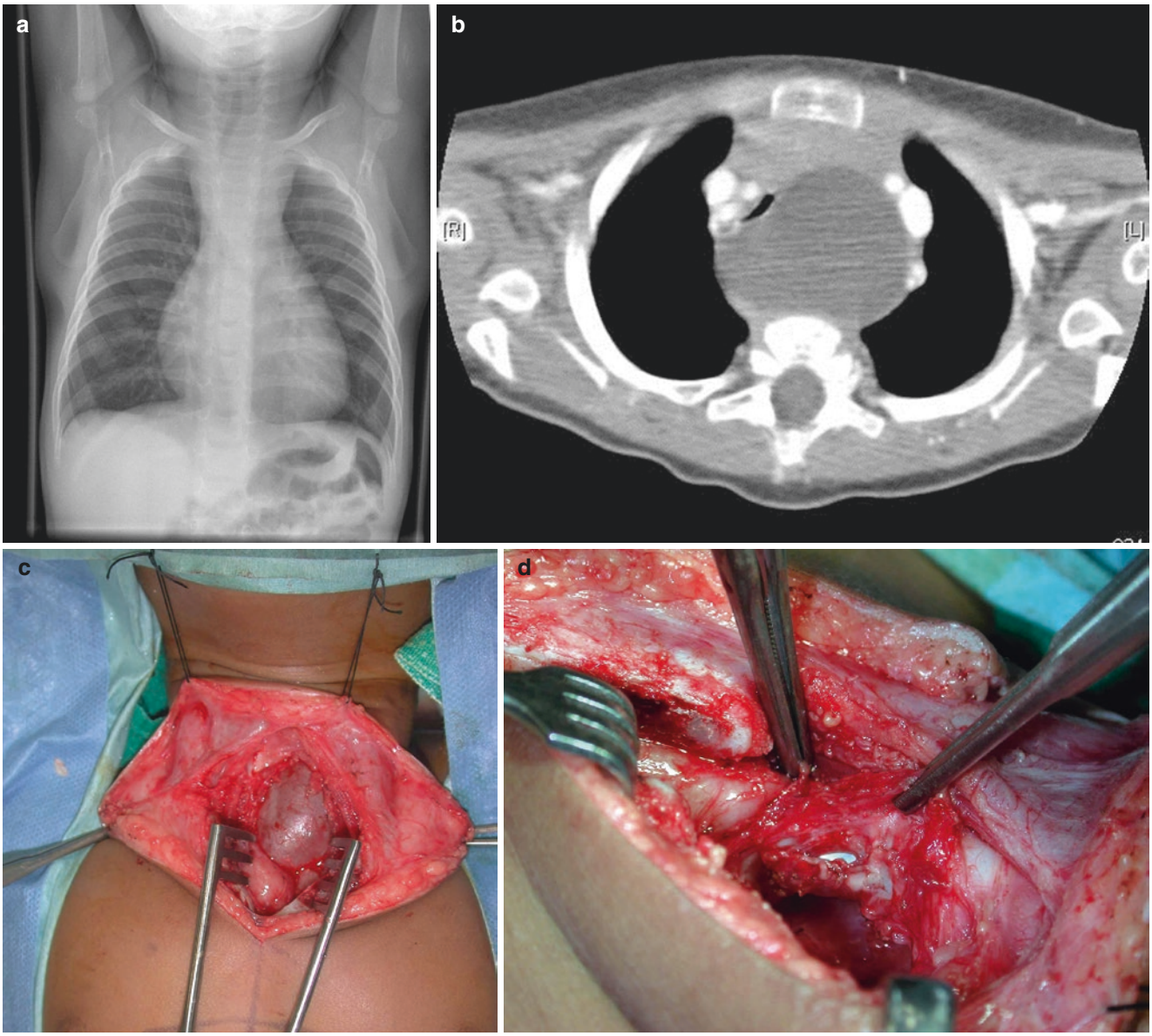

Fig. 11.13 (**a**) Chest radiograph reveals mediastinal mass with significant tracheal compression and deviation. (**b**) Axial CT shows cystic mass within the upper mediastinum compressing trachea. (**c**) Exposure of mass via low neck incision and partial sternotomy. (**d**) The mass was adherent to the left tracheal wall and when excised, a tracheal defect remained that required primary repair. (**e**) H&E. Histopathology of the cyst wall reveals the presence of cartilage, smooth muscle, and respiratory epithelium. (**f**) H&E. The cyst wall is lined by ciliated columnar cells that are typical of respiratory epithelium, deep to it within the submucosa are collections of secretory glands. (**g**) H&E. Focal smooth muscle hyperplasia is noted within the muscularis propria of the cyst wall

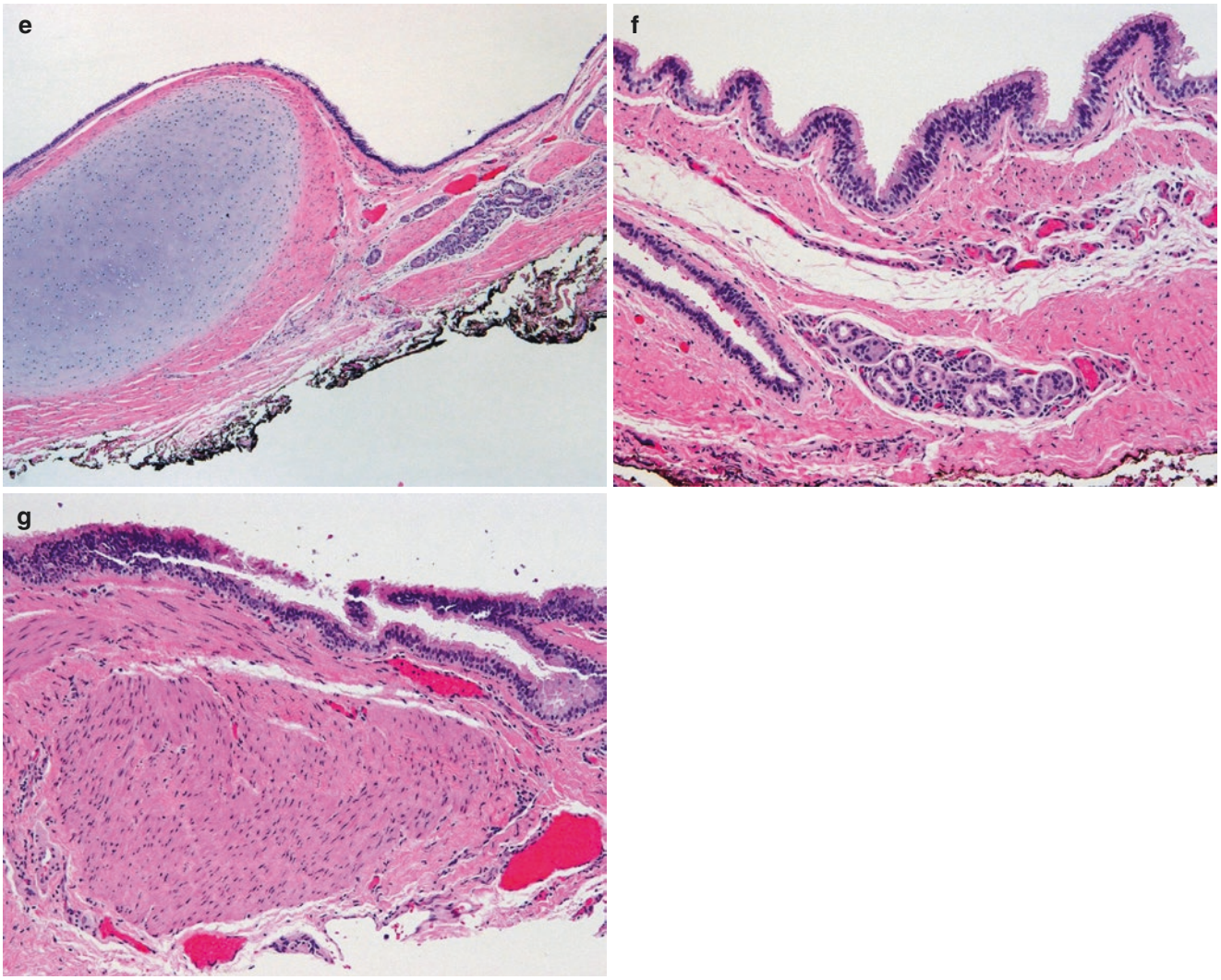

Fig. 11.13 (continued)

Differential Diagnosis

Teratoma, bronchogenic cyst, chondroma, and carcinoid tumor.

Radiological Features

Plain radiographs may demonstrate abnormal calcification and tracheal deviation with extraluminal masses or hyperinflation of lungs with intraluminal lesions due to air-trapping.

Cross-sectional imaging with computed tomography or magnetic resonance will demonstrate a mass lesion with densities consistent with the normal surrounding tissue.

Management

Surgical resection is the preferred method to manage these lesions to relieve the airway obstruction and confirm the diagnosis.

Clinical Examples

A newborn male required intubation at birth due to respiratory distress. He experienced intermittent episodes of acute oxygen desaturation and cyanosis if the end of the endotracheal tube migrated superiorly. A rigid bronchoscopy was therefore performed and revealed a soft tissue mass within the upper third of the tracheal lumen (Fig. 11.14a). The mass extended through the anterior

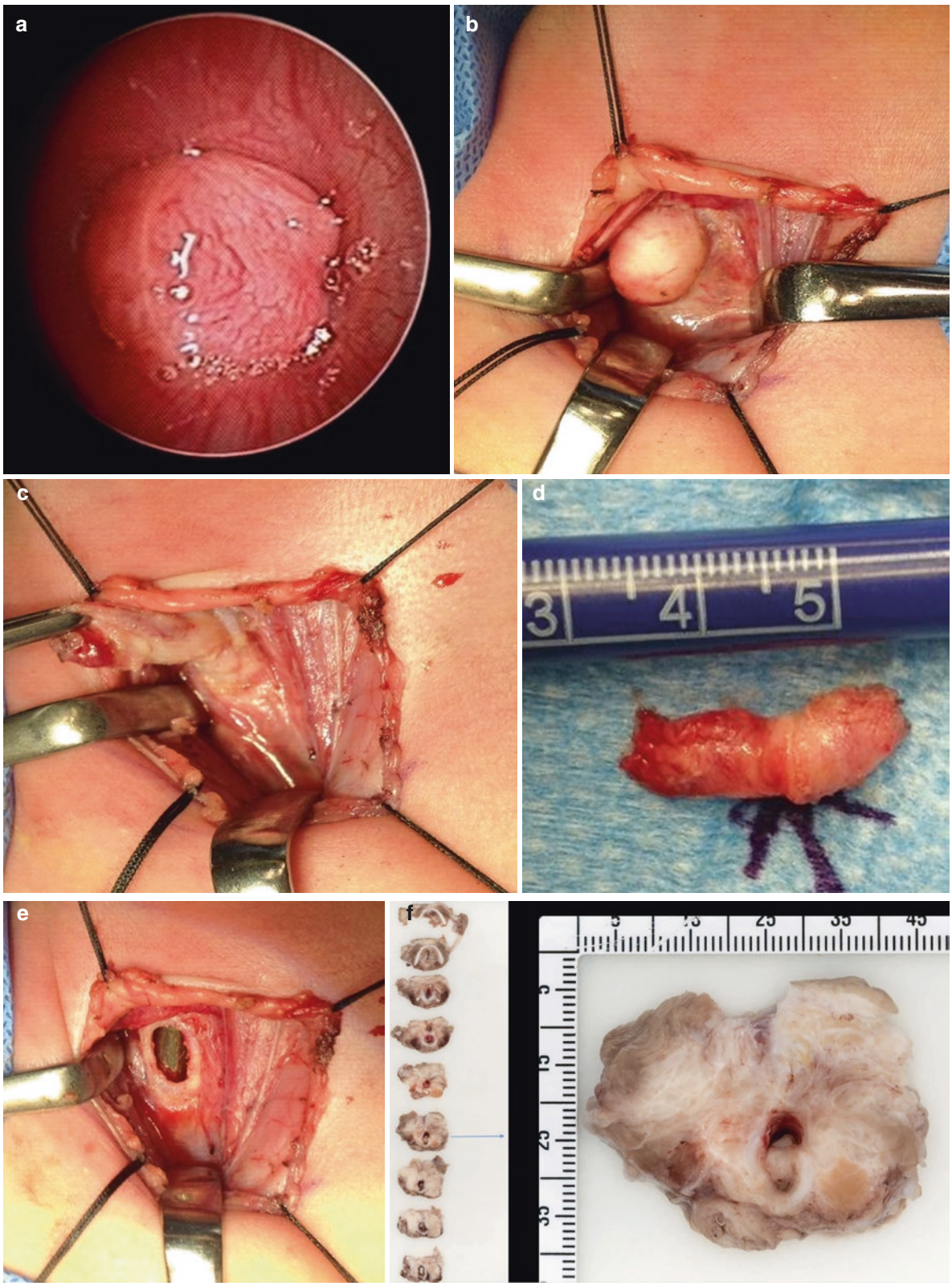

Fig. 11.14 (**a**) Soft tissue mass within the upper third of the tracheal lumen seen at rigid bronchoscopy. (**b**) Mass exposed through cervical neck incision. (**c**) Mass in continuity with tracheal wall. (**d**) Excised specimen including both intratracheal and extratracheal components. (**e**) Small tracheal defect after removal of lesion repaired primary repair. (**f**) Postmortem examination showing extensive fibromatosis of the mediastinum encasing and invading the airway

wall of the trachea and could be palpated in the anterior neck. At surgery performed via a cervical horizontal incision (Fig. 11.14b), the external and intratracheal components of the mass were excised in continuity (Fig. 11.14c and d). This resulted in a tracheal defect that was repaired primarily (Fig. 11.14e). Postoperatively, the patient was extubated uneventfully and experienced no further airway symptoms. However, approximately 6 months later, progressive stridor and increased work of breathing ensued. He developed an aggressive fibromatosis of the mediastinum that required a mediastinal dissection and tracheostomy to support his airway. Unfortunately, the fibromatosis persisted and further collapsed his trachea. A postmortem cross-section of the upper trachea demonstrates the extensive fibromatosis surrounding and invading the trachea (Fig. 11.14f).

Carcinoid Tumor of Bronchus

Definition

According to the World Health Organization, carcinoid tumors are considered neuroendocrine tumors and are subclassified as either *typical* or *atypical* carcinoid tumors [53]. Typical carcinoids are more common (80–90%). They are well differentiated, have a distinct histologic pattern, and demonstrate rare mitoses. In contrast, atypical carcinoids are intermediate grade neuroendocrine tumors with a more aggressive clinical course. They demonstrate nuclear atypia and high mitotic indices.

Clinical Presentation

Patients may be asymptomatic or present with cough, hemoptysis, recurrent pneumonia, and chest pain. Approximately 1–5% of bronchial carcinoids are associated with ectopic ACTH secretion and may present with Cushing's syndrome (central obesity, hypertension) and in some cases with neuropsychological symptoms (depression, irritability, cognitive deficits) [54].

Bronchial carcinoids are very rare in children and are not usually suspected when children present with airway symptoms. Diagnosis is usually established following rigid bronchoscopy and biopsy on an intraluminal lesion.

Differential Diagnosis

Hamartoma and other neuroendocrine carcinoma.

Radiological Features

Plain radiographs of the chest may reveal hyper-inflation or collapse of lung fields, pleural effusion, or hilar changes. Cross-sectional imaging of the chest is required to determine the size of the tumor and presence of hilar adenopathy.

In the setting of Cushingoid symptoms, a brain MRI may be required to rule out the possibility of a pituitary adenoma.

Management

These tumors are managed by surgical resection which may include pulmonary lobectomy and pneumonectomy. If possible, parenchyma-saving procedures such as sleeve resection of the bronchus and bronchoplasty should be considered [55]. At the time of resection, hilar and mediastinal lymph nodes dissections should be performed for staging purposes.

Resection by an endoscopic approach may be attempted with very small, focal lesions.

Clinical Examples

A 14-year-old male presented with shortness of breath and admitted with a diagnosis of pneumonia. Cross-sectional imaging confirmed the presence of a right lung mass (Fig. 11.15a) prompting a rigid bronchoscopy and biopsy. The bronchoscopy demonstrated a large granular mass obstructing the right bronchus intermedius (Fig. 11.15b). Pathology confirmed a diagnosis of carcinoid tumor of the bronchus (Fig. 11.15c–h). He was treated surgically with right middle and lower lung lobectomy (Fig. 11.15i and j).

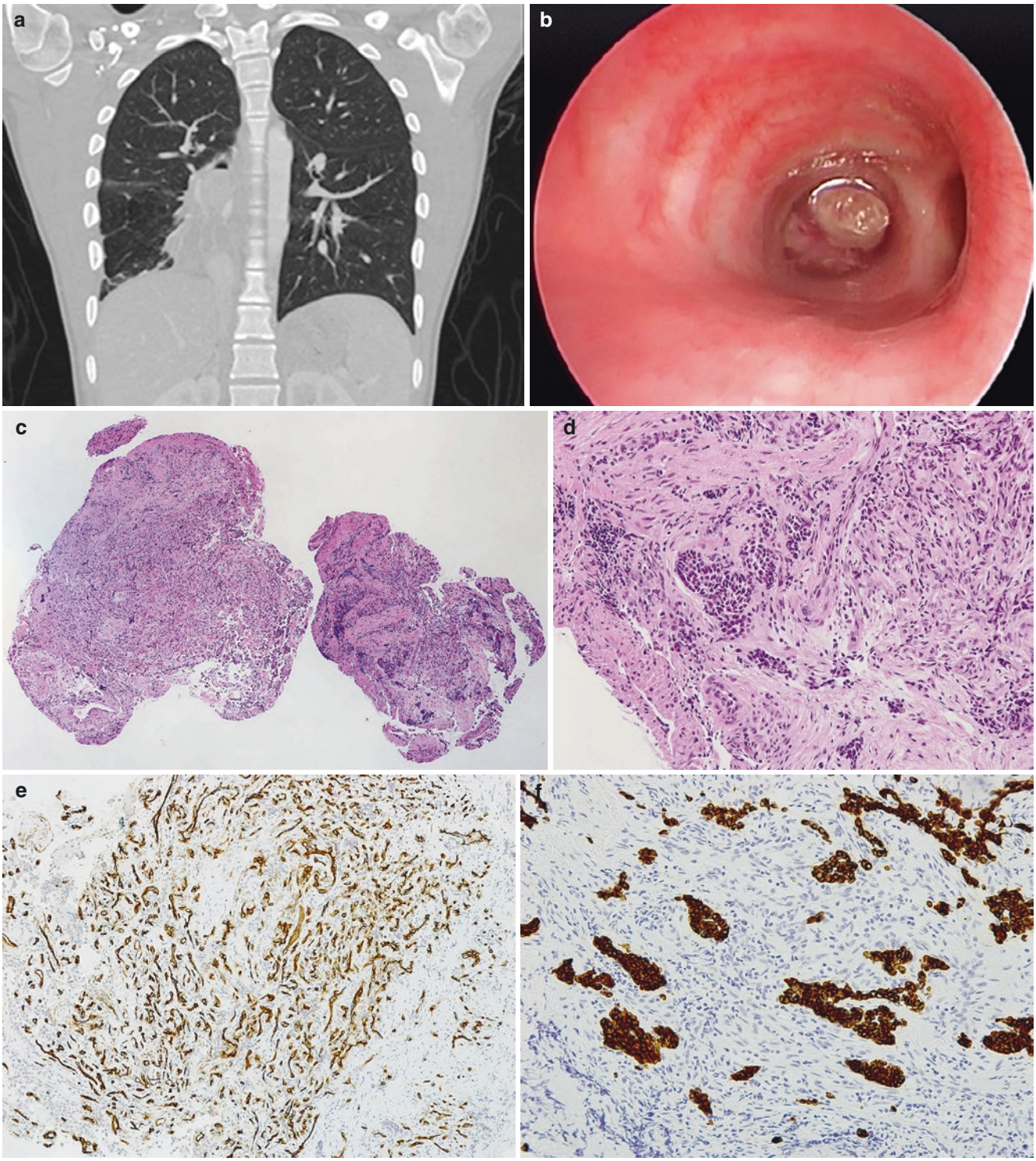

Fig. 11.15 (**a**) Coronal MRI showing right pulmonary mass. (**b**) Bronchial tumor obstructing bronchus intermedius. (**c**) H&E biopsies of the bronchial mass show tumor infiltrates that replace normal respiratory type mucosa with mucous glands. (**d**) H&E. High magnification reveals infiltrative nests of small tumor cells with hyperchromatic nuclei and small amounts of eosinophilic cytoplasm. (**e**) Immunostain for blood vessels (CD34) shows the tumor stroma is well vascularized. (**f**) Immunostain for low molecular weight cytokeratin shows positively stained brown nests of infiltrative tumor cells within the fibrotic bronchial mucosal mass. (**g**) Positive immunostain for Chromogranin reveals the endocrine cell origin of the tumor infiltrates. (**h**) Immunostain for serotonin shows weak staining (light brown cytoplasmic reactions) of the infiltrative tumors; the stain result also supports the endocrine cell origin of this tumor. (**i**) A cross-section made into the bronchial lumen of the resection specimen shows an intrabronchial tumor growth; typical of endocrine tumor (carcinoid) involvement of the bronchial tree. (**j**) Sections made in the longitudinal plane of the bronchial tree show this pale tan luminal mass is located at the bifurcation. The distal portion of the bronchial tree distal to the tumor obstruction is dilated and contains entrapped bronchial mucous secretions

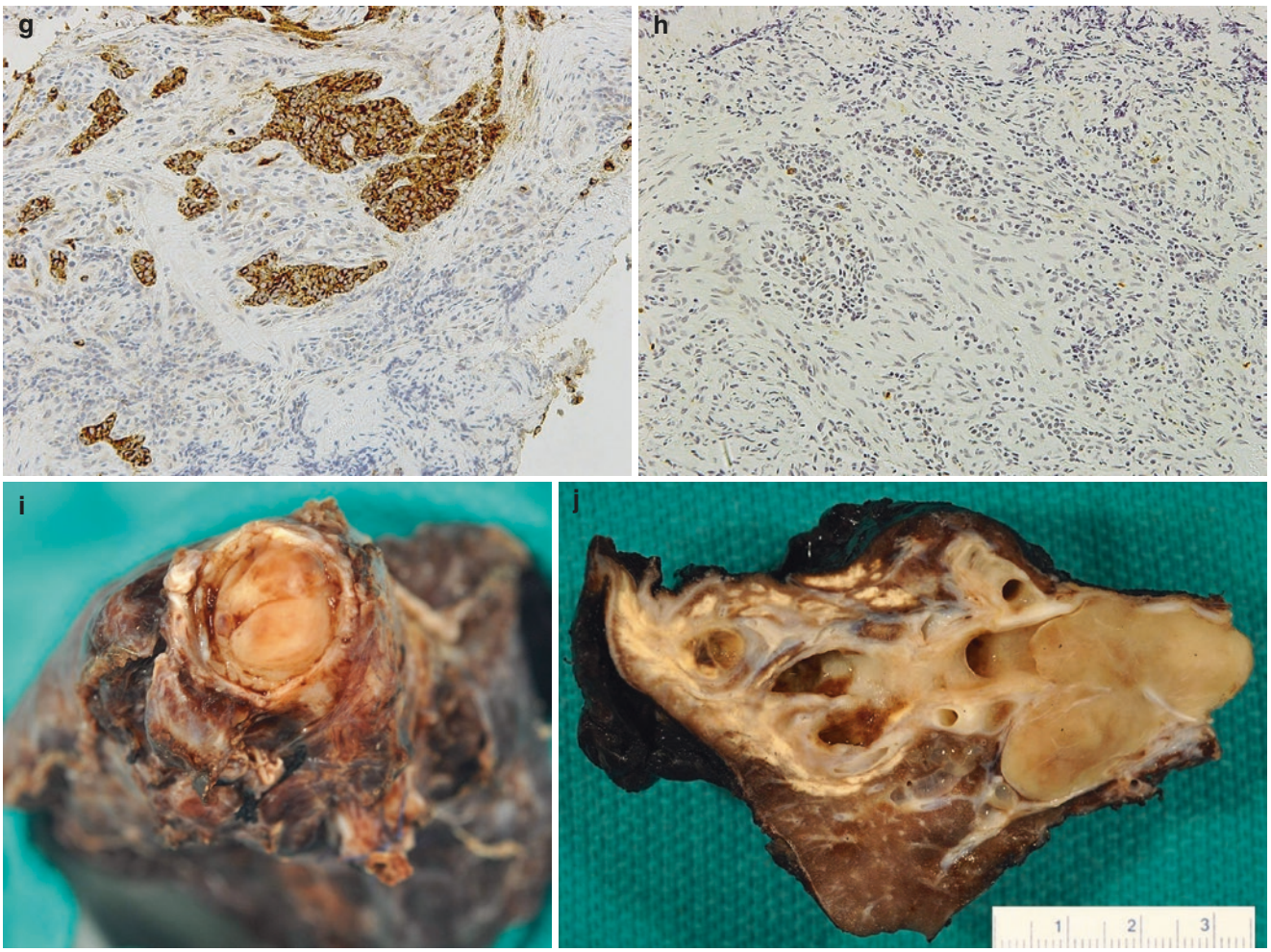

Fig. 11.15 (continued)

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