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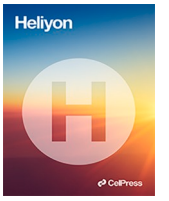

Tracheobronchial mucosal keratosis: A literature review of this rare disorder

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ABSTRACT

Background: Tracheobronchial mucosal keratosis (TBMK) is a rare airway disease that may cause refractory cough and airway stenosis. The characteristics of this disease remain unknown. In the present study, we describe this disorder based on a review of the current literature, emphasizing its diagnostic and therapeutic aspects.
Methods: A comprehensive search of TBMK was performed in Medline, Google Scholar, Web of Science, Cochrane Library (UK), Embase, China National Knowledge Infrastructure (CNKI) (China), and Wan Fang Med Online (China). The following data were collected: patient characteristics, chest imaging findings, bronchoscopy, histopathologic findings, pathogen testing, treatment, and prognosis.
Results: As of 2023, eighteen cases of TBMK have been reported. The main clinical manifestations were cough and expectoration. Chest imaging findings were non-specific. The main bronchoscopy findings were nodular protrusion of airway lumen and yellow-white purulent moss above the nodular lesion. The lesions were mainly located in the trachea and mainstem bronchus. The main pathological manifestations include keratinocytes or keratinocyte beads, squamous metaplasia, and mucosal inflammatory changes. The treatments that were administered include antibiotics, symptomatic treatment, and glucocorticoids. All methods were ineffective except for bronchoscopy-guided high-frequency electric knife and recombinant human epidermal growth factor treatment.
Conclusions: TBMK is a rare respiratory disease with atypical clinical manifestations and chest computed tomography findings. Bronchoscopy revealed that nodular hyperplasia of the airway and purulent fur-covered lesions are typical manifestations. The final diagnosis needs to be confirmed by histopathological examination. There is a lack of effective treatment for this disease, and bronchoscopy-guided intervention therapy may be a candidate treatment.

Introduction Background

Laryngeal keratosis is common in clinical practice, but tracheobronchial mucosal keratosis (TBMK) is extremely rare and manifests

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as hyperkeratosis of tracheal or mainstem bronchial mucosa on pathological examination [1]. Early TBMK related case reports are more common in Japan [2]. In 2005, Qin et al. first reported two cases of tracheal mucosal keratosis in China [3]. The patients were young soldiers who were admitted to the hospital owing to chronic cough and increased sputum production. Chest computed tomography and pulmonary function examination revealed normal findings. However, bronchoscopy revealed multiple nodular protrusions on the mucosa of the tracheal lumen, showing paving stone-like changes. Finally, the two patients were diagnosed with TBMK using pathological examination. Xia et al. found that the disease mainly affected the tracheal and mainstem bronchial mucosa, and it was first proposed to name the disease as TBMK to distinguish it from laryngeal keratosis [4]. So far, 18 cases have been reported worldwide. Since the literature on TBMK includes mostly case reports and lacks systematic research, there is a lack of in-depth understanding of the epidemiology, pathogenesis, diagnosis, treatment, and prognosis of the disease. The clinical symptoms and imaging findings of TBMK lack specificity, and the disease is often misdiagnosed as asthma, chronic obstructive pulmonary disease, and pneumonia [1,5]. Currently, effective anti-keratotic drugs for this disease are lacking. Although symptomatic treatment could help improve clinical symptoms, it does not address the keratosis itself [6]. The histopathological changes found in TBMK are similar to those of laryngeal keratosis, and whether TBMK has malignant potential remains unknown. Therefore, establishing an early and correct diagnosis of this condition and identifying the most suitable therapy are challenging. In this article, we retrospectively analyzed the epidemiology, clinical features, diagnosis, treatment, and prognosis of these 18 patients to improve the comprehensive understanding of this disease for clinicians and researchers.

Methods

A comprehensive search in Medline (National Library of Medicine, USA), Google Scholar, Web of Science, Cochrane Library (UK), Embase, CNKI (China), and Wan Fang Med Online (China) was conducted to identify relevant studies published before June 30, 2023, using the following terms: “tracheal keratosis” OR “respiratory tract keratosis” OR “tracheal leukoplakia” OR “tracheobronchial keratosis” OR “tracheal cutification” OR “tracheal keratinocyte hyperplasia” OR “tracheal pachydermia.” The studies were selected based on the following criteria: (1) histopathological diagnosis and (2) relatively complete case data (including information on patient demographics, history, bronchoscopy, etc.). The exclusion criteria include repeated reports of cases. The references from the retrieved articles that matched our inclusion criteria were manually searched, and the results were not restricted to articles available in the English language.

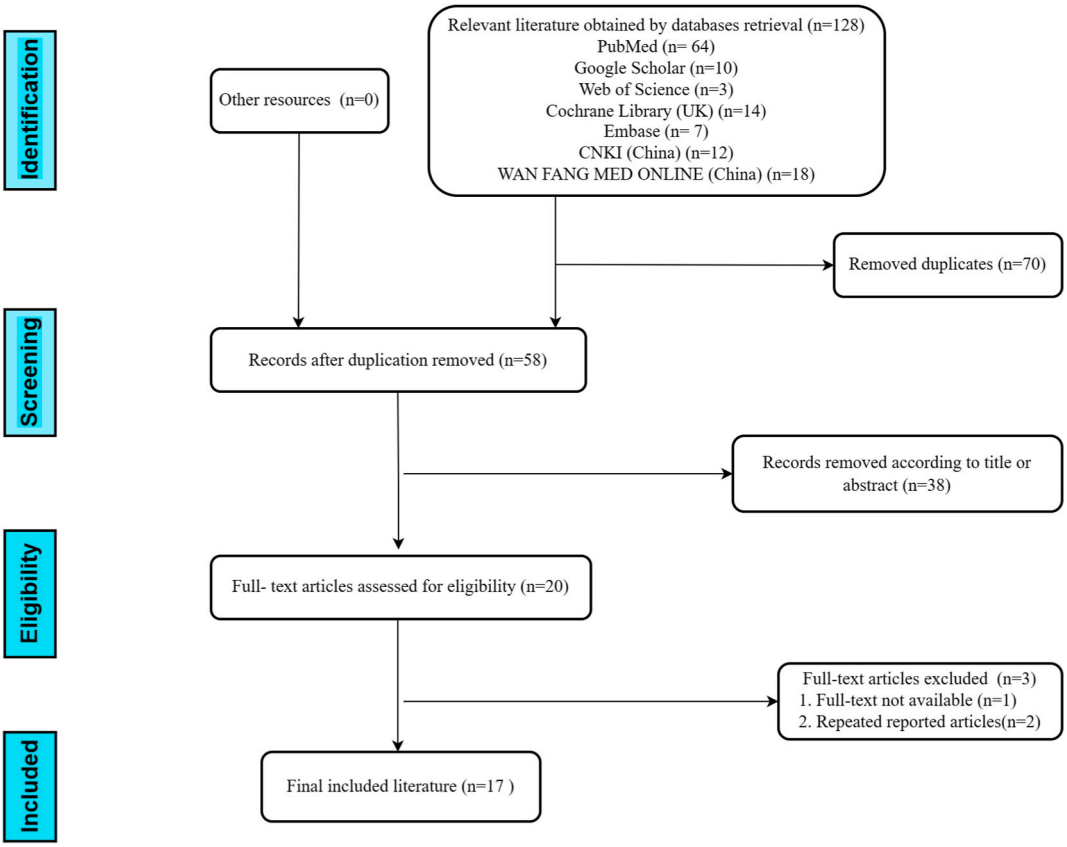

Fig. 1. Flow chart of the study selection process.

Table 1
Clinical features of tracheobronchial mucosal keratosis.

	No. of cases	Proportion (%)		No. of cases	Proportion (%)
Gender			Bronchoscopy		
Man	12	66.70 %	Mucosal hyperemia and swelling	9	50 %
Female	6	33.30 %	Nodular protrusion	17	94 %
Age			Yellow-white purulent moss	10	56 %
< 35	7	38.90 %	**Pathological manifestations**		
35-55	6	33.30 %	Keratinocytes or KB	18	100 %
> 55	5	27.80 %	Mucosal inflammatory changes	13	72 %
Average age	42.6		Squamous metaplasia	16	89 %
Geographical distribution			SSCH	8	44 %
US	1	**5 %**			
Japan	2	**11 %**			
China	14	**78 %**			
France	1	**5 %**			
Risk factors					
None smoke	15	83 %	Submucosal calcification	1	5 %
Smoke	3	16 %	Dysplasia	2	11 %
Dust	2	11 %	**Pathogen testing**		
Toxic gas	2	11 %	α-hemolytic streptococcus	1	5 %
Past history			β-hemolytic streptococcus	1	5 %
URTI	1	5 %	*Klebsiella pneumoniae*	1	5 %
SP	1	5 %	Stenotrophomonas maltophilia	1	5 %
Pneumonia	2	11 %	Pseudomonas aeruginosa	2	11 %
Hypoosmia	1	5 %	Neisseria	1	5 %
Chronic bronchitis	1	5 %	Staphylococcus saprophyticus	1	5 %
Clinicalmanifestations			Morganella morganii	1	5 %
Cough	15	83 %	Aspergillus	2	11 %
Expectoration	15	83 %	Mycobacterium tuberculosis	1	5 %
Chest pain	3	16 %	G+	3	16 %
Shortness of breath	2	11 %	G-	2	11 %
fever	1	5 %	Not detected	5	28 %
Hoarse	2	11 %	**treatment**		
Chest tightness	2	11 %	Antibiotic Case 1: Azithromycin, 2 weeks Case 2: Pseudomonas aeruginosa was detected. Firstly, levofloxacin, 13 days; followed by CS for 3 weeks Case 3: Levofloxacin, 2 weeks Case 4: Morganella morganii was detected. Firstly, cefazoxime 2g, intravenously,2 times/d, 4 weeks; netilmicin 0.2g, intravenously, 1 time/d, 2 weeks. Secondly, CS 3g, intravenously, 2 times/d, 2 weeks, followed by moxifloxacin 400 mg, orally, 5 weeks. Case 5: CT 2.0 g, 2 times/d, 10 days Case 6: Ciprofloxacin and ceftriaxone, dosage and course unknown Case 7: Anti Aspergillus and Pseudomonas aeruginosa treatment, drugs unknown Case 8: Penicillin sodium and pefloxacin, dosage and course unknown Case 9: Mycobacterium tuberculosis was detected.Prescription: isoniazid 0.3g/time, 1 time/d; pyrazinamide 0.5g/time, 3 times/d; ethambutol hydrochloride 1.0g/time, 1 time/d; rifampicin 0.6g/time, 1 time/d, with a period of 6 months. Case 10–12: Drugs unknown	12	67 %
Difficulty breathing	3	16 %	Bronchoscopy-guided therapy	2	11 %
CT Chest			Glucocorticoid	3	16 %
Normal	9	50 %	Vitamins	2	11 %
Patchy shadows	7	39 %	TCM	1	5 %
Tracheal calcification	2	11 %	Symptomatic treatment	4	22 %
Lumen stenosis	1	5 %	Refusal of treatment	1	5 %
Thickening of the airway wall	1	5 %	Sodium bicarbonate	1	5 %
Pulmonary nodules	2	11 %	RHEGF	1	5 %
Atelectasis	2	11 %	Anti-tuberculosis treatment	1	5 %
SMLN	1	5 %	**Prognosis**		
Lung function			Cure	2	11 %
Normal	3	16 %	Get better	4	22 %
Abnormal	1	5 %	stable	4	22 %
Unknown	14	77 %	Unknown	8	44 %
Lesion			**Follow up**		

(*continued on next page*)

Table 1 (*continued*)

	No. of cases	Proportion (%)		No. of cases	Proportion (%)
Trachea	3	17 %	Unknown	10	55.60 %
Trachea and bronchus	12	66.70 %	Known	8	44.40 %
Trachea and larynx	2	11 %	Average age	6–108 M	
Trachea, bronchus and larynx	1	5 %			

URTI = upper respiratory tract infection; SP=Spontaneous pneumothorax; SMLN=Swollen mediastinal lymph nodes; SSCH=Submucosal spinous cell hyperplasia; KB=Keratinocytes beads; TCM = Traditional Chinese Medicine; RHEGF=Recombinant Human Epidermal Growth Factor; CS = cefoperazone sodium and sulbactam sodium, CT=Cefoperazone Sodium and Tazobactam Sodium.

Results

Study selection

A total of 128 records were identified by searching the seven databases. After removing 70 duplicate articles, we screened the titles and abstracts of 58 articles. A total of 38 articles that did not meet the inclusion criteria were excluded. A full-text review of 20 articles was conducted, and 3 of these were excluded, resulting in 17 eligible studies being used for further research (Fig. 1).

Gender distribution and age at diagnosis

Eighteen cases of TBMK were collected, twelve in males and six in females. The male-to-female ratio was 2:1. The minimum and maximum ages at the time of diagnosis were 21 and 67 years, respectively, with an average of 42.6 years. Most of the patients (38.9 %) were below 35 years of age, followed by those aged 35–55 years (33.3 %) and over 55 years (27.8 %). TBMK affected people at any age,

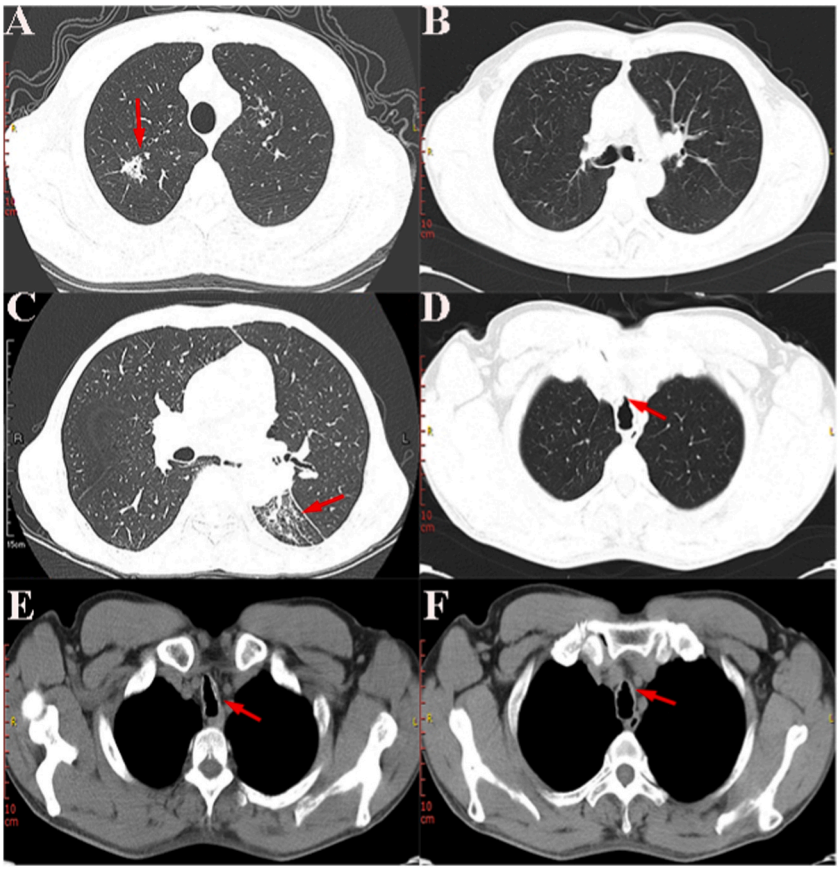

Fig. 2. Chest CT of TBMK. A: Patchy shadows in the left upper lobe (red arrow). B: Normal finding in bilateral lung. C: Local atelectasis of the left lower lobe (red arrow). D: Tracheal lumen stenosis (red arrow). E: Local calcification of tracheal cartilage (red arrow). F: Thickening of the tracheal wall (red arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

but mostly young and middle-aged adults.

Relationships between risk factors and TBMK

Three of the eighteen patients were smokers, while fifteen were non-smokers. Two patients had a history of dust exposure, and two had a history of toxic gas exposure. Six patients had a history of respiratory disorders (33.3 %), including upper respiratory tract infection, pneumonia, hyposmia, chronic bronchitis, and spontaneous pneumothorax. Twelve patients had a negative history of respiratory disorders (66.7 %). Therefore, we believe that the etiology and pathogenesis of TBMK may be related to chronic inflammation of the airways and respiratory tract injury on occupational and environmental exposures. Considering that most of these patients have no smoking history, the role of cigarette smoking in TBMK remains unclear (Table 1).

Reason for admission

All patients had specific indications for hospital admission. Repeated cough and expectoration were the most common indications (83 %). The other reasons for admission were chest pain (16 %), difficulty in breathing (16 %), shortness of breath (11 %), chest tightness (11 %), hoarseness (11 %), and fever (5 %) (Table 1).

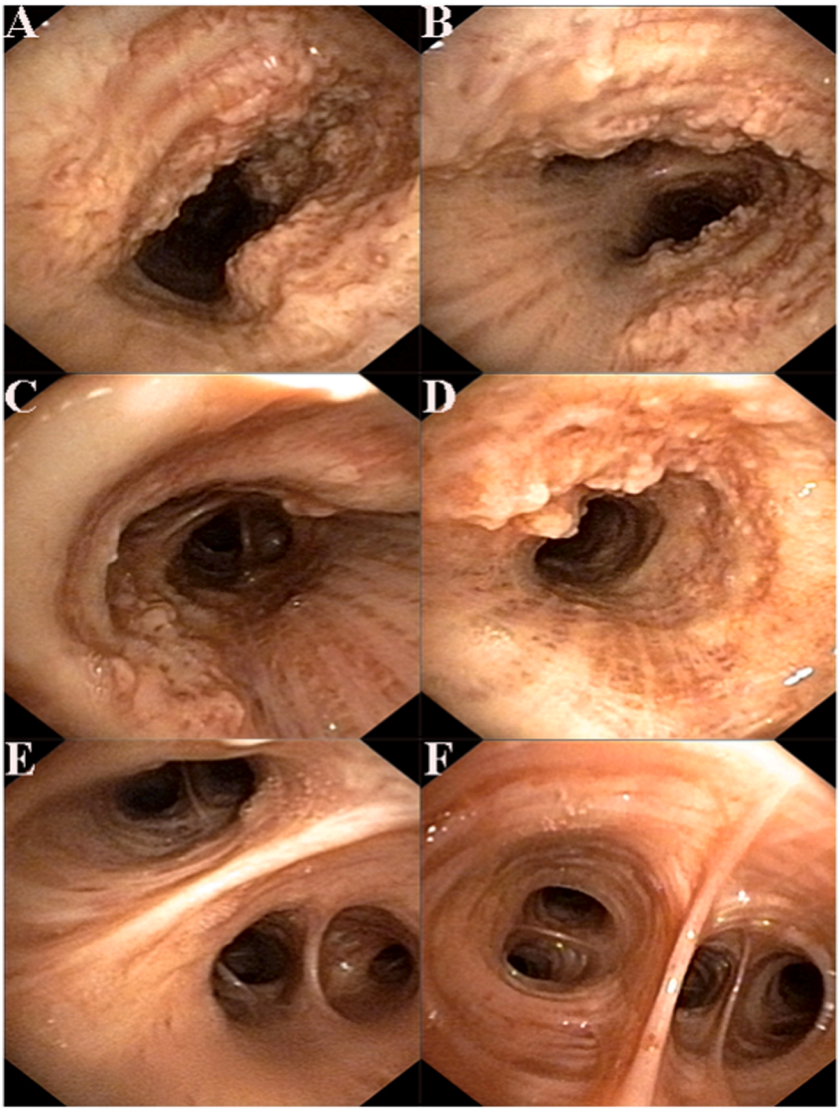

Fig. 3. Bronchoscopy of TBMK. A–D: Nodular protrusion of airway lumen and yellow-white purulent moss-like secretions. E–F: Normal lower lobe bronchus in both lungs. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Imaging and microbiology of TBMK

An exhaustive diagnostic evaluation was performed using chest X-rays, computed tomography (CT), spirometry, bronchoscopy, pathogen testing, and biopsies (Table 1). Notably, chest X-rays and chest CT did not establish the diagnosis of TBMK. Although chest X-ray findings were not reported for 6 of the 18 patients (33.3 %), except for the signs of infection detected in the lung, no abnormal changes were found in the other 12 patients. All patients underwent chest CT, and its characteristic findings were patchy shadows (39 %; Fig. 2A), normal findings (50 %; Fig. 2B), atelectasis (11 %; Fig. 2C), nodular lesions (11 %), lumen stenosis (5 %; Fig. 2D), tracheal calcification (11 %; Fig. 2E), thickening of the airway wall (5 %; Fig. 2F), and swollen mediastinal lymph nodes (5 %; Fig. 2). Thus, TBMK cannot be diagnosed solely by chest X-rays and CT scans owing to the lack of characteristic imaging manifestations. All patients underwent bronchoscopy. The findings were categorized as shown in Table 1, Fig. 3, and supplementary materials, which include the following: (1) mucosal hyperemia and swelling [9 patients (50 %); Fig. 3AcB]; (2) nodular protrusion of airway lumen [17 patients (94 %); Fig. 3A–D]; (3) yellow-white purulent moss-like secretions [10 patients (56 %); Fig. 3C and D], and (4) normal lower lobe bronchus in both lungs [Fig. 3E and F]. Moreover, all patients underwent bronchoscopy-guided biopsies except for one patient who had a blood loss of 50 ml after the biopsy, whereas others only had slight hemorrhage. Pathogens were detected from the culture of lower respiratory tract specimens in 13 patients (72 %) and included *Pseudomonas aeruginosa* (5 %), *Aspergillus* (11 %), *α-hemolytic Streptococcus* (5 %), *β-hemolytic Streptococcus* (5 %), *Klebsiella pneumonia* (5 %), *Stenotrophomonas maltophilia* (5 %), *Neisseria* (5 %), *Staphylococcus saprophyticus* (5 %), *Morganella morganii* (5 %), and *Mycobacterium tuberculosis* (5 %). No pathogenic microorganisms were detected in five patients (28 %). Although spirometry plays an important role in diagnosing airway stenosis and airflow obstruction, only a few patients in this review underwent this test. Three (17 %) patients showed normal findings, while one (5 %) patient showed abnormal findings. In addition, the findings of 14 patients were not known (77 %).

Localization of TBMK

The abnormal lesions were most often located in the trachea (100 %) followed by the mainstem bronchus (72 %). Only three cases were accompanied by laryngeal involvement (17 %; Table 1). Laryngeal keratosis is very common, but tracheobronchial keratosis is extremely rare. Therefore, when laryngeal keratosis is diagnosed, further examination is needed to rule out the possibility of lower respiratory keratosis.

Histological examination

Histological examination was performed for all 18 patients. The results of the biopsy specimens most often showed keratinocytes or keratinocyte beads (100 %; Fig. 4A and B), squamous metaplasia (89 %; Fig. 4A and B), mucosal inflammatory changes (79 %; Fig. 4A and B), and submucosal spinous cell hyperplasia (44 %). Dysplasia (11 %) and submucosal calcification (5 %) could also be detected. In the reports we reviewed, pathological examination revealed mucosal hyperkeratosis as the main feature of this disease, followed by mucosal squamous metaplasia, mucosal inflammatory changes, submucosal spinous cell proliferation, and keratinocytes in secretions.

Treatment of TBMK

Among the 18 cases, a specific treatment was reported in the following six categories for 17 patients (Table 1): (1) antibiotics (67 %); (2) symptomatic treatment (22 %); (3) glucocorticoid treatment (16 %); (4) vitamins (11 %); (5) bronchoscopy-guided treatment, including high-frequency electrocautery and cryotherapy (11 %); and (6) traditional Chinese medicine (5 %). One patient refused treatment for economic reasons (5 %). All methods proved ineffective, except for flexible bronchoscopy-guided therapies that were

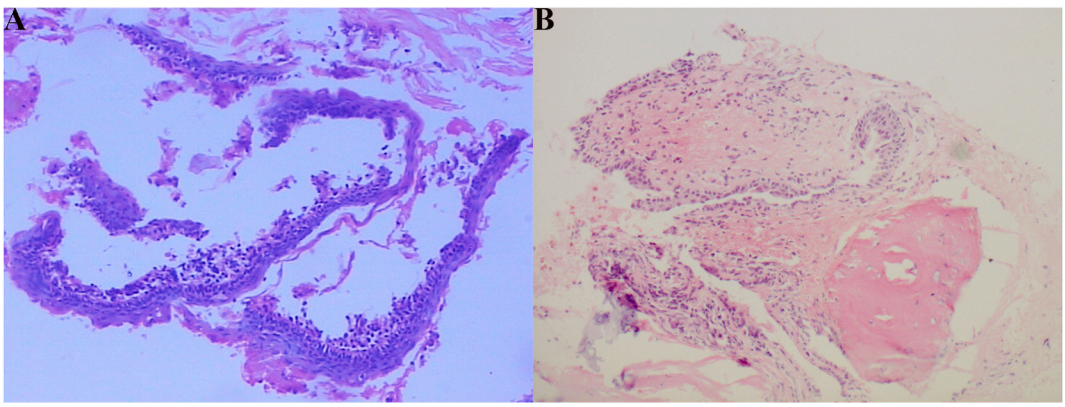

Fig. 4. Histological examination of TBMK. A, B: The biopsy specimens showed keratinocytes and keratinocyte beads, squamous metaplasia, mucosal inflammatory changes, and submucosal spinous cell hyperplasia.

performed to successfully manage two cases. Moreover, one cured patient also received bronchoscopy-guided lavage treatment with recombinant human epidermal growth factor and sodium bicarbonate. The average follow-up time was 20 months, and TBMK had a relatively good prognosis. Although only two patients were cured (11 %), four patients received relief from the clinical symptoms (22 %), four cases were stable (22 %), and the outcome of ten cases was unknown (44 %).

Discussion

Mucosal keratosis of the respiratory tract always occurs in the oral cavity, pharynx, and larynx, and mainly manifests as oral mucosal leukoplakia, tonsil keratosis, and vocal cord leukoplakia, among which laryngeal keratosis is the most common [7,8]. Laryngeal keratosis often manifests as hoarseness with histopathological findings of keratosis in the local squamous epithelium [9]. It has been broadly classified as simple keratosis and keratosis with dysplasia, which is generally considered to be precancerous lesions [10]. Although upper respiratory tract keratosis is very common, TBMK is very rare. As of June 30, 2023, only 18 cases have been reported and are reviewed here. The pathogenesis of this disease was not clear, and there were no relevant research reports. However, TBMK had histopathological findings similar to those of oral mucosal leukoplakia and laryngeal keratosis, and they probably have common risk factors. Previous studies have confirmed that smoking, drinking, vocal cord abuse, occupational environment, male sex, chronic inflammation, and advanced age were risk factors for the occurrence of laryngeal keratosis, which can be cancerous [9,11–13]. In this study, among the 18 patients, 39 % had a history of prolonged exposure to dust, irritating gases, and smoking, while 33 % also had a history of chronic respiratory disease, which could be important risk factors for the occurrence of TBMK; however, such factors could not be identified in 61 % of the cases.

Although the clinical symptoms of TBMK were diverse, they were not typical [1,14]. The common manifestations were repeated cough, sputum production, chest pain, and shortness of breath. TBMK could hardly be differentiated from COPD, bronchiectasis, tuberculosis, and asthma based on symptoms alone. Chest imaging had poor specificity for the diagnosis of this disease [15]. Although the specificity and sensitivity of chest CT is significantly higher than that of chest X-ray, it also had a limited value for TBMK. The probable reason may be that the disease mainly involved the airway mucosa. Unless there was obvious airway wall thickening or airway stenosis, chest CT often failed to show the location and extent of the lesion. In this review, the most common imaging finding was of pulmonary patchy shadows, followed by atelectasis and tracheal calcification, whereas lumen stenosis and thickening of the airway wall were extremely rare. Although spirometry plays an important role in diagnosing airflow limitation, the number of patients with TBMK who completed spirometry tests is relatively small, which may be related to the average age of patients (seen in young and middle-aged adults), and the lack of typical manifestations of COPD or asthma. Moreover, spirometry testing requires certain technology and equipment, which is not routinely available. Although only four of the eighteen patients underwent pulmonary function tests, three of them had normal pulmonary function, while one patient had severe obstructive ventilatory dysfunction due to COPD. In the microbiological examination, pathogens were detected in 72 % of patients. Among them, 10 patients with purulent moss-like secretions underwent sputum culture examination and all patients had bacterial or fungal infections, indicating that there may be a close relationship between the purulent moss-like secretions and infection. Although there was no obvious specificity in these pathogens, the high infection rate suggests that there may be a close relationship between infection and TBMK [16].

Bronchoscopy was the main diagnostic modality for TBMK, and its typical findings included several nodular protrusions adhering to the tracheal and the mainstem bronchial mucosa, which had a tough texture, with hardly any bleeding during the biopsy, and with paving stone-like changes. The nodules were often covered with yellow-white purulent moss-like secretions, and the lumen of the lesion could become narrowed [1,14,15,17]. The disease mainly occurs in the central airway, especially the trachea, followed by the mainstem bronchus [1,18,19]. According to the course of the disease, bronchoscopy showed a certain regularity [1]: 1 month after onset, TBMK mainly showed congestion and swelling of the airway mucosa with purulent moss-like secretions adhering to the mucosa, while nodular changes were not obvious; 4 months after onset, nodular changes with purulent moss-like secretions attached to the mucosal surface; 1 year after onset, gradual fusion of mucosal nodules and the attachment of little purulent moss-like secretions was seen.

Histopathological examination is the chief modality for the final diagnosis of TBMK. The typical pathological manifestations were tracheobronchial mucosal keratinization, followed by squamous epithelial cell metaplasia [1,14,18,20]. Although there was proliferation of the spinous cells, they were mature. Moreover, basal cells were intact and not abnormal. Occasionally, mucosal keratinized beads could be seen in the sputum [1]. Although the literature reports that TBMK is benign, we found that two patients had dysplasia (11 %): a 29-year-old female patient with mild dysplasia [15] and a 67-year-old male patient with moderate dysplasia [21]. Moreover, this finding suggests that the disease has the potential of malignant transformation and requires close follow-up.

TBMK needed to be differentiated from tracheobronchopathia osteochondroplastica, tracheobronchial tuberculosis, tracheobronchial amyloidosis, and bronchial Dieulafoy's disease. Although tracheobronchopathia osteochondroplastica consists of benign lesions of the tracheal and bronchial mucosa with multiple nodular hyperplasias of bone or cartilage protruding into the lumen [22,23], it is possible to confuse it with TBMK in the presence of infection. The following subtypes of tracheobronchial tuberculosis can be detected via bronchoscopy: actively caseating, edematous-hyperaemic, fibrostenotic, tumorous, granular, ulcerative, and non-specific bronchitis [24]. If tracheobronchial tuberculosis shows the actively caseating, ulcerative necrosis, and granular subtypes, it needs to be differentiated from TBMK. Tracheobronchial amyloidosis is a systemic disease involving abnormal extracellular deposition of amyloid and autologous fibrillar protein material in β-pleated sheets [25]. It can also manifest as a nodular protrusion of the airway mucosa and local thickening of the tracheal wall. Although bronchial Dieulafoy's disease is usually seen as a nodular protrusion into the lumen on bronchoscopy, the superficial mucosa is smooth, the diameter and height of the lesions are always less than 5 mm, their color is usually normal or mildly hyperemic, with or without pulsatility, and sometimes a white cap may be present [26]. Therefore, the diagnosis of

TBMK based on bronchoscopy alone is not conclusive, and pathological examination is necessary to establish the final diagnosis. These were essentially different from the characteristics of an abnormal metaplasia, ossification, and nodular neoplasia of the elastic tissue that can be seen under the mucosa of tracheobronchopathia osteochondroplastica [27]. The typical pathological manifestation of tracheal tuberculosis was the formation of caseous necrotizing granuloma. Moreover, the PCR examination of tuberculosis was often positive, which is significantly different from the findings of TBMK [24]. The pathological characteristics of tracheobronchial amyloidosis include the deposition of homogeneous eosinophilic material in the mucosa, with positive Congo red staining, which is also different from TBMK [28]. In addition, the histopathological examination of bronchial Dieulafoy's disease shows typical findings, such as superficial, dysplastic, tortuous, and dilated bronchial artery under the bronchial epithelium, which is projecting or directly communicating with the lumen [26,29]. This is also significantly different from the findings of TBMK.

Currently, there is no specific treatment for TBMK because of the lack of in-depth understanding of the pathophysiological mechanisms of TBMK. Antibiotics, glucocorticoids, and vitamins did not affect mucosal keratosis and squamous metaplasia, but they were effective in improving the clinical symptoms of the patients. In this review, bronchoscopy-guided interventional therapy has played an important role in TBMK, but the number of cases is relatively small and further evaluation of its value and risk is needed. One patient was diagnosed with TBMK and tracheal tuberculosis. Although standard anti-tuberculosis treatment and bronchoscopy-guided cryotherapy were administered, bronchoscopy showed that these treatments were ineffective. Based on the previous treatment, the patient was completely cured after repeated bronchoscopy-guided lavage with recombinant human epidermal growth factor, dexamethasone, and sodium bicarbonate, and there was no recurrence after 4 years of follow-up [30]. The other case was cured after being treated with bronchoscopy-guided high-frequency electrocautery, and no recurrence was found after 4 months of follow-up [31]. Retinoic acid (RA), a metabolite of retinol, functions as a ligand for nuclear RA receptors that regulate development of chordate animals [32]. RA is usually classified in one of the three generations. Briefly, naturally occurring and non-aromatic retinoids are classified as the first generation, while monoaromatic vitamin A derivatives are classified as the second generation. Moreover, retinoids containing a cyclic polyene side-chain are considered as the third generation [33]. RA exists in several isoforms of which the most common are all-trans retinoic acid (ATRA) and 9-cis retinoic acid [32]. ATRA deficiency, which is mediated by cytochrome P450 or other mechanisms, may be associated with cancer progression [34]. Viaminati is a derivative of RA, which has a structural formula similar to ATRA [35], and is often used to treat laryngeal keratosis. Studies have shown that this drug can induce differentiation and apoptosis. It can reduce the size of keratinocytes, increase fragility, and decrease the cohesiveness of the stratum corneum, thereby exerting the anti-keratosis effect [35]. However, it has not yet been used to treat TBMK.

In this review, eight of the eighteen patients had follow-up records. The shortest follow-up period was of 6 months and the longest period was of 9 years. There were no reports of cancerous TBMK during follow-up, but the other 10 patients had no follow-up records. This article also has some limitations. First, TBMK is a rare disease, and the conclusions of this article cannot fully reflect all the characteristics of the disease. Next, this article is a retrospective analysis; therefore, there is limited clinical data that can be extracted as well as lack of basic research, such as genetic testing and its underlying mechanism. Moreover, there is limited help for in-depth understanding of the disease. Given the currently small number of cases and the lack of relevant studies focusing on the pathological mechanism, genomics and proteomics can be used in the future to find the differential genes, proteins, and signaling pathways of TBMK to explain the specific mechanism and identify more therapies for its management.

Conclusions

TBMK is extremely rare and could cause refractory cough and airway stenosis. The clinical manifestations and chest CT of this disease are not specific. Its diagnosis chiefly requires bronchoscopy and histopathological examination. Although this disease has often been considered to be benign, it has the potential for malignant transformation. Currently, effective treatments for this disease are lacking. For patients with severe airway obstruction, bronchoscopy-guided intervention therapy can be considered; however, its effect needs to be evaluated further.

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Informed consent

Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

Ethics approval

This is a retrospective and review study. The Research Ethics Committee of Hospital of Chengdu University of Traditional Chinese Medicine confirmed that no ethical approval is required.

What is already known on this topic

Although tracheobronchial mucosal keratosis (TBMK) is gradually reported in the literature and is generally considered to be a rare disease that may be a cause of refractory cough and airway stenosis, the characteristics of this disease are not known and lack of effective treatments.

What this study adds

The clinical manifestations and chest CT findings of TBMK are atypical. Nodular hyperplasia of the airway and purulent fur-covered lesions are typical manifestations of TBMK under bronchoscopy. Many positive pathogen are detected from the culture of lower respiratory tract specimens of TBMK. Keratinocytes or keratinocyte beads, squamous metaplasia, and mucosal inflammatory changes are the main pathological manifestations of TBMK. Bronchoscopy-guided intervention therapy may be a candidate treatment for TBMK.

How this study might affect research, practice or policy

TBMK is associated with refractory cough and airway narrowing, and epidemiological studies of this disease need to be strengthened.

The relationship between airway infection and TBMK is unclear and requires further verification.

Although the effect of bronchoscopy-guided intervention therapy in TBMK is effective, the sample size is small and needs more clinical trials to confirm.

Data availability statement

Data included in article/supp. material/referenced in article.

CRediT authorship contribution statement

Pengcheng Zhou: Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Wei Yu:** Writing – original draft, Formal analysis, Data curation. **Qianming Xia:** Supervision, Methodology, Conceptualization. **Chengshi He:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

None.

Appendix ASupplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e23701.

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