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Case Report

Epiglottic Tuberculosis in a Patient Treated with Steroids for Addison's Disease

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Egeli, E., Oghan, F., Alper, M., Harputluoglu, U. and Bulut, I. *Epiglottic Tuberculosis in a Patient Treated with Steroids for Addison's Disease.* Tohoku J. Exp. Med., 2003, **201** (2), 119–125 —— Isolated epiglottic tuberculosis (TBC) is uncommon and has rarely been described. We report the case of a 40-year-old man with tuberculous involvement of the epiglottis and primary adrenal insufficiency. Endoscopic examination showed a severely swollen epiglottis with granulomatous and partially necrotic mucosa. The patient has been treated with glucocorticoids for four years due to primary adrenocortical insufficiency. We therefore assume that tuferculous involvement of epiglottis is due to the reactivation of pulmonary TBC. We also discuss differential diagnosis and management of epiglottic TBC and Addison's disease. ———— epiglottic tuberculosis; primary adrenal insufficiency; glucocorticoids

In 1993, WHO (World Health Organization) declared to take precaution immediately for tubenculosis (TBC) that is a widespread contagious disease on all over the world. It was thought that about 90 million people would be infected with TBC between the years of 1990–2000. In Turkey, officially the number of people infected with TBC yearly is about 22 000–27 000, but the actual number was estimated to be about 35 000–40 000 (Azap et al. 1999). There are several risk factors for TBC in Turkey, such as drugs (e.g., antichemotherapeutics, corticosteroids), diseases (e.g., HIV) causing immunosupression, and residence in long term care facilities.

Laryngeal TBC was the most common disease involving the larynx in the early stage of the twentieth century (Agarwal et al. 1998). Today, laryngeal involvement of TBC infection is less than 1% among TBC patients. Furthermore, it is more common in developing countries than developed countries. Consistent with the high incidence of hoarseness, the glottis is the most common site of involvement, but other regions of the larynx can be involved, such as epiglottis seen in our case.

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The causes of adrenal insufficiency are categorized as primary and secondary. Primary adrenal insufficiency is relatively rare and may occur at any age, and affects both sexes equally. On the other hand, because of the common therapeutic use of steroids, secondary adrenal insufficiency is relatively common (Williams eand Dluhy 2001). The common factor in many cases of adrenal insufficiency is destruction of the adrenal cortex, either by infection or an autoimmune-mediated process, with the latter being more likely (Brenner 2001).

The adrenal is a frequent site for chronic granulomatous diseases, predominantly TBC but also histoplasmosis, coccidiodomycosis, and cryptococcosis. TBC used to be responsible for 70 to 90% of the cases, but the most frequent cause now is idiopathic atrophy, which may be caused by an autoimmune mechanism (Williams and Dluhy 2001). Hydrocortisone is the agent of choice for the treatment of acute adrenal insufficiency because it acts rapidly and has both glucocorticoid and mineralocorticoid activity (Brenner 2001).

In this case report we present a patient with epiglottic TBC who has primary adrenocortical insufficiency. Even though the cases with epiglottic TBC are rare, otorhinolaryngologists should keep in mind the possibility of TBC in the differential diagnosis of laryngeal tumors, as the incidence of TBC in developing countries is steadily increasing due to current tending in using immunosupressive treatment.

Case Report

A 40 year-old-man who had hoarseness, fatigue, weariness, cough, anorexia and difficulty in swallowing for fifteen days applied to our clinic. He had 7 kg weight loss for the last 2 months and had a history of symptoms of a common cold for the last 2 years. There was no smoking and alcohol history. He has been treated with the replacement treatment of methylprednizolone (16 mg/day) and fludrocortisone (0.1 mg/day) for the last 4 years due to primary adrenal insufficiency. Endoscopic laryngeal examination revealed a lesion located on the epiglottis and the contours of the epiglottis were irregular. The epiglottis was swollen and partially destructed, with necrotic and granulomatous lesions (Fig. 1). The laryngeal appearance prompted us to suspect of a carcinoma. The irreguler lesions of the epiglottis are localized on the superior third of the epiglottis. Other laryngeal parts appeared not to be affected. Chest x-ray showed multiple cavities

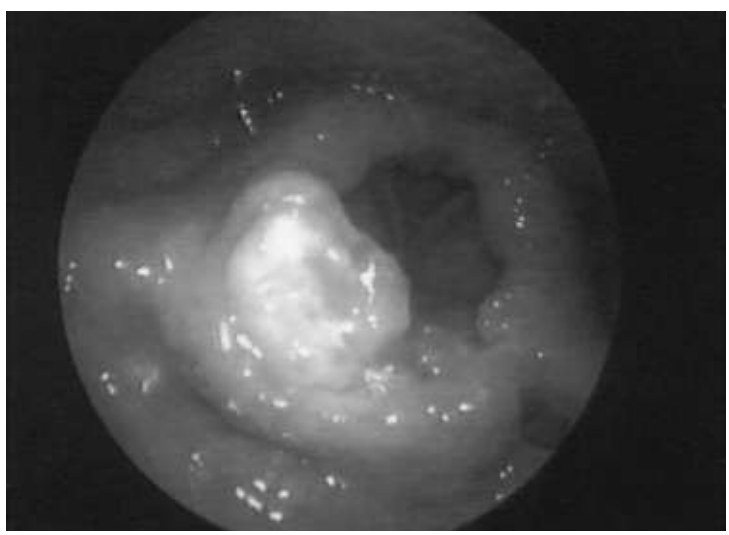

Fig. 1. The lesions of the epiglottis revealed by the first endoscopic examination. The epiglottis was swollen with necrotic mucosa and granulomatous lesions.

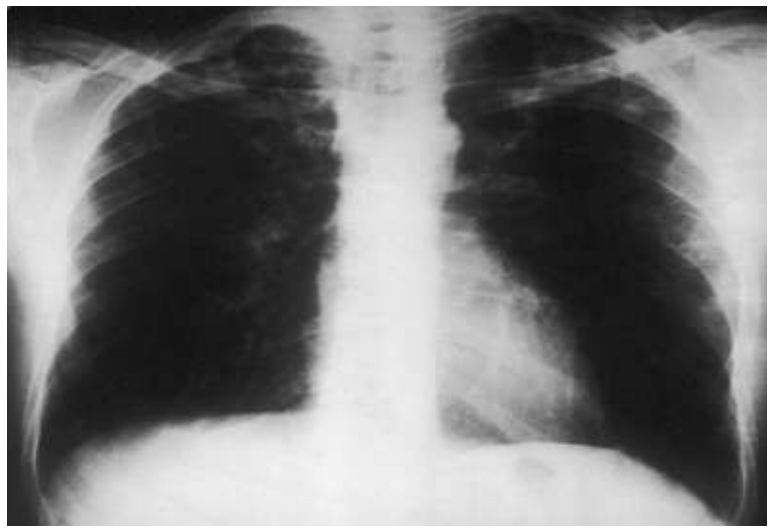

Fig. 2. Chest x-ray showed multiple cavities and fibrosis with nodular shadowing in both upper lobes.

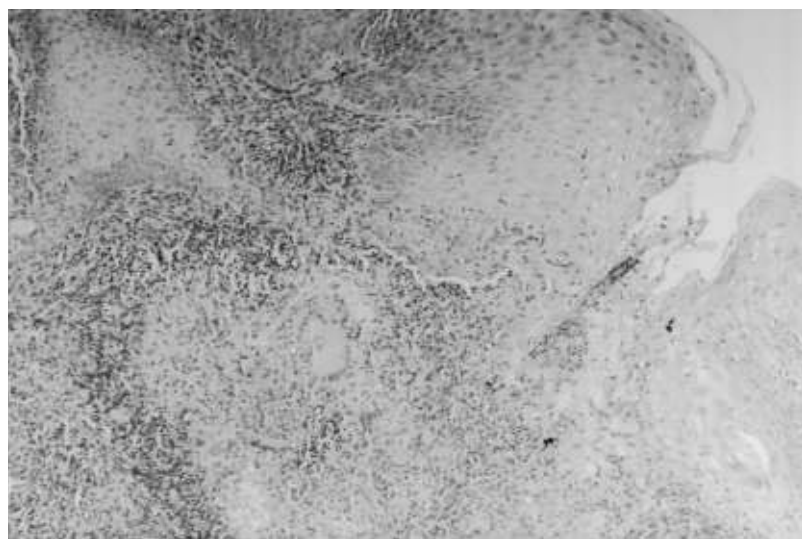

Fig. 3. Epiglottitis with granuloma surrounded by lymphocytes and plasma cells (H & E, ×100).

and fibrosis with nodular shadowing in both upper lobes (Fig. 2) and the erythrocyte sedimentation rate was high raised at 40 mm/hour. The chest radiography findings raised the possibility of TBC. Acid-fast bacilli on a Ziehl-Neelsen stain were seen on microscopy of sputum and gastric fluid samples. Under local anesthesia endoscopic laryngoscopy was performed; one biopsy specimen was sent for bacteriologic evaluation and was found to be positive for acid-fast bacilli. Mycobacteria tuberculosis grew in subsequent cultures. Histologic examination of a second biopsy specimen from epiglottis showed an epithelioid giant cell granuloma with microfocal caseous necrosis surrounded by lymphocytes and plasma cells (Fig. 3). On the basis of the bacteriologic, radiologic, and histologic findings, the diagnosis of pulmonary TBC with epiglottic involvement was established. For further treatment, the patient was transferred to the pneumology department because this infection could be was

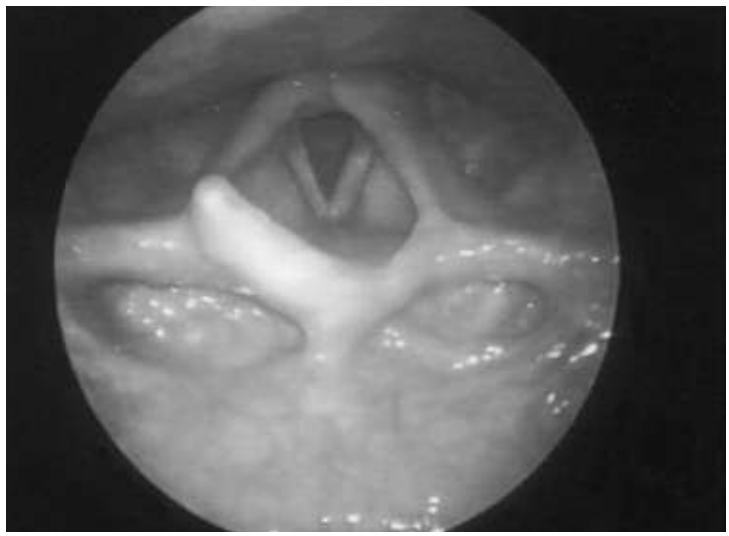

Fig. 4. The granulomatous lesions of the epiglottis disappeared after antituberculous treatment.

secondary to reactivation of the patient's pulmonary TBC. The patient was given antimycobacterial therapy comprising isoniasid, rifampicin, ethambutol hydrochloride, and pyrazinamide. Within 2 weeks, the patient's conditions markedly improved. After 6 months of treatment, on the endoscopic examination the lesions of the epiglottis disappeared (Fig. 4). He had a good response to this treatment and has been followed up in the outpatient clinic. All complaints such as hoarseness and swallowing difficulties disappeared.

DISCUSSION

The existing prevalance figures clearly indicate that Addison's disease has become more common. Before 1950 this disease was closely related to TBC, and idiopathic adrenocortical failure was rare (Guttman 1930). With the declining proportion of tuberculous adrenalitis, the increase in autoimmune adrenal failure has become more evident (Lovas and Huseybe 2002). Because of the fact that the biopsy specimen obtained 4 years ago did not show any infectious origin in the present case, autoimmune-mediated process was considered to be responsible for the destruction of adrenal cortex. The patient has been treated with cortisol and mineralocorticoid replacement due to primary adrenal insufficiency for 4 years. Treatment of other medical conditions with steroids can potentially reactivate a latent TBC or increase the risk for primary infection.

Recent incidence of laryngeal TBC is less than 1% among TBC patients. Nedwicki (1970) described 2 patients who underwent direct laryngoscopy and biopsy and were found to have laryngeal TBC. Bull (1966) reported 7 patients with laryngeal TBC masquerading as carcinomas, and Smallman et al. (1987) reviewed 6 cases of laryngeal TBC in a 10-year period. Isolated epiglottic TBC is uncommon but in the last decade there has been a changing pattern of laryngeal TBC. Singh et al. (1996) found epiglottic TBC in 1 of their 8 non-HIV-positive patients. Kandiloros et al. (1997) reported 9 cases of laryngeal TBC and found the lesion in epiglottis in 2 cases. Thaller et al. (1987) reviewed 15 patients with laryngeal TBC and found only 1 patient with isolated epiglottic involvement. Agarwal et al. (1998), in a series of 31 cases of tuberculous laryngitis, found 1 patient with epiglottis involvement as the only site of laryngeal lesion. Tu et al. (1997) reviewed 46 patients with laryngeal TBC and stated that the epiglottis was affected in 39% of the

cases in addition to other parts of the larynx. Galli et al. (2002) reported a case of isolated epiglottic tuberculosis that was presented as a laryngeal carcinoma. Richter et al. (2001) reported a patient with tuberculous involvement of the epiglottis suffering from unsuspected pulmonary tuberculosis. The clinical symptoms of patients with TBC and carcinoma of the larynx may be similar, including hoarseness, dysphagia, dyspnea, cough, and sore throat. Patients often report a history of weight loss and tobacco or alcohol abuse (Ramadan et al. 1993). In our case, there was no smoking and alcohol history but weight loss was present.

The resurgence of TBC in this decade has affected many populations, especially immunocompromised patients. These patients may need corticosteroid therapy for various concomitant diseases that might predispose a patient to develop primary TBC infection or reactivate latent TBC infection (Cisneros et al. 1996). Cell-mediated immunity plays a very important role in fighting TBC and, wheres by altering this immunity, corticosteroids can increase the risk of reactivating latent disease. Millar and Horne (1979) described 11 patients who developed either pulmonary or extrapulmonary TBC while receiving long-term corticosteroid therapy. Haanaes and Bergmann (1983) evaluated 1355 cases of TBC to determine how frequently the development of TBC was associated with corticosteroid therapy. In their study, 40 patients (3%) had received corticosteroids within 6 months prior to developing TBC. All patients demonstrated reactivated TBC infection; none developed a new infection. Because of the fact that autoimmune deficiency syndrome (AIDS) and other immunosuppressive diseases or treatments may contribute to increase the incidence and spectrum of tuberculosis, we also investigated the presence of such infections and diseases by history and laboratory studies. In our case, we believe that TBC has been reactivated due to long term corticosteroid replacement therapy. Corticosteroids demonstrate both adverse and beneficial effects in patients with TBC. Steroids may adversely suppress or modify cell-mediated immunity (Masud and Kemp 1988). Tuberculin reactivity is reduced after patient recieves prednisone 15 mg/day (or equivalent) for 2–3 weeks (Selwyn et al. 1989). Frenkel (1960) presented evidence for the view that the endogenous steroids of the adrenal cortex permitted the selective, progressive multiplication of tubercule bacilli which resulted in Addison's disease. It is clear, therefore, that excessive glucocorticoids reduce resistance to infection in general. Corticosteroids are used as replacement therapy in patients who develop Addison's disease secondary to tuberculous infection (Dedon et al. 1992). In our case, the patient had been treated with steroids due to Addison's disease that is caused by idiopathic atrophy of adrenal glands. Autoimmune Addison's disease can develop slowly over many years before symptoms appear (Ten et al. 2001).

The patients, who were instructed to spend a large part of their time during their illness in bed, tended to develop lesions of the posterior larynx (Soda et al. 1989). Our present study agrees with the reports (Anderson and Stevens 1981; Espinoza et al. 1981; Hunter and Millar 1981; Levenson et al. 1984) that lymphatic/hematogenic spread and disease of the anterior larynx is now more commonly encountered. In our case, TBC lesion was limited to the epiglottis, but was initially suspected of an epiglottic malignancy. However, unlike our case, patients with malignancy are usually older than 60 years age, with a history of heavy smoking and alcohol. It is therefore important to note that the TBC lesions can be confused with laryngeal tumors. For instance, Khan (1983) reported a case of tuberculous granuloma of the epiglottis that resembled carcinoma on laryngoscopic examination, and only histologic examination of the biopsy material was diagnostic. Our case suggests that the physicians dealing with the patients who has been treated with steroids should be aware of the possibility

of laryngeal TBC and should be careful to distinguish the lesion from tumors or chronic laryngitis.

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