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Infectious Esophagitis

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Abstract

Esophagitis is the inflammation of the lining of the esophagus, which is characterized by its swelling and irritation. The esophagus is tubular structure which helps in the swallowing, and it links the back of the throat to the stomach. The swelling is commonly caused by acid reflux. Sometimes, this swelling can also be caused by infections. Infectious esophagitis can be set off by fungi, yeast, viruses, bacteria and other types of organisms. Anyone can get infectious esophagitis, but people with weakened or comprised immune system are more likely to develop the disease. Anyone can get it, but people are more likely to develop it if their immune system is weakened or compromised. The purpose of this chapter is to review the clinical manifestations, etiology, pathophysiology, histopathology, diagnosis, treatment/management, prevention, prognosis and other healthcare issues of infectious esophagitis.

Keywords: Infectious esophagitis, fungi, yeast, virus, bacteria, diagnosis, treatment, prevention

1. Introduction

Esophagitis is the swelling and irritation of the esophagus. Thus esophagitis refers to inflammation or injury to the esophageal mucosa. The esophagus is the tube that is used in swallowing and it connects the back of the throat to the stomach. There are many causes of esophagitis and essentially the presentation is similar which include retrosternal chest pain, heartburn, dysphagia or odynophagia [1, 2]. The most common cause of swelling and irritation of the esophagus is stomach acid that flows back into the esophagus, called gastroesophageal reflux, which can lead to erosive esophagitis. Other etiologies include radiation, infections, local injury caused by medications, pill esophagitis, and eosinophilic esophagitis (EoE) [3]. Patients with EoE may present with food impaction. If the esophagitis is severe and leads to strictures, fistulization, and perforation, patients may present with symptoms related to those entities.

In addition, infections can also cause swelling and irritation of the esophagus. Fungi, yeast, viruses, and bacteria can all set off the condition, called infectious esophagitis. Anyone can get it, but a person is more likely to develop it if their immune system is weakened [4].

The incidence of infectious esophagitis has become prevalent in immunocompromised patients with cancers and organ transplant because of their survival rates due to advances in medical practice and management techniques. The causative agent is normally *Candida albicans*. However, organisms like herpes simplex

virus (HSV) and cytomegalovirus (CMV) have often been known to invade the esophagus. Patients with acquired immunodeficiency syndrome (AIDS) may develop more fulminant forms of fungal and viral esophagitis (including human immunodeficiency virus [HIV] esophagitis), accentuating the need for early diagnosis and treatment. The purpose of this chapter is to review the clinical manifestations, etiology, pathophysiology, histopathology, diagnosis, treatment/management, prevention, prognosis and other healthcare issues of infectious esophagitis.

2. Etiology

The causes of infectious esophagitis are many and they involve [5–13]]:

- Fungi, like *C. albicans*, which is the most common pathogen. However, other *Candida* group of organisms, for example *C. tropicalis*, *C. glabrata* and *C. parapsilosis* have also been identified as rare causes of esophagitis.
- Other types of fungi such as *Aspergillus*, *Histoplasma*, *Cryptococcus*, *Blastomyces* etc.
- Viruses such as Herpes simplex (HSV), Cytomegalovirus (CMV), Varicella-zoster virus (VZV), Epstein–Barr virus (EBV), Human papillomavirus (HPV), Poliovirus etc. It is important to note that people infected with the human immunodeficiency virus (HIV), CMV, HSV, *Mycobacterium avium*-intracellulare are idiopathic in nature.
- Bacteria such as normal flora, *Mycobacterium tuberculosis*, *M. avium*-intracellulare, *Saphylococcus*, *Streptococcus*, *Lactobacillus*, *Norcadia* etc.
- Parasitic agents such as Chagas disease, *Trypanosoma cruzi*, *Cryptosporidium*, *Pneumocystis*, *Leishmania donovani* etc.

The risk factors of infectious esophagitis include antibiotics and steroids use, chemotherapy, radiation therapy, malignancies and immunodeficiency syndromes like the acquired immunodeficiency syndrome (AIDS). Additional diseases linked to increase in the incidence of *Candida* esophagitis include esophageal stasis, alcoholism, malnutrition, and advanced age. Occasionally, *Candida* esophagitis can occur in otherwise healthy individuals with no underlying esophageal or systemic disease [7–13].

Additional typical risk factors such as acute onset of symptoms such as dysphagia and odynophagia are also remarkable in some cases of infectious esophagitis. The disease may coexist with heartburn, retrosternal pain, nausea and sometimes vomiting. Occasionally, patients can present with abdominal pain, anorexia, weight loss and cough. Infectious esophagitis is frequently caused by *Candida* organisms. Other important causes include CMV and HSV infection.

Again, people presenting with generalized sepsis, low neutrophil counts, AIDS, burns, trauma etc., can have rare infectious esophagitis. Severe esophagitis with very deep ulcers and fistulous tracts to the mediastinum, pleural space, tracheo-bronchial tree, skin and other tissues can be due to actinomycosis. The appearance of characteristic sulfur granules on endoscopic biopsy specimens can confirm the diagnosis of infectious esophagitis. The most notable risk factor for infectious esophagitis in people with HIV is reoccurring low CD4 count. However, it has also

been suggested that people can develop fungal esophagitis during the seroconversion phase of the process [5, 7–13].

3. Pathophysiology

Many agents like fungi, bacteria, parasites, viruses and other microorganisms can cause infectious esophagitis. The disease is more prevalent in immunocompromised people, but it can also occur in healthy people, including adults and children [13, 14]. The least common of all causative agents for infectious esophagitis is bacteria, but the most common cause of infectious esophagitis is .

The steps involved in the pathophysiology of infectious esophagitis include:

- colonization with mucosal adherence and proliferation is the first step in pathophysiology of infectious esophagitis.
- impairing the host defense mechanisms

Whilst *Candida Albicans* is a normal component of oral flora, it can also become a problem if their number increases, for example, with the use of antibiotics or if the patient is immunosuppressed because of treatment with corticosteroids. HSV is the most common cause of viral esophagitis, and it infects the squamous epithelium leading to vesicles and then ulcerations. CMV, Epstein–Barr (EBV) and varicella-zoster (VZV) are other viral causes of viral esophagitis.

Individuals may become susceptible to acquiring opportunistic infections like neutropenia, impaired chemotaxis and phagocytosis, impaired T-cell lymphocyte function and alteration in humoral immunity due to wide range of abnormalities in the host defense.

People suffering from various systemic diseases such as adrenal dysfunction, alcoholism, diabetes etc., and older citizens can be prone to catching infectious esophagitis due to altered immune function steroids, radiation, cytotoxic agents and immune modulators can also lead to the impaired host immune function.

The mucosal protective barriers and antibiotics that suppress the normal bacterial flora disruption may contribute to the invasive ability of commensal organisms [14]. Categories of infectious are as follows [11–14]:

- i. Fungal esophagitis, for example, *Candida* Esophagitis
- ii. Viral esophagitis, for example, HPV esophagitis and CMV esophagitis etc.
- iii. Bacterial esophagitis, for example, tuberculosis, actinomycosis etc.
- iv. Tuberculous esophagitis as stated in point (iii) above
- v. Other infections that can cause esophagitis

Fungal overgrowth in the esophagus, or impaired cell-mediated immunity or both can result in the development of *Candida* esophagitis.

The setting of esophageal stasis leads to cause of fungal overgrowth resulting from:

- a. abnormal esophageal motility like achalasia
- b. scleroderma or mechanical causes such as strictures.

Dysfunctional cell-mediated immunity can be caused by:

- a. immunosuppressive treatment, for example with cytotoxic agents or steroids that might suppress both granulocytes and lymphocytes functions
- b. Malignancy
- c. AIDS

Candida esophagitis also associated with chronic mucocutaneous candidiasis, which is a congenital immunodeficiency state.

Diseases that interfere with esophageal peristalsis like achalasia, esophageal cancer and progressive systemic sclerosis may lead to fungal esophagitis.

Primarily, esophagitis caused by HPV is presented by small vesicle developments that rupture eventually forming superficial ulcers on the mucosa that are discrete in nature.

The host promotes healing of the ulcers in immunocompetent people. However in severely immunosuppressed people, the disease may progress from discrete areas of ulceration hemorrhagic esophagitis that is diffused. Candidiasis may heavily infect necrotic herpetic ulcers.

The esophagus is normally involved by erosion of concerned mediastinal lymph nodes abutting the esophagus in tuberculous esophagitis.

In addition, infection of the esophagus by bacteria occurs in the immunocompromised host, is usually polymicrobial, and derives from oral flora. This entity is underdiagnosed in severely granulocytopenic patients, given that bacteria are difficult to identify on routine histologic examination. In such patients, bacterial infection often coexists with viral or fungal organisms that are more readily detected. Suppression of gastric acid production (by proton pump inhibitors) may predispose to bacterial and fungal esophagitis. The diagnosis is made by endoscopic biopsy, and in these specimens, clusters of bacteria are mixed with necrotic epithelial cells. Treatment consists of broad-spectrum antimicrobial therapy.

Although infectious esophagitis is usually caused by fungal or viral organisms, other rare causes include *Staphylococcus*, *Streptococcus*, *Klebsiella*, *Blastomyces*, *Cryptosporidium*, *Torulopsis glabrata*, and *Lactobacillus acidophilus*.

4. Clinical presentation

4.1 Patient history

The history findings vary based on the type of esophagitis. Esophageal food impaction can be the initial presentation of proton pump inhibitor (PPI)-responsive eosinophilic esophagitis [15].

4.2 Symptoms

Immunosuppressed people are prone to developing infectious esophagitis. Fungi like *Candida* organisms and viruses such as HPV and CMV are the most common causes of infectious esophagitis. The diagnosis of infectious esophagitis is supported by immunocompromisation, steroid treatment, systemic disease or recent antibiotic use. Whilst some people may not have any symptoms of infectious esophagitis, notable symptoms of the disease are [1–15]:

- Experiencing pain when swallowing
- Having trouble swallowing
- Pain in the mouth
- Pain in the chest and heartburn
- Feeling nauseous or vomiting
- Feeling feverish or experiencing chills
- Loss of appetite, anorexia, loss of weights
- Coughing
- Pain in the abdomen
- Intermittent hematemesis

As the symptoms of infectious esophagitis may mimic other diseases, it is important that proper investigation and diagnosis are made in order to have better outcome for the patients.

In people with one or more predisposing factors for *Candida* esophagitis, it is often manifested clinically by dysphagia and/or odynophagia. Symptoms differ in characteristics and features that differ in intensity like mild/moderate achalasia to severe odynophagia, which makes it very hard for sufferers to eat food or swallowing. Some people may develop retrosternal pain or bleeding in the gut. However, some people do not have any symptoms.

Esophagitis caused by HPV is commonly present in immunosuppressed people with AIDS, existing cancer or long term serious diseases or people that had received steroids, chemotherapy or radiation treatments [13–15]. In healthy people with no existing medical conditions, herpes esophagitis can sometimes occur as acute self-limiting disease. Acute onset of severe odynophagia is usually present in people with herpes esophagitis. Difficulty in swallowing, pain in the chest and bleeding in the upper gut are other presenting symptoms in herpes esophagitis.

The development of severe odynophagia, dysphagia or both in people with AIDS is as a result of the manifestation of CMV. Evidence of CMV infection may be present in other organs and tissues like the colon, retina and liver in infected people. Patients may develop fear of eating sometimes in cases of severe odynophagia.

People with ulcers due to HIV normally show acute onset of severe odynophagia, dysphagia or both. A characteristic maculopapular rash may be visible on the upper half of the body if the ulcers manifest at the time of seroconversion.

People with advanced pulmonary or mediastinal tuberculosis or in immunodeficiency that have disseminated tuberculosis or other mycobacterial illnesses develop tuberculous esophagitis.

5. Diagnosis and differential diagnoses strategies

In considering the diagnosis and differential diagnosis of infectious esophagitis, it would be important to look at the diagnostic considerations and diagnosis considerations for the different types of infectious esophagitis in order to have

understandings of the various issues to note for making decisions on the suitable treatments for better outcomes for the patients.

5.1 Diagnostic considerations

The possibility of a systemic illness causing the esophageal manifestations should always be considered (for example, AIDS, scleroderma, systemic lupus erythematosus (SLE) and pemphigus). Similarly, cardiac causes of chest discomfort should also be considered, and the appropriate treatment should be given. If the diagnosis is unclear, admission for further evaluation is suggested. Do not misdiagnose cardiac chest pain as esophageal pain. Pain can be similar, particularly in elderly patients and women.

Conditions that may mimic symptoms of esophagitis include the following [12–15]:

- Coronary artery disease
- Pericarditis
- Aortic aneurysm
- Nonulcer reflux disease
- Functional dyspepsia
- Stricture

5.2 Diagnosis considerations for the different types of infectious esophagitis

The diagnosis considerations for the various types of infectious esophagitis are discussed below.

5.2.1 Diagnosis of Candida esophagitis

Reflux esophagitis, herpes esophagitis, superficial spreading carcinoma and glycogenic acanthosis, may produce findings similar to those seen in *Candida* esophagitis. However, it is also important to note that elderly people who do have any symptoms of the esophagus and the more rounded appearance of the mucosal nodules of glycogenic acanthosis do indeed present with glycogenic acanthosis, but the candidiasis plaques are more linear in appearance.

A nodular mucosa of reflux esophagitis can also be present in patients. However, the nodules are difficult to identify than those found in candidiasis, and they are normally infectious with the gastroesophageal junction.

Multiple plaquelike lesions in the gullet are sometimes due to herpes esophagitis, which is normally linked to small superficial ulcers. Cancers that are spreading superficially may also present as a nodular mucosa with poorly defined nodular borders, leading to a confluent area of disease.

The plaques of candidiasis may resemble the insoluble effervescent particles and debris in the gullet. Hence the performance of a double-contrast study should be undertaken without the use of effervescent granules if infectious esophagitis is suspected.

5.2.2 Diagnostic factors for herpes simplex (HSV) esophagitis

Esophagitis due to the HSV can be identified by discrete superficial ulcers in the upper/mid gullet in the absence of the linked plaques, in the appropriate clinical environment. On the other hand, Candida esophagitis ulceration usually manifests on a background of extensive formation of plaque. Double-contrast investigations can be used in the diagnosis of Candida and herpes esophagitis without performing an endoscopy. It is also important to undertake endoscopic evaluation for confirmation of diagnosis when radiographic findings are ambiguous or when the problem do not respond to the treatment given to them.

Drug-induced esophagitis and Crohn disease are other causes of small superficial ulcers in the upper/mid esophagus, but these diseases can be differentiated from infectious esophagitis via detailed and careful patient history.

5.2.3 Diagnostic factors for CMV esophagitis

Endoscopy with biopsy is the most effective diagnostic tool for CMV. Large punched out lesions are seen in mid esophagus on inspection. Enlarged cells in the sub-epithelial layer with inclusions within the cells' nucleus and its cytoplasm can be seen in histological analysis of the lesions. Fluorescent staining with an immunoperoxidase stain is very specific in addition to the histological investigation. The diagnosis of CMV esophagitis cannot be made effectively with radiologic imaging tests like X-rays or CT scans alone, but they can be helpful in discovering of any resulting fistulae or strictures.

The presentation of large/giant ulcers in a patient may suggest the diagnosis of CMV esophagitis in AIDS patients because herpetic ulcers really becomes as big as those of infectious esophagitis, but giant/large ulcers can also be caused by HIV in HIV positive people.

Giant esophageal ulcers can also be caused by nasogastric intubation; endoscopic sclerotherapy; caustic injuries and oral medications, such as nonsteroidal anti-inflammatory drugs (NSAIDs), potassium chloride, and quinidine [13–15]. Efficient patient's clinical history is normally helpful in suggesting the correct diagnosis of CMV esophagitis [14, 15].

Again, CMV can be transmitted through many ways, which include mother to child transmission, which is common after birth and spreading of CMV through blood or sex, but transmission via tears, saliva, and skin contact is not common. Therefore patient education is very important in this regard.

5.2.4 Diagnostic factors for HIV esophagitis

It is important to rule out CMV esophagitis by performing endoscopy before confirming the HIV esophagitis diagnosis because most HIV ulcers are not distinguishable from CMV ulcers on the basis of just the clinical and radiological criteria alone. In addition, specimens from biopsy, brushings and viral cultures from the esophagus may be needed in order to be certain about the diagnosis and offer the patient the correct treatment.

During the period of transient chills, fever, malaise and rash of early infection with HIV, multiple, small, aphthoid lesions are observed on patients. In addition, giant deep ulcers measuring several centimeters can be seen later. Large ulcers may be complicated by fistula formation, perforation, hemorrhage, or superinfection in patients.

As most cases of HIV esophagitis responds well to oral steroids treatments, but CMV esophagitis is treated with toxic antiviral agents like ganciclovir, it is essential to differentiate between these infections. Hence endoscopic investigation should be undertaken before treating the patients.

5.2.5 Diagnostic factors for varicella-zoster virus (VZV) esophagitis

Severe esophagitis can be caused by Varicella-zoster virus (VZV), and finding its concurrent demographic lesions is extremely important to its diagnosis and also development of effective treatment plan for the patients.

On esophagogastroduodenoscopy (EGD), VZV has different features, which can range from infrequent vesicles of ulcerative lesions to a confluence of ulceration with necrosis. Epithelial cells with VZV display ballooning degeneration, edema and multinucleated giant cells with eosinophilic inclusion bodies on histologic investigation. In differentiating VZV from HSV, immunohistochemical staining utilizing monoclonal antibodies is usually helpful in the process.

5.2.6 Diagnostic factors for Epstein-Barr virus (EBV) esophagitis

Epstein-Barr virus (EBV) causes different syndromes in people. Crohn's disease and ulcerative colitis are common diseases that can be manifested by EBV, but the incidence and prevalence of EBV are still not well stated in both immunocompetent and immunodeficient people, hence, it should be seriously considered in any person presenting with symptoms of the esophagus. EBV esophagitis in an immunocompetent individual is a rare occurrence, and thus represents either a primary infection, reactivation/reoccurrence, which is usually characterized acute onset of symptoms and extensive ulcerative involvement of the upper/mid third of the esophagus. Oral hairy leukoplakia has similar histologic features of esophageal lesions linked to the EBV.

5.2.7 Diagnostic factors for human papillomavirus (HPV) esophagitis

Multiple epithelial lesions and cancers that are predominantly found on cutaneous mucosal surfaces are caused by the human papillomavirus (HPV), which is a non-enveloped, double stranded, circular DNA virus. The virus has over 100 subtypes, and people with persistent HPV infection, especially those with many sexual partners are at very high risk for contracting more subtypes of HPV. At present, the HPV infection can be classified as non-genital/cutaneous; mucosal or anogenital and epidermodysplasia verruciformis (EV).

In some cases, the clinical lesions of HPV can be visibly identifiable, but in other cases, latent lesions of HPV may require testing for viral deoxyribonucleic acid (DNA) before confirming the diagnosis. In majority of the cases, HPV infections are latent and most lesions manifest as warts rather than malignancy in clinic.

Nowadays, the HPV has been identified as the etiological agent for laryngeal, oral, lung and anogenital cancer. HPV subtypes six and 11 are low risk and usually manifest with the formation of condylomata and low grade precancerous lesions. However, HPV 16 and 18 are high risks that are responsible for high grade intraepithelial lesions, which progress to malignancies.

It is also crucial to note that HPV alone does not cause cancer, but it requires triggers such as folate deficiency, smoking, immunosuppression, and pregnancy and ultraviolet (UV) light exposure.

Esophagitis caused by HPV is an asymptomatic illness. Lesions of the disease are usually found in the middle to distal esophagus in patients and they may

look like erythematous macules, white plaques, nodules, or exuberant frondlike lesions. The diagnosis of HPV esophagitis is made based on histology, and koilocytosis, giant cells, and cytologic atypia are visible on immunohistochemical stains.

5.2.8 Diagnostic factors for tuberculous esophagitis

The development of transverse or longitudinal sinus tracts or esophageal-airway fistulae can be as a result of the erosion of caseating nodes into the esophagus. People suffering from radiation esophagitis, Crohn's disease esophageal cancer or some sorts of trauma also display similar fistulae and tracts, but the clinical presentations of these patients normally portray the right diagnosis.

Intrinsic tuberculosis is very uncommon and it features of mucosal plaques, fistulae, strictures and ulcers. In a patient with tuberculosis, the development of difficulty in swallowing, cough and choking on swallowing indicates the involvement of the esophagus.

6. Treatment and management of infectious esophagitis

Treatment of infectious esophagitis is based on the patient's immune status, disease severity, and risk of complications [5, 16, 17]. The goal of medical care is to treat the underlying cause and minimize morbidity. The treatments strategies for the different types of infectious esophagitis are discussed below.

6.1 Treatment of fungal esophagitis

Antifungal drugs are normally used in the treatment of candidiasis in the throat, mouth or esophagus. The treatments for are categorized thus [18]:

- Active topical drugs such as oral amphotericin B, clotrimazole and nystatin
- Absorbable agents that are administered orally like fluconazole and itraconazole
- Agents like amphotericin B, flucytosine nad fluconazole that are administered parenterally

An antifungal medication that is applied to the inside of the mount between seven to 14 days is normally used in the treatment of mild to moderate infections of the throat or mouth. These drugs include clotrimazole, miconazole or nystatin. The most common treatment for severe fungal infections is fluconazole, which is an antifungal medicine that is taken by mouth or administered intravenously. If the patient does not respond to fluconazole, a different antifungal drug should be prescribed. The treatment for *Candida* esophagitis is fluconazole. However, another type of antifungal medication should be given to people who cannot tolerate fluconazole or who do not respond to the treatment with it.

It is important to note that treatment option chosen for a patient will depend on the severity of infection and the extent of the host defense impairment. For exam0ple, majority of immonocompetent people with fungal esophagitis can be treated with a topical antifungal medicine, which do not have adverse side effects, have only few or even any drug to drug interactions as the drugs are not absorbable in nature.

6.2 Treatment of HSV esophagitis

HSV esophagitis diagnosed at endoscopy can be treated with medications such as acyclovir (Zovirax); valacyclovir (Valtrex); famciclovir (Valtrex), an acyclovir analog; and foscarnet (for acyclovir-resistant cases). Pain relief medicines bought over the counter at pharmacies may also help in relieving pain caused by HPV esophagitis. Long term prescription of antiviral drugs can also be used in the prevention of the development of recurrent outbreaks of HSV esophagitis.

6.3 Treatment of CMV esophagitis

CMV is similar to HSV, as it is a member of the *herpesviridae* family of viruses. Induction therapy for three to six weeks is used in the treatment of CMV esophagitis, but the optimal period of the treatment is not yet well defined. The maintenance treatment for CMV is controversial. Overall, intravenously administered ganciclovir 5 mg/kg or foscarnet 90 mg/kg is the recommended treatment for induction therapy. As both ganciclovir and foscarnet are potent viral agents that have significant bone marrow and renal toxicities, extra care should be taken before they are prescribed to patients, by taking careful medical and drug histories from the patients, including any side effects they had had in the past.

It is also important to note that HIV esophagitis is treated differently from CMV esophagitis, but the two diseases cannot be simply separated on the basis of the clinical and radiographic results. Hence endoscopic investigation should be undertaken for a confirmatory diagnosis before patients are treated in order to achieve a better clinical outcome. In addition, endoscopy has over 95% sensitivity in the diagnosis of CMV esophagitis.

6.4 Treatment of HIV esophagitis

HIV esophagitis is treated with oral corticosteroid therapy normally for over one month with antiretroviral therapy for HIV in contrast to CMV esophagitis.

6.5 Treatment of VZV esophagitis

Acyclovir, famciclovir or foscarnet (for acyclovir-resistant cases) are typically used in the treatment of VZV esophagitis.

6.6 Treatment of EBV esophagitis

Acyclovir is used in the treatment of EBV esophagitis. In order to suppress oral hairy leukoplakia, long term maintenance therapy may also be required for the patient.

6.7 Treatment of HPV esophagitis

No treatment is normally required, as HPV esophagitis is usually asymptomatic. Some medicines such as systemic interferon alfa, bleomycin and etoposide have been used in patients' treatments with variable outcomes.

6.8 Treatment of *M. tuberculosis* esophagitis

In the immunocompetent people, standard antituberculous therapy has been used in the treatment of mycobacterium tuberculosis esophagitis.

6.9 Treatment of bacterial esophagitis

In healthy individuals, infection by normal flora that is usually seen in immunosuppressed people are rare. Polymicrobial infections such as *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus viridans* and *Bacillus* species are often seen in patients with Bacterial esophagitis.

A broad-spectrum beta-lactam antibiotic with an aminoglycoside is used in the treatment of Bacterial esophagitis. It is also important to note that the treatment is adjusted based on the results of response and culture.

7. Epidemiology of infectious esophagitis

The incident of esophagitis is low in children, but esophagitis is prevalent in adults [19, 20], and reflux esophagitis is the most common type.

The most type of infectious esophagitis is *Candida* esophagitis. Incidence of reflux esophagitis occur monthly in up to 44% of the general population, and up to 10% of people have daily symptoms of esophagitis [20].

In this section, we will look at the international statistics of the diseases and their prevalence in association with other disorders as described and discussed below.

7.1 International statistics

The prevalence of esophagitis is lower than the incidence of the symptoms of reflux sensation.

Patients presenting with symptoms of esophagitis to a General Practitioner (GP) in the United Kingdom (UK) show esophagitis rate in the range of 40–65%. The results of a retrospective review of results of over 800 diagnostic endoscopies in Hampshire, England, UK should that reflux esophagitis accounted for about 23% of all upper gastrointestinal diseases identified [21]. However, the incidence of infectious esophagitis is small in the studied population.

Another review of the Swedish National Register estimated that the prevalence of esophagitis diagnosed via endoscopy is about 5% or less in people aged 55 [22], and prevalence has also been estimated to be about 2% in other reports [23–25]. Again the incidents for infectious esophagitis low as indicated in the reports.

7.2 Prevalence in association with other disorders

In people with AIDS, leukemia and lymphoma, the prevalence of symptomatic infectious esophagitis is high, but it is less than 5% in the general population, which is low.

As noted stated previously, the most common type of infectious esophagitis is *Candida* esophagitis. The second most common infectious esophagitis is HSV esophagitis, which has been reported in about 1% of immunosuppressed patients, and in as many as 43% of the patients in autopsy investigations [23–28].

Another etiological agent for esophagitis is CMV. A big percentage of the global population has been exposed to CMV and asymptomatic CMV infection is common around the world [29, 30].

CMV esophagitis was usually discovered on post-mortem analysis prior to the AIDS epidemic, and the first clinical case of CMV esophagitis was reported in 1985 [30].

CMV does not occur in immunocompetent people unlike HSV esophagitis, and the majority of the people with CMV esophagitis have AIDS [29, 30]. Since the

advent of highly active antiretroviral therapy, the incidence of CMV esophagitis like those of other types of infectious esophagitis has declined among people with AIDS [29, 30]. On the other hand, there has been reported increase of CMV esophagitis in people who had undergone solid organ transplant, and in whom the onset of the disease was delayed due to the increasing routine of early CMV prophylaxis [31].

In AIDS patients in whom no other infectious etiological factors can be identified [32–36], giant esophageal ulcers have been observed [37], which have been called idiopathic HIV ulcers because they are believed to be caused by HIV, as electron microscopic investigation had confirmed the presence of HIV-like viral particles in the ulcer lesions [32–37].

Most patients have been found to have chronic AIDS with CD4 counts less than 100 cells/uL, despite the fact that some patients with HIV ulcers may have undergone recent seroconversion [38–41]. Ulcers associated with HIV have been under recognized generally, as it accounts for about 40% of all reported esophageal ulcers in AIDS patients [32–42].

8. Complications of infectious esophagitis

Unless a person has a medical condition that weakens his/her immunity, the complications of infectious esophagitis are rare, and they may include the following [43, 44]:

- Infection, which can spread to the other parts of the body
- Narrowing of the esophagus by scar tissue
- Bleeding from ulcers in the esophagus
- Perforation or fistula in the esophagus, including the formation of stricture
- Barrett esophagus, which occurs when the normal epithelium of the esophagus is replaced with columnar epithelium that is associated with cancer development.
- A serious and rare complication of perforation with mediastinitis
- Inability to swallow may cause volume depletion and weight loss
- If the gastric contents are refluxed up to the level of the larynx, laryngitis, aspiration bronchospasm and pneumonitis may occur.
- Failure to thrive and apnea may manifest in infants and children

9. Prognosis

The prognosis of infectious esophagitis is good with quick diagnosis, including effective and efficient treatment. Ultimately, prognosis depends on the underlying disease process.

Mild symptoms of esophagitis results in minimal morbidity and mortality. People with moderate-to- severe symptoms may suffer anxiety and lost time from work, which could lead to medical evaluations for more serious causes of pain.

Esophageal strictures (typically long, smooth, tapered areas of narrowing), malnutrition, and, rarely, perforation or bleeding can occur as a result of complicated esophagitis.

Barrett esophagus and adenocarcinoma are serious gastrointestinal complications of esophagitis in addition to strictures. In children, gastric content aspiration is a potentially serious respiratory complication that occurs frequently, that can be linked to apnea, pneumonitis and bronchospasm.

Odynophagia, malnutrition, dyspnea and pain may be as a result of severe esophagitis. On rare occasions, death may occur as a result of life threatening bleeding, but outcomes and survival in these patients are associated to the severity of their underlying systemic diseases.

Due to the fact that recurrence is a frequent problem in patients with reflux, many patients require maintenance therapy to prevent relapse of symptoms.

As *Candida* esophagitis is often self-limiting, many patients responds antifungal therapy [42, 43]. However, mycetoma, a fungus ball that causes obstruction may be formed from necrotic mucosal debris and fungal mycelia in the esophagus. The formation of strictures as a result of severe *Candida* esophagitis can also be seen in some patients. Rare fistula development into the tree of the bronchi, including ulceration and hemorrhage are other complications of infectious esophagitis, which will give poor outcome for the patients [43, 44].

Herpes esophagitis usually resolves spontaneously in immunocompetent patients within one to two weeks with conservative treatment involving analgesia and sedation. Rare complications of herpes esophagitis include perforation, tracheoesophageal fistulas, and dissemination to other organs.

Generally, most healthy individuals with infectious esophagitis recover within two to four weeks with proper therapy. However, recovery in people with comprised immunity (immunosuppressed people) recovery may take longer due to various factors.

10. Patient education and preventive measures

Clinicians should work closely with people who are recovering from infectious esophagitis and encourage them to keep all their follow-up medical appointments in order to monitor their progress and treatments outcomes.

The clinicians can suggest the following steps to patients that have ongoing symptoms of painful or difficulty in swallowing:

- Quit smoking and the use of tobacco and its products
- Stop alcohol and caffeine consumption
- Avoid over the counter drugs such as ibuprofen, aspirin and other non-steroidal anti-inflammatory drugs, which can irritate the esophagus
- Beverages and food that can cause heartburn should be avoided
- Try to lose weight if they are obsessed or overweight
- Eating smaller foods or meals more often
- Stop eating for three hours before going to bed

- Sleeping in flat position should be avoided, and the head of the bed should be elevated by several inches, i.e., six inch blocks. It is also important to discourage patients from sleeping with extra pillows as this may increase intra-abdominal pressure caused by people bending at the waist level.

The importance seeking early medical evaluation at the onset of symptoms should be emphasized to the patients and the general population in health education/health promotion campaigns. In addition, the importance of taking medicines with plenty of water while sitting upright in order to avoid the complications of drug-induced esophagitis should be highlighted to the patients.

Clinicians should also avoid the prescription of certain medications like alendronate in patients with obvious esophageal varices. It should also be noted that giving alendronate to patients who are cirrhotic could precipitate gastrointestinal bleeding from erosions over an esophageal varix.

11. Conclusion

Infectious esophagitis is a rare disease caused by viral, bacterial, or fungal agents or other organisms and infections. Patients who are immune suppressed, including people with granulocytopenia, lymphopenia etc., are usually prone to infections. Infection with *Candida* is the common cause of infectious esophagitis, but infections with HSP, bacteria and CMV are rare and accounts in up to 16% cases of infectious esophagitis in people with immunosuppression. Endoscopic observable ulcers with erythema, exudate and hemorrhage characterized bacterial esophagitis, and persistent symptoms include severe dysphagia and odynophagia, which may be a source of bacterial sepsis that will require prompt antibiotic treatment. Thus, infectious esophagitis causes morbidity in patients and careful diagnosis and treatment processes need to be followed in order to achieve better prognosis and outcomes for sufferers.

Conflict of interest

The authors declare no conflict of interest.

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