

# Head and Neck Infections in Diabetic Patients

Pookamala Sathasivam

## Abstract

Globally, the burden of diabetes is increasing very rapidly as is the diabetic related complications. Infections in diabetes mellitus are relatively more common and serious. Diabetic patients run the risk of acute metabolic decompensation during infections, and conversely patients with metabolic decompensation are at higher risk of certain invasive infections. Infections in diabetic patients result in extended hospital stays and additional financial burden.<sup>1</sup> Medicine in modern world has seen tremendous advancements like newer generation of anti-diabetic drugs, modern insulin therapy, better intensive care facilities and more potent antibiotics. Despite all these advancements, infection still remains one of the major cause for increasing morbidity and mortality in diabetic patients<sup>2</sup>. This article focuses on the common diabetes related infections in the Head and Neck region of the body. Some of the life threatening infections like malignant otitis externa and rhino-cerebral mucormycosis affect this region of body.

## Introduction

Patients with diabetes mellitus are more prone for infections. Infection can affect any region of the body and some of the common infections in the head and neck region include furunculosis involving the skin of ear canal and nasal vestibule, cellulitis, necrotising fasciitis, malignant otitis externa, rhino-cerebral mucormycosis,

parotid abscess and parapharyngeal abscess. Among these infections malignant otitis externa is almost always seen in diabetics only. Some of these infections are very difficult to treat and have a greater mortality rate. Treatment of all these diabetes associated head and neck infections is quite challenging and many a times patient need long term hospitalisation for anti-microbial therapy and better

glycemic control. Such long term hospitalisation incurs greater treatment cost and increased absence from work place which in turn causes huge financial burden to the family. Nevertheless if a prompt diagnosis of a major life threatening infection is made at an earlier stage, one can avoid the onset of major complication which in turn can reduce overall morbidity and mortality. Thus the aim of this article is to give an overview of common diabetic infections in head and neck region, their management and prevention strategies.

## Pathophysiology

There are certain pathogenic mechanisms that make diabetic patients more susceptible to infection. It includes hyperglycemic environment increasing the virulence of some pathogens; lower production of interleukins in response to infection; reduced chemotaxis and

Senior Lecturer in ENT, Insaniah University College,  
Kedah, Malaysia  
Received: 09.04.2017; Accepted: 24.12.2017

## Abstract

Globally, the burden of diabetes is increasing very rapidly as is the diabetic related complications. Infections in diabetes mellitus are relatively more common and serious. Diabetic patients run the risk of acute metabolic decompensation during infections, and conversely patients with metabolic decompensation are at higher risk of certain invasive infections. Infections in diabetic patients result in extended hospital stays and additional financial burden.<sup>1</sup> Medicine in modern world has seen tremendous advancements like newer generation of anti-diabetic drugs, modern insulin therapy, better intensive care facilities and more potent antibiotics. Despite all these advancements, infection still remains one of the major cause for increasing morbidity and mortality in diabetic patients<sup>2</sup>. This article focuses on the common diabetes related infections in the Head and Neck region of the body. Some of the life threatening infections like malignant otitis externa and rhino-cerebral mucormycosis affect this region of body.

## Introduction

Patients with diabetes mellitus are more prone for infections. Infection can affect any region of the body and some of the common infections in the head and neck region include furunculosis involving the skin of ear canal and nasal vestibule, cellulitis, necrotising fasciitis, malignant otitis externa, rhino-cerebral mucormycosis, parotid abscess and parapharyngeal abscess. Among these infections malignant otitis externa is almost always seen in diabetics only. Some of these infections are very difficult to treat and have a greater mortality rate. Treatment of all these diabetes associated head and neck infections is quite challenging and many a times patient need long term hospitalisation for anti-microbial therapy and better glycaemic control. Such long term hospitalisation incurs greater treatment cost and increased absence from work place which in turn causes huge financial burden to the family. Nevertheless if a prompt diagnosis of a major life threatening infection is made at an earlier stage, one can avoid the onset of major complication which in turn can reduce overall morbidity and

mortality. Thus the aim of this article is to give an overview of common diabetic infections in head and neck region, their management and prevention strategies.

## Pathophysiology

There are certain pathogenic mechanisms that make diabetic patients more susceptible to infection. It includes hyperglycemic environment increasing the virulence of some pathogens; lower production of interleukins in response to infection; reduced chemotaxis and phagocytic activity; immobilization of polymorphonuclear leukocytes; glycosuria; gastrointestinal and urinary dysmotility.<sup>3</sup> In short all these effects are caused by hyperglycemia. Hyperglycemia causes protein glycation and formation of AGEs, which can have a diverse impact on host cell function. It can cause impairment of host proteins involved in complement activation, bacterial uptake, phagocytic killing, and scavenging of biolimiting nutrients and change the binding of host surface receptors for pathogens.<sup>4</sup>

In addition hyperglycemic environment also blocks the antimicrobial function by inhibiting glucose-6-phosphate dehydrogenase (G6PD), thereby increasing apoptosis of polymorphonuclear leukocytes, and reducing polymorphonuclear leukocyte transmigration through the endothelium<sup>5</sup>. Glycation of immunoglobulin occurs in patients with diabetes in proportion with the increase in HbA1c, and this may harm the biological function of the antibodies.<sup>5</sup> Some studies have also demonstrated that when the glycated hemoglobin (HbA1c) is <8.0%, the proliferative function of CD4 T lymphocytes and their response to antigens is not impaired,<sup>5</sup> thereby stressing the importance of long term glycaemic control.

## Effect of infection on Diabetes

Stress and infections in diabetic patients can lead to hyperglycemia and diabetic ketoacidosis. Hyperglycemia is due to augmented gluconeogenesis, increased glycogenolysis and poor utilization of glucose in the tissues.<sup>6</sup> Diminished insulin levels, increased concentrations of cortisol, catecholamines and glucagon contribute to both hyperglycemia and ketoacidosis.<sup>6</sup> Uncontrolled glucose

level makes the disease more aggressive and as the disease becomes aggressive glycaemic control becomes more challenging and it forms a vicious cycle.

## High risk patients

Compared to patients without diabetes, people with type-1 diabetes were 7.2 times more at risk of *S. aureus* infection whereas people with type-2 were 2.7 times more at risk. Also more at risk were those suffering from other complications such as heart/circulation problems and diabetic ulcers. Kidney problems associated with diabetes were one of the highest risk factors, with a 4.2 times increased risk. The risk of infection also increases with the number of years a patient has had diabetes; those who had suffered for 10 years or more were 3.8 times more at risk. The extent to which patients had control over their diabetes is also important, those with poor management of their diabetes (HbA1c > 7%) show a greater risk for infections.<sup>7</sup>

## Furunculosis of ear canal and nasal vestibule

Furunculosis refers to staphylococcal infection of the hair follicle. Furunculosis is common in diabetics. Many a times, initial diagnosis of diabetes is usually made out during the workup for recurrent furunculosis. In the Head and Neck region furunculosis commonly involves skin of external auditory canal and nasal vestibule. Furunculosis in mid facial region around external nostril (Nasal vestibulitis) is quite dangerous as they have tendency to cause cavernous sinus thrombosis due to the extensive communication between the valve less veins of orbit and face.

Regarding the furunculosis of ear canal, when the infection involves anterior wall of ear canal, patient usually presents with pain on chewing of food rather than ear pain. This is due to proximity of anterior canal wall to temporo-mandibular joint. Such presentation can cause a delay in diagnosis and treatment. Ear canal furunculosis if left untreated can easily develop into rapidly spreading cellulitis and osteomyelitis. Thus furunculosis in these two sensitive regions of Head and Neck must be treated aggressively. Patients must be advised not to do repeat scratching

or rubbing over the lesion as it can enhance the spread of lesion. Localized furunculosis should ideally be treated with oral antibiotics. However intra venous antibiotic therapy is required when there is cellulitis with evidence of local spread. Infection with MRSA strain should be considered when there is history of recurrent furunculosis, or nosocomial infection or with a positive nasal swab and antibiotic therapy must be tailored accordingly. Topical mupirocin or fusidic acid cream can be applied locally for a period of 2 weeks to prevent bacterial colonization especially when there is MRSA infection.

### **Malignant otitis externa**

It refers to the infection of the ear canal which has tendency for rapid spread into bone of entire temporal bone and thence into other bones of skull base. Hence it is also known as skull base osteomyelitis. Such an extensive skull base involvement causes greater morbidity and mortality due to excruciating pain and lower cranial palsy. The disease has aggressive clinical course, with poor treatment outcome and relatively increased mortality rate. Such features mimic that of a malignancy and hence the name malignant otitis externa. Malignant otitis externa is almost always seen in diabetic individuals only hence it is one of the diabetes defining infections.

Infection is usually caused by *Pseudomonas aeruginosa* in 98 % of cases.<sup>8</sup> Occasionally other bacteria like *Staphylococcus*, MRSA, *E-coli* and *Protues* species have also been isolated. Initial clinical symptoms include severe ear pain with purulent ear discharge. Ear pain is usually unbearable, it worsens at night and they spend sleepless nights. Ear discharge is yellowish in colour and it is persistent. It is associated with diffuse swelling of the pinna and ear canal. Sometimes patients ignore the initial symptoms and seek treatment only when they develop facial palsy and also when the pain becomes unmanageable anymore.

When a diabetic patient presents with such severe pain and ear discharge, a diagnosis of malignant otitis externa should be suspected and an urgent referral to an Otorhinolaryngologist must be made. ENT examination usually will reveal diffuse edema of pinna and ear canal with purulent

discharge. Evaluation of ear under microscopy will reveal granulations in ear canal and biopsy of the same must be done to rule out any malignancy. Depending upon the extent of disease spread, clinical examination may also reveal facial palsy, conductive/ sensory neural hearing loss, nystagmus. Features of lower cranial nerve palsy like palatal weakness, absent gag reflex with nasal regurgitation, vocal cord palsy with aspiration, tongue muscle weakness with reduced mobility is seen when the disease has spread beyond jugular foramen. Such an advanced stage of disease at presentation carries poor prognosis.

To confirm the diagnosis and to assess the disease progress a series of investigations needs to be done. It includes culture and sensitivity of ear discharge, biopsy of granulations from ear canal and audiometry to assess the type and degree of hearing loss. Imaging usually includes high resolution CT scan of the temporal bone and technitium Tc 99/ Gallium 67 bone scan. MRI of brain and temporal region is done when any intra cranial complication is suspected. Haematological investigations will usually reveal a very high ESR level (above 80mm/hr) at presentation and ESR level usually begin to settle during the course of treatment.

Treatment includes strict glycemic control, long term intra-venous antibiotics for a minimum period of 6 weeks and oral antibiotic for another 6 weeks. Anti-pseudomonal antibiotics like ciprofloxacin, piperazillin-tazobactam, netilmycin, ceftazidime are the antibiotics of choice. Ideally one penicillin group of antibiotic must be combined with either fluroquinolone or aminoglycoside for optimal outcome. Many a time's patients usually cannot tolerate such a higher dose of antibiotics on long term due to associated renal or hepatic derangement. Nevertheless such aggressive treatment is crucial because the infection has involved the bone of skull base which has poor perfusion due to diabetic microangiopathy and *Pseudomonas* induced vasculitis. Medications with ciprofloxacin and acetic acid combination is used a topical ear drops.

While the patient is on long term iv antibiotics, charting of pain score, weekly monitoring of ESR and regular monitoring of renal profile is done.

Declining trend of ESR and improved pain score indicates good response to treatment. Bone scan especially Gallium 67 scan (if available) should be done at the end of treatment to look for complete resolution of inflammation.

### **Rhino-cerebral Mucormycosis**

Mucormycosis is a rare opportunistic invasive fungal infection caused by fungi of the following genus namely *Rhizopus*, *Mucor* or *Cunninghamella*.<sup>9</sup> Mucormycosis in diabetic patients commonly involves nose and para nasal sinuses and from there it can spread into orbit and cranial cavity via angio and perineural invasion, hence the name rhino-cerebral mucormycosis. The classical triad is characterized by paranasal sinusitis, ophthalmoplegia with blindness and unilateral proptosis with cellulitis.<sup>10</sup> The disease is highly fatal with a survival rate of 38-50%<sup>11</sup> only and death can occur in one or two days if treatment is not initiated immediately.

Fungus causing mucormycosis is a saprophytic fungus and it is commonly found in decaying vegetable matter, bread mold and soil. They are easily susceptible to phagocytic activity of macrophages in healthy individuals and hence they rarely cause infection in immune-competent individuals. They thrive well in conditions with acidic pH, hyperglycemia and reduced phagocytotic activity. All these factors make persons with diabetic ketoacidosis more prone for mucormycosis. The fungus has the tendency to invade blood vessels and cause thrombosis and tissue necrosis. Aggressive clinical course of this infection is mainly due to angio-invasion, which provides a channel for rapid spread of infection along the vessels into orbit, cavernous sinus and intra cranial cavity. Also the ensuring tissue necrosis provides a viable medium for fungus to grow where penetration of anti-fungal drugs is poor due to loss of tissue perfusion.

Initial symptoms usually include headache, facial and periorbital pain mimicking that of acute sinusitis. Sometimes patients or even physicians tend to ignore these initial symptoms. Once the fungus has started spreading beyond the sinuses, patients will start getting facial swelling with discoloration, ophthalmoplegia, loss

of vision, palatal discoloration.<sup>12</sup> Facial and palatal discoloration is caused by ischemic necrosis. To begin with the discoloration is of pale white in color and then the color changes into white, grey hue and finally black (gangrene). The necrotic area is often well demarcated, appear black in color and such features can be seen easily in hard palate, periorbital region of face and nasal septum. Presence of ophthalmoplegia and vision loss usually indicates cavernous sinus involvement. The disease shows a very rapid clinical progression and the progressive tissue discoloration due to ischemia happens within few minutes. So treatment must be initiated soon after a diagnosis of mucormycosis is suspected. CT-scan and MRI of Para nasal sinuses and Brain is done to assess the disease extent and to guide for debridement

Treatment must be very aggressive as is the disease. Soon after admission, sample of necrotic tissue must be sent for fungal- KOH study and culture. In case of mucormycosis, KOH study usually reveals aseptate fungal hyphae with right angled branching. Anti-fungal therapy with Amphotericin-B must be initiated soon after admission along with other measures to control hyperglycemia and ketoacidosis. Urgent surgical debridement of the necrotic tissue is also crucial for disease control as fungus in necrosis will evade anti-fungal treatment due to absent tissue perfusion in these areas. Thus urgent anti-fungal therapy, glycemic control and surgical debridement form the main triad of treatment.

Most of the times, it is very difficult to stabilise the patients for a major debridement surgery. In such situations, debridement under local anaesthesia must be considered

as the necrotic tissue is pain free and does not bleed much. Necrotic tissue involving nasal cavity, para nasal sinuses, palate can be debrided easily using endoscope. Orbital involvement usually necessitates orbital exenteration. Craniotomy and debridement is required when there is significant intra cranial spread. Anti-fungal therapy must be initiated soon after establishing a diagnosis of mucormycosis. Amphotericin B is given at a dose of 1 to 1.5 g/kg body weight/day. Total cumulative dose of 2 to 3 mg is ideal. Given the potential nephrotoxic effect of this drug, periodic monitoring of electrolytes and renal profile is done during the entire course of treatment. Liposomal amphotericin B is considered in patients with deranged renal function. Currently amphotericin B is the only anti-fungal drug which is showing potential activity against mucormycosis infections. However in certain refractory cases other antifungal agents like posaconazole, caspofungins can be considered as adjuvant therapy along with amphotericin B.<sup>13</sup>

### Parotid Abscess

Parotid abscess is one of the common infections in diabetic patients. Infective agent is a mixed flora of gram positive and anaerobic organisms as they usually ascend from oral cavity via parotid duct. Clinical presentation includes fever, pain and swelling in the parotid region. Infection is usually aggressive in diabetics and many a time's patients do present with severe trismus, discoloration of overlying skin, facial palsy<sup>14</sup> (rarely) and with systemic features of sepsis. Treatment includes glycemic control, intravenous broad spectrum antibiotics with anaerobic cover and aspiration of pus. Incision and drainage is done

for localised abscess. Debridement of devitalized tissue and necrotic skin may be required in selected cases showing gangrenous changes.

### Deep Neck Space Infections / Abscess

Deep neck space abscess refers to the collection of pus between the fascial planes of Head and Neck region. Of all the deep neck space infections, parapharyngeal abscess is seen more commonly in diabetics. Majority of the lymph nodes and major vein of Head and Neck region lies in the parapharyngeal space. So any odontogenic or upper respiratory infection, easily spreads into this space via the draining nodes. Most common infective agents include *Streptococcus viridans*,  $\beta$ -hemolytic *Streptococcus*, *Staphylococcus*, *Klebsiella* and anaerobic *Bacteroides*.<sup>15</sup> Clinical presentations includes fever, neck swelling with pain, dysphagia, reduced mouth opening. Respiratory difficulty is seen when there is significant airway obstruction due to swelling.

Imaging studies like contrast enhanced CT scan and MRI are done to see the disease extent and for treatment planning. Treatment includes control of hyperglycemia, intra venous antibiotics and aspiration of pus. Localised pus collection is easily managed by image guided aspiration. However surgical drainage is required when there is poor response to antibiotic therapy, multiloculated collection and in refractory cases.

### Prevention

In view of the significant morbidity and mortality associated with these infections, it becomes essential to educate patients about various preventive measures. To reduce the chance of getting ear infection, susceptible patients should be educated to avoid manipulation of the ear canal (i.e.,) they should not cause ear trauma while using cotton swabs to clean their ears and to minimize exposure of the ear canal to water with a high chloride concentration.<sup>16</sup> Patients must be advised to seek medical care at the earliest possible time when they develop symptoms like severe ear pain, nodule with swelling near external nostril, peri-orbital swelling, diplopia, neck swelling and difficulty in mouth

opening. When patients seek medical care, a prompt diagnosis should be made and efforts must be made to avoid any significant treatment delay. Also anticipating serious complications of common infections in patients with diabetes is as important as appreciating rare disease entities that affect these patients disproportionately. Finally, one must not forget the importance of regular exercise, strict dietary control and good compliance with diabetic medication.

## References

1. Smita Gupta, Janak Koirala, Romesh Khadori, Nancy Khadori. Infections in Diabetes Mellitus and Hyperglycemia. *Infectious Disease Clinics* 2007; 21:617–638.
2. Zargar AH, Wani AL, Masoodi SR, Laway BA. Mortality in Diabetes mellitus- data from a developing region of the World. *Diabetes Res Clin Pract* 1999; 43:67-74.
3. Juliana Casqueiro, Janine Casqueiro, and Cresio Alves. Infections in patients with diabetes mellitus: A review of pathogenesis. *Indian J Endocrinol Metab* 2012; 16(Suppl1): S27–S36.
4. Yunn-Hwen Gan .Host Susceptibility Factors to Bacterial Infections in Type 2 Diabetes. *PLOS Pathogens*, December 26, 2013 <http://dx.doi.org/10.1371/journal.ppat.1003794>.
5. Peleg AY, Weerathna T, McCarthy JS, Davis TM. Common infections in diabetes: Pathogenesis, management and relationship to glycaemic control. *Diabetes Metab Res Rev* 2007; 23:3–13.
6. Diabetic ketoacidosis. David E. Trachtenbarg. *Am Fam Physician* 2005; 71:1705-1714.
7. Jesper Smit, Mette Søgaard, Henrik Carl Schönheyder, Henrik Nielsen, Trine Frøslev, Reimar Wernich Thomsen. Diabetes and risk of community-acquired Staphylococcus aureus bacteremia: a population-based case-control study. *Eur J Endocrinol* 2016; 174:631-639.
8. Rubin Grandis J, Branstetter BFT, Yu VL. The changing face of malignant (necrotising) external otitis: clinical, radiological and anatomic correlations. *Lancet Infect Dis* 2004; 4:34-39.
9. Severo CB, Guazzelli LS, Severo LC. Chapter 7: zygomycosis. *J Bras Pneumol* 2010; 36:134-41.
10. Artal R, Agreda B, Serrano E, Alfonso JI, Vallés H. Rhinocerebral mucormycosis: Report on eight cases. *Acta Otorrinolaringol Esp* 2010; 61:301–5.
11. Young Kyung Yoon, Min Ja Kim, Yong Gu Chung, Young Shin. Successful Treatment of a Case with Rhino-Orbital-Cerebral Mucormycosis by the Combination of Neurosurgical Intervention and the Sequential Use of Amphotericin B and Posaconazole. *J Korean Neurosurg Soc* 2010; 47:74–77.
12. Safar A, Marsan J, Marglani O, Al-Sebeih K, Al-Harbi J, Valvoda M. Early identification of rhinocerebral mucormycosis. *J Otolaryngol* 2005; 34:166–71.
13. Reed C, et al. Combination polyene-caspofungin treatment of rhino-orbital-cerebral mucormycosis. *Clin Infect Dis* 2008; 47:364.
14. Primuharsa Putra, Sabir Husin Athar, Zakinah Yahya, Marina Mat Baki, Asma Abdullah Facial Nerve Paralysis: A Rare Complication of Parotid Abscess. *Malays J Med Sci* 2009; 16:38–39.
15. Tung-tsun Huang, Fen-yu Tseng, Tien-chen Liu, Chuan-jen Hsu, Yuh-shyang Chen. Deep neck infection in diabetic patients: Comparison of clinical picture and outcomes with non-diabetic patients. *Otolaryngol Head Neck Surg* 2005; 132:943-7.
16. Ophir Handzel, Doron Halperin. Necrotizing (Malignant) External Otitis. *Am Fam Physician* 2003; 68:309-312.