

Mumps and Sterility: A comprehensive review

Bushar Jabbar Hamad¹, Nabeel Mahdi Abed², Rasha Salih Nuhaier¹

Biology department, science collage, university of Thi-Qar¹
Physiology, Vet-medicine, university of Thi-Qar²



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ABSTRACT

Mumps is an acute infectious viral disease characterized by hypertrophy and pain of the parotid glands. Although symptoms of mumps are generally limited to infectious parotitis, serious complications such as orchitis, pancreatitis, and meningitis can occur. Unvaccinated postpubertal males diagnosed with mumps virus frequently develop complications such as mumps orchitis between puberty and after puberty males. The mumps virus damages testicular tissue as a result of that infertility occurs. Therefore, it is important for men as well as doctors to be aware of the relationship between mumps and infertility. Here we review the etiology, epidemiology, systemic symptoms and signs, diagnostic methods and complications of mumps orchitis, as a complication of mumps virus, with particular emphasis on orchitis and sterility.



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1. INTRODUCTION

Mumps is an acute, contagious, systemic viral infection characterized by unilateral or bilateral swelling of salivary glands, especially the parotid ones. Gonads, meninges, pancreas and other organs may also be affected [20], [43]. Mumps is known as an important vaccine-preventable childhood viral disease. The clinical pictures of mumps virus infection is characterized by pain and swelling of the parotid glands, but can involve various other tissues and organs. It is an acute contagious RNA paramyxovirus disease (by a single stranded RNA virus belonging to the genus Rubulavirus and the family Paramyxoviridae) that results in a painful swelling of the parotid gland. Infection rate was more common in males and less than 15 years old [21]. It is transmitted by direct contact with infected nuclei or fomites contained within infected saliva and possibly even urine. The incubation period is 2–3 weeks and can result in infertility and hospitalization in severe cases [29], [14], [30]. The virus has no animal reservoirs and is purely a human disease. There is only one serotype of the virus, which can be further divided into 10–11 genotypes [37]. Once infected, most people recover from mumps without any long-term health issues, however, complications occasionally arise and can lead to hospitalization. Complications include orchitis, meningitis, oophoritis, mastitis, encephalitis, and deafness [30].

Individuals almost acquire lifelong immunity once infected, however, mumps orchitis is the most common complication in pubertal and postpubertal males, at 5–37%; of these cases, 16–65% are bilateral. As a result, a patient with mumps orchitis may present to the urologist with an acutely painful testicle [29], [18]. Mumps is the best-known cause inflammation of the testicles, reduced testosterone level, failure of sperm production and lead to infertility [33]. It is a considerable cause of infection-induced infertility with a high

prevalence rate of exposure [17]. Infertility is defined as the inability of couples to have a baby after one year of regular unprotected intercourse, affecting 10–15 percent of couples [4]. According to the latest WHO statistics, about 50–80 million people worldwide suffer from infertility [10], [27]. The mumps virus damages testicular tissue as a result of parenchymal oedema. This leads to congestion of the seminiferous tubules and perivascular infiltration of lymphocytes, with subsequent necrosis of the seminiferous tubules from pressure [29]. This leads to hyalinization of the seminiferous tubules which can cause fibrosis and atrophy of the testes while, infertility is in fact a rare complication, but subfertility occurs in an estimated 13% of patients, and can occur in patients with no signs of testicular atrophy [46].

2. EPIDEMIOLOGY AND ETIOLOGY

2.1 EPIDEMIOLOGY

Mumps is endemic worldwide with epidemic outbreaks occurring approximately every five years in unvaccinated regions. In countries where there is no vaccination against mumps [19]. although mumps is a benign clinical disease, it has become an important re-emerging pathogen. The reemergence of mumps virus infection will continue to threaten people unless additional preventive measures are implemented. Mumps was a serious disease that cause significant morbidity and mortality worldwide before the program of mumps vaccination starting [34]. In the pre-vaccine era, mumps was characterized by inter-epidemic periods every 4–5 years that most commonly affected of approximately 40–726 cases per 100,000 population per year [31]. Mumps is highly contagious and spreads rapidly among people living in close quarters [28]. The mumps virus is spread between humans either by direct or indirect contact. The virus is transmitted by respiratory droplets or direct contact with an infected person [3].

Mumps disease can be spread through saliva or mucus. The person can be infected by mumps virus through coughing, sneezing, talking, sharing items and touching of other patients. Mumps can spread rapidly, even before the swelling of salivary gland and up to five days after the mumps can occasionally cause complications [2]. Up to 10% of mumps patients developed aseptic meningitis; a less common but more serious complication is encephalitis, which can result in death or disability; and permanent deafness, orchitis and pancreatitis are other untoward effects that can be prevented by vaccination [19]. Mump infections frequently occurred in crowded population centers, e.g., prisons, kindergartens, boarding schools, military barracks, and other similar crowded settings. Several risk factors have been reported in mumps infection including age, exposure, and compromised immunity, time of year, travel, and vaccination status. Although there is no evidence of a deference on occurrence of mump virus infections between the sexes, males seemly have higher risk to present complications [40], [16].

2.2 ETIOLOGY

Mumps virus is a single stranded non-segmented, negative sense RNA virus belonging to the Paramyxoviridae family [48]. It is a negative-sense, single stranded RNA virus consisting of a ribonucleocapsid core enveloped by a lipid membrane derived from host cell, which causes mumps disease [9]. The transmission of mumps virus is occurring through droplet infection, contaminated fomites, direct contact and possibly urine [14]. The incubation period for mumps ranges from 12–25 days post exposure and parotitis typically occurs 16–18 days after exposure. The virus enters the body through the upper respiratory tract and replicates within the local reticulo-endothelial and lymphoid systems. Subsequently, viraemia persists for 7–10 days. During this period other organs can become infected [46]. There are at least 12 genotypes which are defined based on the sequence of the small hydrophobic (SH) gene. Currently, the most frequently detected mumps genotype in recent outbreaks worldwide is genotype G [45], [23].

3. SYSTEMIC SYMPTOMS AND SIGNS

Mumps is categorized by non-specific symptoms such as headache, fever, pain, tenderness, and parotitis. Parotitis refers to swelling of one or both of the parotid glands as well as the salivary glands in the cheek and jaw. Initially, this swelling occurs near the lower part of the ear. Because of this initial swelling, mumps can be confused as lymph node swelling leading to incorrect diagnosis [30]. The symptoms ranging between severe to symptomless in some mumps patients that may do not know they are infected with the disease. Rarely, adults can contract mumps with same symptoms and slightly complications [50]. The main symptom is parotitis, found in around 95% of symptomatic patients – although most begin with fever, malaise and sometimes a blotchy red rash. Initially there is unilateral parotitis, although 90% progress to bilateral parotitis. The glands are tender, and pain occurs on chewing. Fever usually settles by day four and symptom [32].

4. DIAGNOSIS

Mumps virus infection is normally diagnosed by serologic testing, it is normally diagnosed by serologic tests. The simplest procedure is the identification of mumps-specific IgM antibodies in sera or plasma by enzyme immunoassay analysis (EIA) [35] in samples obtained during the acute phase, preferably at around seven days after onset of symptoms. When the infection cannot be confirmed by serologic tests, the diagnosis can be made by direct methods such as isolation of the virus in cell cultures or detection of the viral genome by molecular analysis [12]. However, when an earlier diagnosis is required or in the case of vaccinated subjects, identification of the viral genome by Real Time PCR in samples taken during the first days of infection is an excellent, simpler diagnostic method, with a greater sensitivity than isolation in cell culture. Molecular diagnosis is an important factor in the diagnosis of mumps infections because of its excellent specificity [26], [12].

5. RELATIONSHIP BETWEEN MUMPS AND STERILITY

The mumps virus damages testicular tissue as a result of parenchymal oedema which lead to congestion of the seminiferous tubules and perivascular infiltration of lymphocytes, with subsequent necrosis of the seminiferous tubules from pressure that can cause fibrosis and atrophy of the testes [29], [4]. Orchitis refers to testicular swelling that occurs in about 20- 30% of infected post pubescent males who usually experience symptoms in only one testis. Though rare, orchitis can cause sterility in infected males [30]. Approximately 18% of mumps patients develop associated orchitis. Testicular symptoms usually develop within the first week after the parotid infection appears, but orchitis develops without parotid involvement [6]. The most common pathologic type of mumps orchitis is the interstitial type, which is characterized by interstitial edema and mononuclear infiltration. Increased intra-testicular pressure leads to atrophy in 40–70% of cases. Testicular atrophy may cause sterility in 37–87% of these cases [25], [6]. Infertile men showed lower sperm concentration and lower motility, lower proportions of normal sperm morphology than fertile control [39]. [1] showed that a significant decreased of the percentage of the active motility sperms, while the percentage of the non motile and sluggish sperms was increased of infertility man in Thi-Qar province at 2003-2006. Clinicians define testicular atrophy as any reduction in testicular size. This is difficult to quantify, as a small reduction can only be assessed from the patient's history or by comparison with the contralateral testes (if unaffected).

Abnormalities of spermatogenesis can occur in up to half of patients for up to 3 months after recovery, this accounts for abnormalities of sperm count, sperm motility and sperm morphology [5], [14]. The more complications of mumps that accompanied with orchitis (testicles inflammation), are Encephalitis and Meningitis (brain inflammation and inflammation of the tissue covering the brain and spinal cord) [9]. The examination of the scrotum, often sensitive and inflammatory, shows a hot and swollen testicle,

characteristic of orchitis. Epididymitis is associated with orchitis in 85% of cases, and often precedes orchitis. The symptoms regress spontaneously in three to 15 days, but the testicle may remain sensitive for several weeks. The complications of orchitis are severe: total or partial infertility and testicular atrophy. On the other hand, the link between mumps orchitis and increased risk of testicular cancer, a time referred to, has been ruled out by several epidemiological studies [41], [49]. Testicular atrophy is a reduction in testicular size that can occur after epididymo-orchitis, testicular torsion, unilateral cryptorchidism, varicocele, or trauma [13]. The specific symptoms and signs of mumps- orchitis are headache and fever followed by unilateral/ bilateral parotid swelling, this is followed 7–10 days later by unilateral testicular swelling. Atypically, those affected can present with bilateral testicular swelling, epididymitis alone or without systemic symptoms [51].

Epididymo-orchitis does not occur if the infection occurs prior to adolescence. In 80% of all mumps orchitis cases, symptoms are first seen in the first 8 days of the parotid swelling but occasionally may precede it and rarely may manifest itself present even without the parotid swelling. It results in severe pain, swelling, and tenderness at the affected site and is often associated with high fever, nausea, vomiting, and abdominal pain. It resolves over a week, though, gonadal tenderness may persist for a long time. In about 20-30% of cases orchitis is unilateral, and 10-30% cases are bilateral. Of the affected testicles, 30-50% show a degree of testicular atrophy [5], [7]. At last, Mumps orchitis is a severe complication of mumps which can lead to sterility in postpubertal males. But, Immunization and education regarding its complications is the best policy to avoid mumps-related complications. However, the treatment needs to remain conservative [11].

6. OTHER COMPLICATIONS FROM MUMPS

6.1 MENINGITIS AND ENCEPHALITIS

Central nervous system (CNS) involvement in the form of aseptic meningitis (inflammatory cells in cerebrospinal fluid) is a most common complication of mumps infection [42]. Mumps virus was the leading cause of meningitis prior to widespread use of vaccines. Clinical signs of meningitis appear from one week before to two weeks after the appearance of parotitis; when it is present because the two manifestations are independent. As for Enterovirus meningitis, mumps virus meningitis is usually benign, spontaneously resolving, and mortality or long-term sequelae are exceptions. Symptoms associated with these meningitis are classic and associate fever, neck stiffness, vomiting, headache, and lethargy [38], [24], [22].

Encephalitis is brain swelling that can be very dangerous, however, it is also quite rare occurring in less than 1% of the population. Although these complications are somewhat unlikely, the consequences are very important as mumps-induced swelling can result in permanent damage such as reproductive infertility [30]. Acute encephalitis may include altered consciousness, focal neurological deficits, epileptic seizures, electroencephalogram abnormalities, or ataxia. These signs decline in a few days to a few weeks [36].

6.2 OOPHORITIS AND MASTITIS

Female specific complications include oophoritis and mastitis. Oophoritis, a complication of mumps, in postnatal women, mastitis occurs in up to 30% and ovarian inflammation (Oophoritis) in about 5% of cases [11]. Mastitis refers to swelling of the breasts and oophoritis refers to swelling of the ovaries which also has the potential to cause sterility. Fortunately, both of these complications occur in less than 1% of the infected adolescent and post-pubescent female population [30]. Among women who acquire mumps during the first 12 weeks of pregnancy, more than a quarter suffer spontaneous abortion; in a large cohort study, the rate of spontaneous abortion in the first trimester due to mumps infection was higher than that due to rubella infection [19].

6.3 PANCREATITIS

Pancreatitis is seen in about 4% of patients with mumps. There is evidence suggesting that mumps virus can infect human pancreatic beta cells, and may trigger the onset of insulin-dependent diabetes mellitus in some individuals [47], [19]. In addition to what has been mentioned complications associated with mumps, there is also deafness, myocarditis, arthralgias, cerebellar ataxia, ascending polyradiculitis, thyroiditis, thrombocytopenia, arthritis, transverse myelitis, nephritis and endocardial fibroelastosis [15].

7. CONCLUSIONS

The causes of male infertility are still unknown, one of the causes may be mumps (especially in unvaccinated pubertal and postpubertal males). Therefore, it is necessary to study the relationship of mumps and infertility, the reasons for their occurrence and how to develop solutions to prevent them. Doctors must also be aware of the relationship between orchitis in mumps (one of the causes of infertility). This condition must also be prevented by administering the MMR vaccine and by educating unvaccinated patients about orchitis and mumps and its possible complications.

8. References

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