

Infection/Inflammation

# Clinical Features of Mumps Orchitis in Vaccinated Postpubertal Males: A Single-Center Series of 62 Patients

Bum Sik Tae, Byeong Kuk Ham, Jae Heon Kim, Jae Young Park, Jae Hyun Bae

Department of Urology, Korea University School of Medicine, Seoul, Korea

**Purpose:** Although the measles-mumps-rubella vaccination covers most children against mumps in Korea, the development of mumps has been reported. However, the clinical manifestations of mumps orchitis in postpubertal vaccinated patients have never been investigated. Herein we report the clinical features of mumps orchitis in postpubertal vaccinated patients.

**Materials and Methods:** This study included a total of 62 postpubertal males who developed acute mumps orchitis from 2005 to 2010. The clinical manifestations such as the incubation period, febrile duration, and the mean duration of orchitis were retrospectively investigated. The laboratory and sonographic findings were also reviewed and compared with the features of previously reported cases of unvaccinated postpubertal mumps orchitis.

**Results:** The mean age of the 62 patients was 17.56 years (range, 15 to 29 years). All patients were serologically confirmed with acute mumps infection (positive immunoglobulin [Ig] M and negative or positive IgG). The mean incubation period was 5.39 days (range, 0 to 23 days), with a febrile duration of 1.8 days (range, 0.5 to 3 days), and a mean duration of orchitis of 4.96 days (range, 0 to 17 days). Sonography revealed unilateral orchitis in 58 patients (93.6%) and bilateral orchitis in only 6 (6.4%).

**Conclusions:** In our study, mumps orchitis in postpubertal vaccinated patients showed a relatively shorter febrile duration. In addition, less scrotal swelling and a lower incidence of bilaterality were found upon physical examination and ultrasonography. In the future, additional long-term follow-up is needed to determine the features of mumps orchitis in postpubertal vaccinated males, and an additional booster vaccination should be considered.

**Key Words:** Mumps; Orchitis; Vaccination; Young adult

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Article History:**

received 16 May, 2012

accepted 11 July, 2012

**Corresponding Author:**

Jae Hyun Bae  
Department of Urology, Korea University Ansan Hospital, Korea University School of Medicine, 123 Jeokgeum-ro, Danwon-gu, Ansan 425-707, Korea  
TEL: +82-31-412-5190  
FAX: +82-31-412-5194  
E-mail: urobae@genetherapy.or.kr

## INTRODUCTION

The mumps virus is a single-stranded, nonsegmented, negative-sense RNA virus belonging to the Paramyxoviridae family. Mumps is an acute, self-limiting viral infection that causes nonsuppurative swelling and tenderness of the salivary glands [1]. However, the incidence of mumps has been reduced by high coverage with effective vaccines. Since the measles-mumps-rubella (MMR) vaccine was incorporated into the National Immunization program in Korea in 1985, the incidence of mumps has decreased. However, mumps

outbreaks have been reported continuously worldwide even in vaccinated children. There continue to be mumps outbreaks every 4 to 5 years, and recently, the periodic epidemics of mumps outbreaks have been shorter than in the past.

Symptoms of mumps are generally confined to infectious parotitis. However, it causes severe complications such as orchitis, pancreatitis, and meningitis, and at least one of these occurs in up to 42% of patients with mumps [2-4]. Of these complications, mumps orchitis is a common complication in pubertal and postpubertal males [5]. Testicular

swelling and pain occurs 10 days after the onset of parotitis in 15 to 40% of males with mumps viral infection; however, these symptoms can occur up to 6 weeks after the onset of parotitis [6]. The mumps virus damages the testicular tissue as a result of parenchymal edema. As a result, testicular atrophy is reported to occur in 30 to 50% of affected testicles and subfertility occurs in an estimated 13% of patients.

Although there have been several reports examining the resurgence in mumps, there have been few studies of the characteristics of postpubertal mumps and mumps orchitis in patients after MMR vaccination [7]. Park et al. [8] reported on an outbreak of mumps in vaccinated males, but they did not include a description of mumps orchitis. To our knowledge, this is the first report describing postpubertal mumps orchitis in vaccinated Korean males.

## MATERIALS AND METHODS

From January 2005 to December 2010, 62 patients diagnosed with acute mumps orchitis were treated at Korea University Medical Center. It was confirmed by questionnaire that all patients had been vaccinated with the MMR vaccine under the national vaccination system of the Korean Center for Disease Control. Patients who did not receive vaccination or had an unknown vaccination history were excluded from our study. Diagnostic criteria for mumps orchitis were complaints of testicular pain, swelling, and tenderness on palpation during the acute illness stage and serologic confirmation of acute mumps infection (positive immunoglobulin [Ig] M with negative or positive IgG). Mumps-specific IgM and IgG were detected by using a commercially available enzyme immunoassay kit (Viracell, Granada, Spain). The test was performed and interpreted in accordance with the manufacturer's instructions. Optical density value above 1.1 were considered positive, those below 0.9 were considered negative, and those between 0.9 and 1.1 were considered indeterminate. The patients' previous history of mumps and vaccination status was obtained from the patients or their parents by questionnaire or telephone survey.

The characteristics of the clinical manifestations, such as incubation period, febrile duration, mean duration of orchitis, and hospital stay, were investigated. Other general symptoms, such as pyrexia, headache, and malaise, were reviewed through medical records. Scrotal symptoms including scrotal swelling and tenderness were present in all patients.

Laboratory findings such as serologic markers (white blood cell counts [WBCs], C-reactive protein [CRP], amylase, and lipase) and urine analysis with urine culture were assessed. Sonographic findings of mumps orchitis, such as the degree of testicular swelling, bilaterality, and direction, were also investigated. Complications of mumps including meningitis and pancreatitis were also recorded.

The clinical features in our patients were compared with the features of previous reports of unvaccinated post-

**TABLE 1.** The general symptoms of postpubertal mumps orchitis in 62 patients

Characteristic	Value
Age (yr)	17.56 (16–29)
Contact with mumps	56 (90.3)
Vaccination history	62 (100)
Parotitis before orchitis	56 (90.3)
Orchitis-associated fever	46 (74.19)
Positive mumps IgG antibody	36 (58.1)
Positive mumps IgM antibody	62 (100)

Values are presented as mean (range) or number (%).  
IgG, immunoglobulin G; IgM, immunoglobulin M.

pubertal mumps orchitis identified through literature review. Searched reports were limited to studies that investigated more than 10 patients with unvaccinated postpubertal mumps orchitis.

Patients were admitted to the hospital unless their general status allowed them to be treated as outpatients. All patients were treated with bed rest, elevation of the scrotum, local cooling (ice bag), and nonsteroidal antiinflammatory drugs or antipyretics (acetaminophen).

## RESULTS

The mean age of the 62 patients was 17.56 years (range, 15 to 29 years). It was confirmed by questionnaire that all patients had been vaccinated with the MMR vaccine under the national vaccination system of the Korean Center for Disease Control. A total of 56 patients (90.3%) had been in contact with a mumps-infected case. All patients were serologically confirmed to have an acute mumps infection (positive IgM with negative or positive IgG) and were hospitalized for supportive treatment. All 62 serum samples obtained at admission were positive for mumps IgM antibodies, whereas 36 (58.1%) were positive for IgG antibodies (Table 1). The mean incubation period was 5.39 days (range, 0 to 23 days), the mean duration of fever was 1.8 days (range, 0.5 to 3 days), the mean duration of orchitis was 4.96 days (range, 0 to 17 days), and the mean hospital stay was 4.88 days (range, 0 to 10 days).

With regard to general symptoms, fever was observed in 46 patients (74.2%), headache in 34 patients (54.8%), and myalgia in 32 patients (51.6%). Also, 56 patients (90.3%) had parotitis before the appearance of acute orchitis.

Laboratory and scrotal findings are shown in Table 2. The mean WBC level was not elevated in any patients (8,396/L; normal range, 4500 to 11,000/L), whereas the mean CRP level was increased over the normal range (24.18 mg/dl; normal range, 0 to 5 mg/dl), and the mean amylase level was 406.08 IU/l (normal range, 28 to 100 IU/l) (Table 1). Scrotal ultrasonography revealed testicular swelling of >20 ml in 17 patients (27.4%), between 15 and 20 ml in 12 patients (19.4%), and <15 ml in 33 patients (53.2%) (Table 3). Bilateral orchitis was present in 4 pa-

tients (6.4%), and 58 patients (93.6%) had unilateral orchitis. Right-sided orchitis was present in 31 patients (50%), and left-sided orchitis was noted in 27 patients (43.5%) (Table 2). Meningitis was present in 5 patients (8%), but there were no other complications, including pancreatitis (Table 3).

To compare the clinical features observed in our study with those of cases of unvaccinated postpubertal mumps orchitis, we reviewed the literature and found four articles that investigated more than 10 patients with unvaccinated postpubertal mumps orchitis. Table 4 shows the comparison between our study and previous reports. The mean duration of fever was shorter (1.8 days) in the population of our study than in unvaccinated patients (3.5 days), and the incidence of bilateral orchitis was lower in our study. However, the mean incubation period, the length of orchitis, and the length of hospital stay did not differ significantly from that in the previous reports (Table 4).

## DISCUSSION

Mumps is usually a self-limiting condition and generally resolves spontaneously without sequelae. About 30 to 40% of patients with mumps do not have parotitis. Complications such as meningoencephalitis, pancreatitis, and oophoritis or orchitis have been observed in up to 42% of patients with mumps [3,4]. In the past, populations not receiving the MMR vaccine clustered in large groups in secondary

schools and colleges. This clustered environment provides a perfect breeding ground for the virus. Students are more susceptible to the virus and its complications, including mumps orchitis. However, the incidence of mumps has been reduced by high coverage with effective vaccines.

However, recent mumps outbreaks have been reported continuously worldwide, even in vaccinated children. Immunization programs against mumps have influenced the age distribution, and recent outbreaks have mainly affected adolescents and young adults. Since the introduction of the mumps vaccine in 1967 (the year the first mumps vaccine was licensed in the United States), a shift in the age of peak incidence of mumps from children aged 5 to 9 years in the prevaccine era to children and young adults aged 10 to 24 years has been observed. This shift in the age at the appearance of mumps [13-16] from children to young adults means a shift toward a period during which the development of mumps complications, such as orchitis, is more frequent [17].

As a result, there has been a resurgence in mumps orchitis, with epidemics being reported more frequently. However, to our knowledge, there have been no reports about the clinical features of postpubertal mumps orchitis in patients who have received the MMR vaccine. Our sur-

**TABLE 2.** Laboratory data of 62 patients

Characteristic	Value
Pyuria	1 (1.6)
Serum white blood cell	8,396.6 (4,500-11,000)
Serum erythrocyte sedimentation rate (mm/h)	38.75 (0-10)
C-reactive protein (mg/dl)	24.18 (0-5)
Amylase (IU/l)	406.08 (28-100)
Lipase (IU/l)	49.89 (0-60)

Values are presented as number (%) or mean (normal range).

**TABLE 3.** Scrotal sonography findings and complications (n=62)

Clinical finding of mumps orchitis	Value
Bilaterality	
Bilateral	4 (6.4)
Right	31 (50.0)
Left	27 (43.5)
Degree of scrotal swelling	
< 15	33 (53.2)
15-20	12 (19.4)
> 20	17 (29.4)
Other complications	
Pancreatitis	0 (0)
Meningitis	5 (8.1)

Values are presented as number (%).

**TABLE 4.** Clinical manifestations of patients with acute mumps orchitis in the present and previous reports

First author, yr	No. of patients	Country	Pre/post pubertal	Postvaccination	Side of orchitis				P-O interval (d)	Fever (d)	Severe testicular swelling (<20 ml)
					B	U	R	L			
Ternavasio-de la Vega, 2000-2001 [9]	67	Spain	Pre, post	N	7	60	36	24	4.9	4.6	60
Yeniyol, 1992-1995 [10]	18	Turkey	Pre, post	N	0	18	10	8	5	3.5	NM
Ku, 1990-1997 [11]	21	Korea	Pre, post	N	6	15	NM	NM	5.9	2-5.4	13
Casella, 1995-1996 [12]	11	Switzerland	Post	N	2	9	5	4	10	3.6	NM
Our study, 2005-2010	62	Korea	Post	V	4	58	31	27	5.4	1.8	17

B, bilateral; U, unilateral; R, right-sided; L, left-sided; P-O interval, parotitis-orchitis interval; N, unvaccinated; NM, not mentioned; V, vaccinated.

vey revealed that all study patients had previously received the MMR vaccination in accordance with Korean national immunization programs.

Most patients with mumps orchitis are hospitalized because of high fever and severe testicular pain. Fevers are frequent in mumps orchitis, although leukocytosis or pyuria are not evident in most patients. Casella et al. [12] investigated the features of mumps orchitis in unvaccinated postpubertal males. They reported that the interval between the initiation of treatment and the disappearance of fever averaged 3.6 days with antiinflammatory drugs administered for an average of 8.6 days. In other studies, the mean duration of fever was about 2 to 5.4 days [10,11,14,15,18-23]. In our study, the mean duration of fever was relatively shorter (1.9 days), although treatment, including bed rest, scrotal support, local cooling, and anti-inflammatory drugs, did not differ from other reports. We found that the febrile duration was relatively shorter in vaccinated postpubertal mumps orchitis patients than in unvaccinated mumps orchitis patients.

Mumps orchitis generally manifests as a gradual worsening of testicular pain and swelling. In particular, testicular swelling can lead to a rise in intratesticular pressure followed by testicular atrophy. Ku et al. [11] measured the testicular volume of 21 patients with acute mumps orchitis and found a mean testicular volume of 18.1 to 19.2 ml. In the same study, 8 of the 44 measured testes (18.2%) reached a volume of 25 ml. Tarantino et al. [24] measured the testicular volume in 12 patients with acute mumps orchitis, and the mean volume of the affected testicles by ultrasound was 18.5 ml. In another series of 11 patients with acute mumps orchitis, the volumes of the affected testes ranged between 15.2 and 47.5 mm<sup>3</sup> (mean, 27.2 mm<sup>3</sup>) [22]. In our study, the volumes of the affected testes in 33 patients (53.2%) were smaller than 15 ml, and severe enlargement of the testis (>25 ml) was observed in only 7 patients (11.3%). We think these results may lead to a lower incidence of testicular atrophy and subfertility, but unfortunately, we did not investigate the development of testicular atrophy and subfertility in this study.

Mumps orchitis is generally unilateral, but occurs bilaterally in 15 to 30% of patients [25]. In unvaccinated postpubertal males, Casella et al. [12] reported that 18% of unvaccinated postpubertal males suffered bilateral mumps orchitis, and Ternavasio-de la Vega et al. [9] reported the incidence of bilateral orchitis to be two times higher in young adults than in adolescents (29% vs. 13%, respectively). However, bilateral orchitis was present in only four (6.4%) of the vaccinated postpubertal patients in our study.

Our findings indicate that the clinical manifestations of mumps orchitis in vaccinated postpubertal males are milder than in unvaccinated patients. The duration of fever was shorter, the incidence of severe testicular swelling was lower, and the incidence of bilateral orchitis was also lower compared with mumps orchitis in unvaccinated postpubertal males. There have been no reports explaining the difference in clinical features of mumps orchitis in vac-

nated postpubertal males. However, possible explanations may be deduced from outbreaks of mumps in vaccinated patients. Park et al. [8] reported that the level of IgG titers and the avidity index in vaccinated unaffected patients were not significantly different from those in patients with a past infection. Alternatively, the low IgG avidity index of the vaccinated unaffected group may represent a qualitative limitation of vaccine-induced humoral immunity in mumps; that is, failure to induce sufficiently mature antibodies, resulting in secondary vaccine failure. Narita et al. [21] reported that a recent mumps vaccination group had a low avidity index. Although recently vaccinated patients have a lower IgG avidity, their IgG avidity level will be higher than that in unvaccinated males. Therefore, the symptoms and the duration of fever may be less severe in these patients than the symptoms of mumps orchitis in unvaccinated males.

The limited short-term follow-up period is the main limitation of this study. Long-term follow-up is needed to investigate the complications of mumps orchitis, such as testicular atrophy or subfertility. Also, it is necessary to carry out more research involving comparisons with unvaccinated patients. In addition, more effort should be directed toward determining the mechanism underlying the reemergence of mumps and mumps orchitis, and an additional booster vaccination should be developed.

## CONCLUSIONS

As shown in our study, the clinical manifestations of mumps orchitis in postpubertal vaccinated patients include a relatively shorter febrile duration, less scrotal swelling, and a low incidence of bilateral orchitis compared with unvaccinated patients. Additional long-term follow-up and large prospective studies are needed to determine ways to prevent outbreaks of mumps and mumps orchitis, and an additional booster vaccination should be considered.

## CONFLICTS OF INTEREST

The authors have nothing to disclose.

## ACKNOWLEDGEMENTS

This study was supported by a grant from Korea University.

## REFERENCES

1. Anderson LJ, Seward JF. Mumps epidemiology and immunity: the anatomy of a modern epidemic. *Pediatr Infect Dis J* 2008; 27(10 Suppl):S75-9.
2. Hviid A, Rubin S, Muhlemann K. Mumps. *Lancet* 2008;371:932-44.
3. Shulman A, Shohat B, Gillis D, Yavetz H, Homonnai ZT, Paz G. Mumps orchitis among soldiers: frequency, effect on sperm quality, and sperm antibodies. *Fertil Steril* 1992;57:1344-6.
4. Feldman G, Zer M. Infantile acute pancreatitis after mumps vaccination simulating an acute abdomen. *Pediatr Surg Int* 2000;16: 488-9.
5. Singh R, Mostafid H, Hindley RG. Measles, mumps and rubella: the urologist's perspective. *Int J Clin Pract* 2006;60:335-9.

6. Gemmill IM. Mumps vaccine: is it time to re-evaluate our approach? *CMAJ* 2006;175:491-2.
7. Davis NF, McGuire BB, Mahon JA, Smyth AE, O'Malley KJ, Fitzpatrick JM. The increasing incidence of mumps orchitis: a comprehensive review. *BJU Int* 2010;105:1060-5.
8. Park DW, Nam MH, Kim JY, Kim HJ, Sohn JW, Cho Y, et al. Mumps outbreak in a highly vaccinated school population: assessment of secondary vaccine failure using IgG avidity measurements. *Vaccine* 2007;25:4665-70.
9. Ternavasio-de la Vega HG, Boronat M, Ojeda A, Garcia-Delgado Y, Angel-Moreno A, Carranza-Rodriguez C, et al. Mumps orchitis in the post-vaccine era (1967-2009): a single-center series of 67 patients and review of clinical outcome and trends. *Medicine (Baltimore)* 2010;89:96-116.
10. Yeniol CO, Sorguc S, Minareci S, Ayder AR. Role of interferon-alpha-2B in prevention of testicular atrophy with unilateral mumps orchitis. *Urology* 2000;55:931-3.
11. Ku JH, Kim YH, Jeon YS, Lee NK. The preventive effect of systemic treatment with interferon-alpha2B for infertility from mumps orchitis. *BJU Int* 1999;84:839-42.
12. Casella R, Leibundgut B, Lehmann K, Gasser TC. Mumps orchitis: report of a mini-epidemic. *J Urol* 1997;158:2158-61.
13. Cardenosa N, Dominguez A, Camps N, Martinez A, Torner N, Navas E, et al. Non-preventable mumps outbreaks in school-children in Catalonia. *Scand J Infect Dis* 2006;38:671-4.
14. Castilla J, Garcia Cenoz M, Barricarte A, Irisarri F, Nunez-Cordoba JM, Barricarte A. Mumps outbreak in Navarre region, Spain, 2006-2007. *Euro Surveill* 2007;12:E070215.1.
15. Centers for Disease Control and Prevention (CDC). Mumps epidemic--United kingdom, 2004-2005. *MMWR Morb Mortal Wkly Rep* 2006;55:173-5.
16. Centers for Disease Control and Prevention (CDC). Update: multistate outbreak of mumps--United States, January 1-May 2, 2006. *MMWR Morb Mortal Wkly Rep* 2006;55:559-63.
17. Falk WA, Buchan K, Dow M, Garson JZ, Hill E, Nosal M, et al. The epidemiology of mumps in southern Alberta 1980-1982. *Am J Epidemiol* 1989;130:736-49.
18. Philip J, Selvan D, Desmond AD. Mumps orchitis in the non-immune postpubertal male: a resurgent threat to male fertility? *BJU Int* 2006;97:138-41.
19. Lopez Pacios JC, Parra Muntaner L, Pineiro Fernandez MC, Gomez Cisneros SC, Sanchez Sanchez E, Rivas Escudero JA, et al. Mumps orchitis; review of 8 cases. *Arch Esp Urol* 1998;51:331-3.
20. Candel S. Epididymitis in mumps, including orchitis: further clinical studies and comments. *Ann Intern Med* 1951;34:20-36.
21. Narita M, Matsuzono Y, Takekoshi Y, Yamada S, Itakura O, Kubota M, et al. Analysis of mumps vaccine failure by means of avidity testing for mumps virus-specific immunoglobulin G. *Clin Diagn Lab Immunol* 1998;5:799-803.
22. Wu L, Bai Z, Li Y, Rima BK, Afzal MA. Wild type mumps viruses circulating in China establish a new genotype. *Vaccine* 1998;16:281-5.
23. Nojd J, Teclé T, Samuelsson A, Orvell C. Mumps virus neutralizing antibodies do not protect against reinfection with a heterologous mumps virus genotype. *Vaccine* 2001;19:1727-31.
24. Tarantino L, Giorgio A, de Stefano G, Farella N. Echo color Doppler findings in postpubertal mumps epididymo-orchitis. *J Ultrasound Med* 2001;20:1189-95.
25. Bartak V. Sperm count, morphology and motility after unilateral mumps orchitis. *J Reprod Fertil* 1973;32:491-4.