The patient is an adult who immigrated from Central America many years ago with no past medical history who presents to the emergency department complaining of right testicle pain and swelling. The pain began about 4 days prior to presentation and was mild at first but became severe 24 hours prior to presentation. The patient denied nausea, vomiting, diarrhea, abdominal pain, or genital lesions, but endorsed one episode of dysuria. They reported that two weeks prior, they had cough and rhinorrhea followed by subjective fevers, intermittent headaches, and cervical lymphadenopathy. The patient has no history of sexually transmitted infection and is sexually active with one partner. An ultrasound exam with doppler of the testicle revealed normal blood flow.

Question: Which of the following is NOT accurate about this patient's condition?

A. The presentation is caused by a reportable infection.
B. Emergent orchiopexy is required.
C. The infection is preventable with a live-attenuated vaccine.
D. Sialic acid plays an important role in pathogenesis.

Answer: B. Emergent orchiopexy is appropriate treatment for testicular torsion, not mumps.

Discussion

This patient ultimately tested positive via PCR for mumps. Mumps is an enveloped negative sense RNA virus that is included in the trivalent MMR live-attenuated vaccine, along with measles and rubella. It is highly contagious, with approximately 85% of vulnerable contacts becoming infected upon first exposure, and most transmission occurs before and within 5 days of the onset of parotid involvement. Transmission is through respiratory droplets or fomites, and highest viral load occurs close to the onset of parotitis and decreases quickly after. After introduction of the MMR vaccine, annual cases in the United States decreased from 150,000 cases a year to a nidus of 154 cases in 2021 during the COVID-19 pandemic. Clinically, patients can present with nonspecific mild symptoms which can include mild fever, myalgia, and malaise. Common mumps signs are pain, swelling, and tenderness in one or both parotid salivary glands. Less commonly, other salivary glands (submandibular and sublingual) may also be inflamed. Infection is usually self-limited, though in some patients, disease can progress to meningoencephalitis, oophoritis, or, as seen in this patient, orchitis. Treatment is focused on supportive care with analgesia and antipyretics; parotid discomfort is classically addressed with warm or cold packs. Though often associated with mumps, parotitis can also be seen in other viral

illnesses, so a broad differential should be considered, particularly in vaccinated individuals. Serology has limited diagnostic utility in vaccinated patients, and PCR testing is recommended for diagnosis (a buccal swab specimen). Confirmed and probable cases must be reported.

Sialic acid is a common receptor for viruses including mumps, which helps explain some of the tropism of the virus—parotid, pancreas, Sertoli, and Leydig cells all contain high levels of sialic acid. Hemagglutinin-neuraminidase (HN) is the viral protein that interacts with the host sialic acid. The hemagglutinin portion of the protein interacts directly with host α2-3 linked sialic acid with unbranched sugars, while the neuraminidase portion of the protein cleaves the sialic acid from progeny viruses which facilitates release from the host cell. Both HN and the fusion protein play important roles in cell to cell fusion as well as virus to cell fusion, further assisting in viral spread. The HN protein is also believed to play an important role in activation of the fusion protein.

Recent outbreaks have raised new concerns regarding the control of mumps infection. Historically considered a disease of early childhood, mumps outbreaks in recent years have increasingly involved adolescents and young adults. A recent review and meta-analysis highlighted this shift, reporting that adults currently experience the highest incidence of disease (Agrawal *et al.* 2025).

The currently recommended two-dose vaccine series provides greater protection than a single dose; however, evidence indicates that immunity wanes in individuals vaccinated more than a decade ago. This has led to recommendations for administering a third dose to previously vaccinated individuals during outbreaks to mitigate disease severity and transmission. Additional studies have demonstrated that a third dose can reduce infection rates, prompting discussion about whether a third dose should be more broadly incorporated into standard vaccination schedules (Agrawal *et al.* 2025).

The increasing frequency of outbreaks highlights a complex interplay of waning vaccine-derived immunity, vaccine hesitancy, viral evolution, and shifting epidemiology, underscoring the importance of continued research.

Case by: Molly McGowan, MD

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