

## ODONTOID OSTEOMYELITIS IN CHILDREN

## Illustrative Case Reports and Review of the Literature

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**Abstract:** Odontoid osteomyelitis is a rare disease which is frequently misdiagnosed as torticollis, leading to a delay in diagnosis. We present 2 illustrative cases and a systematic literature review summarizing previously reported cases. Odontoid osteomyelitis should be considered in children presenting with decreased head movements and with elevated erythrocyte sedimentation rate, particularly without improvement while receiving antiinflammatory treatment. Plain radiographs can be misleading, and magnetic resonance imaging should be performed for better visualization.

**Key Words:** osteomyelitis, dens, odontoid peg, children

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Odontoid osteomyelitis (OOM) is a rare disease. It mostly occurs in adults, either associated with an underlying condition<sup>1-4</sup> or rarely in healthy individuals.<sup>5,6</sup> In children, only few cases have been described. The diagnosis of OOM seems particularly challenging in infants and young children for several reasons: (i) the differential diagnosis of neck pathologies particularly the ones of infectious etiology are broad and include cervical lymphadenitis, abscesses (peri-, retrotonsillar and epidural), central venous infections, malignancies or infections of the spine, (ii) the interpretation of images of cartilaginous and osseous parts of the cervical vertebrae is difficult and (iii) most patients present in good clinical condition and afebrile. The aim of this review is to summarize risk factors and clinical criteria for OOM and to outline appropriate methods for investigation.

## CASE 1

A 14-month-old boy presented with symptoms of an upper respiratory tract infection (including rhinitis, cough and mild cervical lymphadenopathy) persisting for 3 days. During the same time interval, he also developed right-sided torticollis and vomiting. There was no preceding trauma recalled. A viral infection was presumed, and he was discharged with an antiinflammatory treatment. Nine days later, he returned to the emergency department for persistent elevated temperature, reduced feeding, drooling and whining. At presentation, the child was systemically unwell with a tilted head and restricted head movements. Physical examination (including oral and neurologic examination) was unremarkable. Laboratory investigations showed a hemoglobin value of 114 g/L,

a total white blood count (WBC) of  $9.7 \times 10^9/L$ , a platelet count of  $506 \times 10^9/L$  and a slightly elevated C-reactive protein (CRP) at 18 mg/L. A magnetic resonance imaging (MRI) of the neck showed cervical lymphadenopathy but was otherwise unremarkable. The child was discharged with symptomatic treatment and physiotherapy for the torticollis which was presumed to be caused by a viral upper respiratory tract infection. Three days later, he was readmitted because of persistent torticollis and elevated temperatures with a maximum of 38°C. The CRP was persistently slightly elevated at 20 mg/L, and the erythrocyte sedimentation rate (ESR)—which was not previously measured—was significantly elevated at >110 mm/h. Radiography of the cervical and thoracic spine was normal. A repeat MRI of the neck showed edema of the basis of the odontoid peg (Fig. A, Supplemental Digital Content 1, <http://links.lww.com/INF/C468>) with contrast enhancement (Fig. C and F, Supplemental Digital Content 1, <http://links.lww.com/INF/C468>), consistent with osteomyelitis. Intravenous treatment with cefuroxime (150 mg/kg/d) was started. A nasopharyngeal swab did reveal normal flora. Blood cultures were not performed. A bone biopsy was considered but not performed because of the high risk of an intervention in this location and the favorable response to treatment. After 5 days of treatment, the CRP normalized and the ESR was 35 mm/h. Antibiotic treatment was changed to oral amoxicillin/clavulanate (90 mg/kg/d) and continued for 4 weeks. On follow-up at the end of antibiotic treatment, the child was asymptomatic with a full range of head movement and normal neurologic examination.

## CASE 2

A 32-month-old boy was referred to our hospital because of persistent torticollis for 3 weeks. He had previously been seen by his general pediatrician. The boy had always been afebrile, in good general condition and inflammatory markers in the blood as well as radiography of the neck were unremarkable (Fig. A, Supplemental Digital Content 2, <http://links.lww.com/INF/C469>). The boy had empirically been treated with antiinflammatory medication, but the neck pain increased, especially during the night and the parents also reported decreased head movement. A fall from his bicycle had been noted shortly before the onset of symptoms 3 weeks earlier. At presentation, the boy had left-sided torticollis, mild cervical lymphadenopathy, cervical paraspinal muscle spasm and pain on head rotation to the left. Oral inspection was unremarkable, apart from a symmetrical tonsillar hypertrophy. Laboratory investigations showed a hemoglobin level of 112 g/L, a total WBC of  $9.6 \times 10^9/L$ , a platelet count of  $514 \times 10^9/L$ , a slightly elevated CRP of 8 mg/L and a significantly elevated ESR of 70 mm/h. A computed tomography (CT) of the cervical spine showed irregular osteolysis of the odontoid peg with soft tissue swelling and pannus formation with contrast enhancement within atlantoaxial joint space and marked enhancement of the odontoid (Fig. B, Supplemental Digital Content 2, <http://links.lww.com/INF/C469>).

Intravenous cefuroxime (150 mg/kg/d) was started. After 6 days of treatment, symptoms resolved. Blood cultures remained sterile. Serology for *Bartonella*, *Salmonella*, *Brucella*, *Francisella tularensis* and an interferon gamma release assay for tuberculosis was negative. After 2 weeks of therapy with cefuroxime, the child developed fever, skin flushing and vomiting, and therefore, the antibiotic treatment was changed to meropenem 75 mg/kg/d. Three weeks after initiation of treatment, an MRI showed contrast enhancement within the dens and atlantoaxial joint space (Fig. C, Supplemental Digital Content 2, <http://links.lww.com/INF/C469>) and the ESR dropped to 10 mm/h. Antibiotic treatment was switched to oral amoxicillin/clavulanate (90 mg/kg/d). After 6 weeks of therapy, the inflammatory markers had normalized,

**TABLE 1.** Clinical Characteristics of the Children With Odontoid Osteomyelitis

Age (mo)	Gender	Symptoms at Presentation	Previous Trauma	Interval to Diagnosis (d)	Laboratory Investigations at Presentation	Initial Presumed Diagnosis	Imaging and Findings	Blood Culture Isolated Pathogen	Treatment	Reference
1	NS	Fever Systemically unwell Drooling Muscular hypotension Left-sided hemiparesis	Not reported	NS	NS	Central nervous system infection	Rx: not done MRI: C1/C2 destruction and epidural abscess	Not performed <i>Staphylococcus aureus</i> (soft tissue)	Abscess evacuation Heml—semi laminectomy Meropenem iv 6 wk followed by vancomycin iv 2 d	7
2	NS	Posterior neck swelling Torticollis Painful, restricted head movements	Not reported	NS	WBC 22.9 × 10 <sup>9</sup> /L CRP 10 mg/L ESR 94 mm/h	Soft tissue infection with abscess and osteomyelitis Dens osteomyelitis	Rx: radiolucent lesions C2, C3 and C4 MRI: soft tissue mass arising from the posterior element of the upper cervical spine with osseous destruction Rx: prevertebral soft tissue swelling MRI: enhancement odontoid peg and atlantoaxial joint space	Not performed <i>S. aureus</i> (aspiration)	Aspiration Nafcillin iv 4 wk plus gentamicin iv a few days followed by dioxacillin oral for 12 wk Antibiotics not further specified iv 6 wk followed by antibiotics not further specified oral 12 wk	8
10	NS	Neck stiffness	Not reported	0	WBC and CRP “mildly elevated” ESR normal	Dens osteomyelitis	Rx: prevertebral soft tissue swelling MRI: enhancement odontoid peg and atlantoaxial joint space	Not performed None	Antibiotics not further specified iv 6 wk followed by antibiotics not further specified oral 12 wk	9
14	Male	Torticollis Restricted head movements Cervical lymphadenopathy Drooling Whining Reduced feeding	Not reported	13	WBC 9.7 × 10 <sup>9</sup> /L CRP 20 mg/L ESR >110 mm/h	Torticollis Upper respiratory infection	Rx: normal MRI: contrast enhancement in the atlantoaxial joint space, edema odontoid peg	Not performed None	Cefuroxime iv 5 d followed by amoxicillin/clavulanate oral 4 wk	Our case
18	Male	Neck stiffness Restricted head movements Weight loss Malaise Cervical lymphadenopathy	Fall from chair	NS	WBC 6.3 × 10 <sup>9</sup> /L ESR 94 mm/h	Torticollis C2 fracture	Rx: prevertebral soft tissue swelling, widened synchondrosis CT: C2 destruction MRI: contrast enhancement odontoid and prevertebral soft tissues, retropharyngeal inflammation CT: C1–C2 irregularities, particularly in the dens MRI: enhancement in odontoid peg with surrounding edema	Negative None	Cervical collar Clindamycin iv, duration NS	10
20	Male	Neck stiffness Restricted, painful head movements Torticollis Cervical muscle spasm Irritability	Not reported	7	WBC 12.1 × 10 <sup>9</sup> /L CRP 37 mg/L ESR 63 mm/h	Torticollis	CT: C1–C2 irregularities, particularly in the dens MRI: enhancement in odontoid peg with surrounding edema	Negative None	Clindamycin iv 2 wk followed by clindamycin oral 4 wk	11
32	Male	Neck stiffness Torticollis Posterior neck pain Restricted head movements Cervical muscle spasm Cervical lymphadenopathy	Fall from bike 1 wk before	21	WBC 9.6 × 10 <sup>9</sup> /L CRP 8 mg/L ESR 70 mm/h	Torticollis Upper respiratory infection	Rx: normal CT: osteolysis of the odontoid peg MRI: contrast enhancement within dens and atlantoaxial joint space	Negative None	Cefuroxime iv 1 wk followed by meropenem iv 2 wk followed by amoxicillin/clavulanate oral 8 wk	Our case
84	Female	Posterior neck swelling Torticollis Reduced, painful head movements	Fall from swing 3 wk before	90	NS	subluxation atlantoaxial joint	Rx: C1 anterior subluxation, C2–C4 lytic lesions in posterior elements	Not performed None	Cervical collar Halo traction Aspiration Spinal fusion C1–C5 Antibiotics, not further specified duration NS	12

NS indicates not specified, C, cervical vertebrae; iv, intravenous; Rx, plain radiographs.

a follow-up MRI showed markedly less contrast enhancement of the odontoid peg. The therapy was stopped after a total of 8 weeks. Follow-up MRI 3 months after the onset of treatment showed further reduction in contrast enhancement. The patient was asymptomatic at 8 months follow-up.

## LITERATURE REVIEW

A systematic literature review was performed using Medline, Embase and Web of Science (1950 to September 2015) using the search terms “OOM” or “osteomyelitis odontoid peg” or “dens osteomyelitis” or “vertebral osteomyelitis.” References were hand-searched for additional articles. Only cases of children with OOM with sufficiently detailed description of clinical presentation, diagnostic methods and treatment were included. The clinical characteristics of the 6 children reported in the literature and our 2 cases are summarized in Table 1.<sup>7–12</sup>

In children with OOM, the median age at presentation was 16 (range, 1–84) months; 7 of the 8 children were below the age of 3 years. The most common presenting symptoms were reduced head movements, neck stiffness or torticollis which was present in all but 1 patient.<sup>7</sup> Cervical lymphadenopathy was described in 3 children<sup>10</sup>; neck swelling,<sup>8,12</sup> cervical muscle span<sup>11</sup> and drooling<sup>7</sup> each in 2 patients. Interestingly, for both children described in our cases, an aggravation of pain during the night was reported. The median interval from the first medical presentation to time of the diagnosis was 17 (range 0–90) days. Four of the 8 patients, including our 2 cases, were initially diagnosed with torticollis and discharged with antiinflammatory medication.<sup>10,11</sup> In 3 patients, a prior trauma affecting the head or neck was described.<sup>10,12</sup>

The majority of children (7 of 8 cases) were not reported to have fever or be systemically unwell. Detailed laboratory results were available from 5 patients.<sup>8–11</sup> ESR and CRP were elevated in all 5 cases with a median level of 94 (range of 63 to >110) mm and 15 (range of 8–37) mg/L, respectively. The WBC was only elevated in 1 child, and the median level was  $9.7$  (range of  $6.3$ – $22.9$ )  $\times 10^9/L$ .

In 3 patients, a concomitant infection was present: thigh abscess,<sup>10</sup> retropharyngeal abscess<sup>7</sup> and staphylococcal pharyngitis<sup>12</sup>). While radiography of the spine was normal or not done in 3 patients (38%), cervical MRI established the diagnosis in all patients in whom it was performed. One patient was diagnosed based on findings in radiography only. In 3 children, blood cultures were taken but remained sterile.<sup>10,12</sup> A pathogen was isolated in 2 patients only, both of which were positive for *Staphylococcus aureus* isolated from an aspirate<sup>7,8</sup>; none of the patients had bone biopsies performed.

Three patients were surgically treated (one each with aspiration,<sup>8</sup> aspiration and spinal fusion,<sup>12</sup> and evacuation of abscess and hemi–semi-laminectomy<sup>7</sup>). All patients received antibiotic treatment for a median duration of 9 (range, 5–18) weeks. Five patients were switched to oral antibiotics after a median duration of 3 (range, 1–6) weeks.<sup>7–9,11</sup> The choice of antibiotics and the duration of therapy were heterogeneous. Seven of the eight patients showed complete resolutions of symptoms on follow-up. Only the youngest patient showed residual changes follow-up CT at 2 months with the absence of normal osseous structures in craniospinal region. He had from reduced head movements on his 3-year follow-up.<sup>7</sup>

## DISCUSSION

Vertebral osteomyelitis is most commonly caused by haematogenous seeding of bacteria, and infections are predominantly localized in the lumbar and thoracic spine, with significantly less

frequent involvement of the cervical spine.<sup>13</sup> Local trauma to bone in the setting of bacteremia may also be a contributing factor. OOM is a rare condition, and diagnosis is challenging as most children present in good general condition and without fever. The most common symptoms at presentation are reduced head movements, torticollis or neck stiffness. Torticollis usually resolves within a few days. In children with persistent symptoms, further investigations are necessary. Possible noninfectious differential diagnoses are muscular strains, fractures or Grisel Syndrome (an atlantoaxial subluxation after inflammation). If persistent torticollis is associated with an elevation of ESR, possible differential diagnoses are cervical lymphadenitis, abscesses (peri-, retrotonsillar and epidural), central venous infections, malignancies or infections of the spine. One consistent finding of patients with OOM is persistence of symptoms and in most cases an elevated ESR above 50 mm/h. Further hints might be drooling or an aggravation of pain during the night. Radiography of the spine may be helpful for diagnosis, but prevertebral softtissue swelling can be subtle and easily be missed. Unossified cartilaginous parts of the atlas and axis in infants, unexpected variants of synchondroses and osseous gaps are difficult to differentiate from osteomyelitis on plain radiographs.<sup>14</sup> Disk space narrowing used for diagnosis of other vertebral osteomyelitis is not usually evident in the cervical spine. CT scans may be useful to show bone destruction and soft tissue swelling or pannus formation. Unexpected synchondroses and osseous gaps can lead to a misdiagnosis of a fracture.<sup>10</sup> The most helpful imaging modality is MRI, particularly in early diagnosis, as it may indicate bone edema, soft tissue enhancement or abscess formation.

Treatment of OOM should include empiric antibiotic medication covering *S. aureus* until culture results are available. Surgical intervention should be performed when deemed necessary and may help to determine the causing pathogen. Despite frequent delay in diagnosis, the outcome of the reported cases is generally favorable, but possible complications include destruction of the vertebral bodies,<sup>7,15</sup> subluxation of the atlantoaxial joint<sup>16</sup> or cervical cord compression.<sup>3,7</sup>

Osteomyelitis of the atlas may present similarly to OOM and require similar treatment.<sup>17</sup> Tuberculous osteomyelitis should be considered, particularly for children exposed to tuberculosis or living in high prevalence countries and/or lack of improvement under initial antibiotic treatment. Tuberculous osteomyelitis is commonly described in spine but the dens seems rarely affected.<sup>18,19</sup>

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*Authors' contributions:* P. Zimmermann drafted the initial manuscript, performed the literature review and approved the final manuscript as submitted. N. Ritz critically reviewed and revised the manuscript and approved the final manuscript as submitted. E. Stranzinger prepared the figures and critically reviewed and revised the manuscript and approved the final manuscript as submitted. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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## SURVIVAL OF AN ENVELOPED VIRUS ON TOYS

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**Abstract:** Children's toys may carry respiratory viruses. Inactivation of a lipid-enveloped bacteriophage, Φ6, was measured on a nonporous toy at indoor temperature and relative humidity (RH). Inactivation was approximately  $2\log_{10}$  after 24 hours at 60% RH and  $6.8\log_{10}$  at 10 hours at 40% RH. Enveloped viruses can potentially survive on toys long enough to result in exposures.

**Key Words:** virus, fomite, influenza, survival, respiratory

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Toys may serve as important fomites for the transmission of viral diseases among children, including lipid-enveloped respiratory viruses such as influenza that spread through hand-to-mucous-

membrane contact. Sampling of shared toys in day cares<sup>1</sup> shows evidence of viral contamination; nucleic acids from respiratory viruses have been isolated from toys in day cares<sup>2</sup> and doctors' offices,<sup>3</sup> and influenza nucleic acids have been isolated from toys in homes.<sup>4</sup> Toys in common play areas in healthcare settings have been implicated as vehicles for outbreaks of viral illness.<sup>2</sup> One challenge of understanding the potential role of toys in viral transmission is that many studies of viral contamination of toys are cross-sectional and based on detection of viral nucleic acids, making it difficult to determine whether infectious viruses are present on toys and how long they persist. Without knowing how enveloped viruses survive on fomites like toys, it is difficult to assess the potential risk of infection and effectively design control measures such as disinfection. Therefore, the purpose of this study is to determine the inactivation of an enveloped virus surrogate, bacteriophage Φ6, on the surface of a nonporous children's toy at temperature and relative humidity (RH) levels typical of indoor environments.

## METHODS

Virus was propagated in host *Pseudomonas syringae* using the soft agar propagation method (bacteriophage and host were kindly provided by Dr. Leonard Mindich, University of Medicine and Dentistry, New Jersey). Thirty milliliter of host bacterial culture was grown for 24 hours with shaking (100 rpm, 25°C). Virus stock (2 mL) was added and incubated with shaking for another 24 hours. This virus culture (0.5 mL) and fresh host culture (0.5 mL) were added to 30 mL of soft agar (0.7% agar), dispensed into tryptic soy bottom agar plates and incubated at 25°C for 24 hours. The top layer was then harvested, pooled, purified by centrifugation ( $5900 \times g$ , 30 minutes and 4°C) and stored as stock in 20% glycerol–tryptic soy broth at –80°C.

A nonporous flexible plastic children's toy (a squeaking frog) was disinfected with 70% ethanol and cut into 1 cm<sup>2</sup> coupons. Virus stock was diluted in phosphate-buffered saline to target a concentration of  $10^7$  plaque-forming units (PFU) in 10 μL. 10 μL was placed on toy coupons. Time 0 carriers were sampled immediately. For the other time points, coupons were placed into controlled humidity environments at 22°C at either 40% ( $\pm 2\%$ ) or 60% ( $\pm 2\%$ ) RH, created by placing saturated salt solutions in sealed glass containers. For sampling, coupons were placed in tubes using sterile forceps. Eluent (5 mL of 1.5% beef extract, pH 7.5) was added into each tube and agitated on a shaker at 100 rpm for 20 minutes. Eluent was assayed using the double-agar layer plaque assay on tryptic soy agar and incubated at 22°C for 24 hours. Virus survival at each time point was expressed as  $\log_{10}(N_t/N_0)$ , where  $N_t$  is the virus concentration in PFU on the coupon at time  $t$ , and  $N_0$  is the initial virus concentration in PFU on the coupon at time 0. Data were analyzed with Excel 2011 (Microsoft Corp.) and GraphPad Prism 5 (GraphPad, San Diego, CA).

## RESULTS

Over 24 hours, there was an approximately  $2\log_{10}$  (99%) reduction in the number of infectious viruses at 60% RH, with approximately  $1\log_{10}$  reduction in the first 8 hours. At 40% RH, there was a more rapid decline, with  $3.2\log_{10}$  reduction at 2 hours and  $6.8\log_{10}$  at 10 hours (Fig. 1). Measurements at 40% humidity were carried out until the detection limit of  $6.8\log_{10}$  was reached at 10 hours.

To determine if the slopes of the inactivation curves were significantly different, data were fitted using the Weibull model, which has been previously applied to describe the effects of humidity on virus survival.<sup>5</sup> The Weibull model is  $\log_{10}(N_t/N_0) = -bt^n$ . Using this model, the slope  $n$  was determined for each humidity level (60%,  $n = 0.47$ ; 40% RH,  $n = 1.08$ ).  $R^2$  values indicated good