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INTRODUCTION

Subdural empyema (SDE) is a collection of pus between the dura and arachnoid layers of the meninges. It is a rare infection of the brain, and it is an almost fatal condition if left untreated, but since using antibiotics, the mortality rate has decreased and now ranges from 14% to 28%. In infants, it complicates neonatal meningitis, but in older children, it develops mainly due to ear, sinus infection, or spread from a hematogenous source. In males, SDE is more frequently seen in males, and it is the most commonly encountered intracranial complication of infection. The patient usually presents with fever, sinusitis, and neurological deficits with less frequent symptoms, including headache and seizures with alteration of the level of consciousness. Laboratory investigations vary from blood to imaging. Computed tomography (CT) and magnetic resonance imaging (MRI) are the most important. Also, white blood cell count, erythrocyte sedimentation rate, and C-reactive protein level may be helpful. Imaging is recommended for every patient suspected to have a subdural abscess.

CASE REPORT

Subdural empyema due to mixed infections successfully treated medically: A case report with review literature

Mostafa Meshref | Anas Zakarya Nourelden | Alaa Ahmed Elshanbary | Yossef Hassan AbdelQadir | Mohamed Sayed Zaazouee | Khaled Mohamed Ragab | Eman Mohammed Sharif Ahmed | Sarya Swed

1MSc neurology, Al-Azhar University, Cairo, Egypt
2Faculty of Medicine, Al-Azhar University, Cairo, Egypt
3International Medical Research Association (IMedRA), Cairo, Egypt
4Faculty of Medicine, Alexandria University, Alexandria, Egypt
5Faculty of Medicine, Al-Azhar University, Assiut, Egypt
6Faculty of Medicine, Minia University, Minia, Egypt
7Department of Obstetrics & Gynecology, Nile Valley University, Sudan
8Faculty of Medicine, Aleppo University, Aleppo, Syria

Correspondence
Sarya Swed, Faculty of Medicine, Aleppo University, Aleppo, Syria.
Email: saryaswed1@gmail.com

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Abstract
Subdural empyema is a rare intracranial infection with an accumulation of purulent material between the dura and arachnoid matter. We report a case of 17 years old presented with an altered conscious level. CSF analysis showed increased WBCs. His situation has improved after treating by acyclovir, ceftriaxone, vancomycin, and dexamethasone.

KEYWORDS
bacterial infection, medical treatment, meningeal irritation, subdural empyema, viral infection

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### TABLE 1: Summary of the previous case reports

| Study ID    | Sex   | Age | Predisposing event                          | Signs and symptoms                                 | Bilateral or unilateral | Location                                      | Specific location                                      |
|-------------|-------|-----|---------------------------------------------|---------------------------------------------------|-------------------------|------------------------------------------------|--------------------------------------------------------|
| Şahin 2015  | Male  | 16  | Sinusitis                                   | Projectile vomiting, lethargy, fever, and headache | Unilateral              | Subdural                                        | Around the right cerebral hemisphere then relapse in the posterior interhemispheric fissure |
| Yuçel 1998  | Male  | 14  | Upper airway infection                      | Deterioration of consciousness, right hemiparesis, edema in the left eyelid and seizures | Unilateral              | Subdural                                        | Frontal                                                |
| Arifianto 2017 | Male  | 17  | Allergic rhinitis                           | Deterioration in consciousness, difficulties in speech, and hemiparesis | Unilateral              | Subdural                                        | Interhemispheric and infratentorial                     |
| Balfour-Lynn 1997 | Female | 16  | Exposure to an active case of pulmonary tuberculosis | Seizure and visual hallucination                  | Unilateral              | Subdural empyema                               | Over the right cerebral hemisphere                      |
| Banerjee 2010 | Male  | 12  | Suspicion of sinusitis                      | Raised intracranial pressure and fever for 1 month and altered sensorium for 2 days | Unilateral              | Subdural empyema                               | Left frontoparietal and interhemispheric                |
| Derin 2015  | Male  | 16  | Dental infection                            | Dental and facial pain and swelling of the left face | Unilateral              | Subdural empyema                               | Frontal                                                |
| Borovich 1990 | All of them are males | Case 1: 17 | Case 1: purulent meningitis                | Case 1: headaches, abdominal pain, and fever of 1 month's duration | Cases 1 & 2: unilateral | All of them are subtentorial collection with marked mass effect | –                                                      |
|             |       |     | Cases 2 & 3: acute meningitis | Case 2: 1 day of headaches and fever | Case 3: otorrhea, fever, and headaches | |                                                     |
| Calik 2012  | Male  | 13  | Upper airway infection                      | Fever and cervical micro lymphadenopathy           | Unilateral              | Subdural empyema                               | Frontal                                                |
| Conlon 1996 | Case 1 | 16  | Upper airway infection                      | Fever and left frontal headache then seizures     | Unilateral              | Subdural empyema                               | Frontal                                                |
|            | Female | 16  | Upper airway infection                      | Photophobia, frontal headache and periorbital swelling | Unilateral              | Cerebritis                                      | Frontal                                                |
| Dolan 1995  | Male  | 16  | Suspected sinusitis                         | Altered mental status and slurring of speech      | Unilateral              | Subdural empyema                               | Frontal                                                |
| Dunn 2013   | Male  | 14  | Migraine headaches and acute sinusitis      | Vomiting and nausea                               | Unilateral              | Epidural and subdural empyema                  | Frontopatellar                                         |
| Harris 1987 | Male  | 12  | Sinusitis                                   | Fever, lethargy and monoplegia                    | Unilateral              | Subdural empyema                               | –                                                      |
| Heilbronn 1984 | Male  | 13  | Pansinusitis                                | Frontal headache early then the patient developed neck stiffness | Unilateral              | Subdural                                       | Frontal and temporal                                   |
|            | Female | 12  | Pharyngitis                                 | Fever, neck stiffness                             | Unilateral              | Subdural empyema                               | Lateral ventricles                                      |
| Holland 2012 | Male  | 15  | Sinusitis                                   | Headache and low-grade fever then motor disability | Unilateral              | Subdural empyema                               | Right frontal sinus                                    |
| Jones 1997  | Female | 14  | Previous infection of mixed coliforms and Enterococcus | Deterioration of consciousness and bilateral abducens nerve palsy | Unilateral              | Sub-tentorial empyema                           | Left cerebellar hemisphere                              |
| Medline Shift | Intra-axial component (yes/no) | CNS infection (causative organism) | Follow-up period | Intervention used | Outcome |
|---------------|-------------------------------|-----------------------------------|-----------------|------------------|---------|
| Present       | None                          | *Streptococcus constellatus*      | 2 months        | Frontoparietal craniotomy | Hemiparesis of the patient improved gradually and SDE regressed completely after ampicillin treatment |
| Absence       | None                          | *Streptococcus pneumonia*         | 2 weeks         | Cranietomy        | Patient lost vision then he responded for treatment and was released from hospital |
| Present       | None                          | *Staphylococcus epidermidis*      | 4 weeks         | Conservative therapy then craniotomy | All the symptoms resolved; the only remaining symptom was limited extraocular muscle movement |
| Absence       | Yes                           | *Burkholderia cepacia*            | 1 year          | Cranietomy        | Initial recovery then deterioration and obliterator bronchitis of the lung although the use of antibiotics |
| Absence       | No                            | Acid-fast bacilli of TB           | 18 months       | Cranietomy        | Full recovery and no recurrence |
| Absence       | No                            | *Streptococcus viridans*          | 8 weeks         | Sinus drainage for pansinusitis and Empiric therapy | Recovery and patient discharge |
| All cases: Absence: No | Case 1: *Pneumococcus and Proteus*. Cases 2 & 3: None mentioned | Case 1: penicillin and gentamicin then left suboccipital craniectomy Case 2: Antibiotics then suboccipital craniectomy Case 3: penicillin and chloramphenicol then external ventricular drainage, drainage of the subtentorial pus, and a bilateral mastoidectomy | – | Cases 1 & 2: Recovery and patient discharge Case 3: The patient died 24 h after surgery |
| Absence       | No                            | None                              | 4 weeks         | Craniotomy and sinusotomy | Recovery and patient discharge |
| Absence       | No                            | Pansinusitis by B hemolytic *Streptococcus group A* | 1 week | Pus aspiration from sinus | Recovery and patient discharge |
| Absence       | No                            | NR                                | NR              | Craniotomy and twist drill ventriculostomy | Recovery and patient discharge |
| Present       | No                            | Threatening                       | 6 weeks         | Bifrontal craniotomy, physical and speech therapies in follow-up | Full recovery and no recurrence |
| Absence       | No                            | NR                                | NR              | Craniotomy         | Recovery and patient discharge |
| Absence       | No                            | Pansinusitis by B hemolytic *Streptococcus group A* | NR | Exploration surgery and resection of necrotized tissue | Patient death |
| Absence       | No                            | NR                                | NR              | Craniotomy         | Recovery and patient discharge with anticonvulsant therapy |
| Present       | No                            | *Pneumococcus*                    | 6 months        | Craniotomy, ventricular drain, speech, and physical therapy | Postsurgical facial droop and unequal pupil dilation, after recovery the patient was discharged with residual left-sided weakness |
| Absence       | No                            | *Enterococcus faecalis*           | 4 weeks         | Craniectomy and radical mastoidectomy | Full recovery and no recurrence |

(Continues)
Table 1 (Continued)

| Study ID     | Sex     | Age     | Predisposing event | Signs and symptoms                                                                 | Bilateral or unilateral | Location                  | Specific location                                      |
|--------------|---------|---------|---------------------|-------------------------------------------------------------------------------------|-------------------------|---------------------------|--------------------------------------------------------|
| Kageyama 2000 | Male    | 18      |                     | Neurological deterioration, mild fever and vomiting                                 | Unilateral              | Subdural empyema          | Paranasal sinuses and convexity                        |
| Kuczkowski 2005 | Male    | 14      | Purulent rhinorrhea and upper respiratory tract infection | Headache, nausea, vomiting                                                          | Bilateral              | Subdural empyema          | Frontal brain lobes                                    |
|              | Male    | 12      | Purulent rhinorrhea and upper respiratory tract infection | Headache, periorbital swelling and meningitis                                        | Unilateral              | Subdural empyema          | Frontal sinuses                                        |
| Kwangong 2002 | All males| 7 patients (9-14) | Sinusitis | Headache, fever, motor deficit, seizures, and altered mental status                  | Unilateral              | Subdural empyema          | Frontal sinusitis                                      |
| Lefebvre 2009 | Male    | 15      | Sinusitis           | Headache and hemiparesis                                                            | Unilateral              | Subdural empyema          | Subdural and maxillary sinus                           |
| Manjila 2017 | Male    | 14      | Sinusitis           | Epistaxis due to suspected carotid artery damage                                    | Unilateral              | Subdural empyema          and cavernous sinus pseudo aneurism | Frontal and temporal regions                           |
| Martins 2014 | Male    | 18      | Sinusitis           | Dysarthria, fever and purulent rhinorrhea                                           | Unilateral              | Subdural empyema          | Maxillary sinus and frontal sinus                      |
| Millar 1996  | Male    | 14      | Flu-like illness    | Hemiparesis, headache and fever                                                     | Unilateral              | Subdural empyema          | Right frontal                                          |
| Mitsuoka 1995 | Male    | 14      | Retrobulbar pain and eye swelling | Seizure and loss of consciousness                                                  | Unilateral              | Subdural and interhemispheric empyema                 | Falc                                                   |
| Morgan 1995  | Male    | 17      | Chronic otitis      | Dysarthria, headache and neck stiffness and decreased sensation                     | Bilateral              | Basal cisterns and subdural                               |
|              | Male    | 15      |                     | Bilateral papiledema, nystagmus, ataxia, and photophobia                           | Unilateral              | Subdural empyema          | –                                                      |
|              | Male    | 17      | Postnasal discharge, fever and retroorbital pain, later he developed limb weakness |                                                                                         | Unilateral              | Subdural empyema          | –                                                      |
| Nica 2011    | Male    | 15      | Meningio-encephalitis | Drowsiness, cervical pain and headache                                            | Unilateral              | Subdural empyema          | Fronto-temporoparietal                                 |
| Ong 2002     | Male    | 13      |                     | Fever, drowsiness, headaches, and nausea later he developed unequal pupils and a suspected hemorrhagic infarct on CT scan | Unilateral              | Subdural empyema          | –                                                      |
| Pattisapu 2008 | Male    | 11      | Otitis media and mastoiditis meningitis | Nuchal rigidity, headache and lethargy                                           | Bilateral              | Subdural empyema          | Subtentorial                                           |
|              | Male    | 11      | meningitis          | Seizures, nuchal rigidity and decorticate posturing                                 | Bilateral              | Subdural empyema          | Subfrontal, parafalcine                                |
|              | Female  | 13      | Ethmoiditis and frontal osteomyelitis | Facial swelling, orbital cellulitis and hemiparesis                                | Bilateral              | Subdural empyema          | Parafalcine                                            |
| Sengul 2009  | Male    | 15      | Left otitis media and meningitis | Fever, headache, earache, and neck stiffness                                      | Unilateral              | Subdural empyema          | –                                                      |
| Medline Shift | Intra-axial component (yes/no) | CNS infection (causative organism) | Follow-up period | Intervention used | Outcome |
|---------------|--------------------------------|----------------------------------|-----------------|------------------|---------|
| Absence       | No                             | *Streptococcus milleri*          | 2 weeks         | Burr holes drainage and barbiturates | Recovery and patient discharge |
| Absence       | No                             | β-hemolytic group C *Streptococcus* |                | Craniotomy       | Full recovery and no recurrence |
| Absence       | No                             | Negative                         |                | Craniotomy       | Death 13 days after surgery |
| Absence       | No                             | *Streptococcus constellatus*     | 6 months       | Craniotomy       | Recurrent interhemispheric empyema then total recovery |
| Absence       | No                             | Methicillin-sensitive *Staphylococcus aureus* | 3 months | Craniotomy and arterial resection and reconstruction | Recovery and patient discharge |
| Absence       | No                             | Alpha hemolytic streptococci     | 2 weeks        | Craniotomy       | Death 3 days after surgery |
| Absence       | NO                            | *Streptococcus species*          | 4 weeks        | Craniotomy       | Full recovery and no recurrence |
| Absence       | NO                            | Anaerobic hemolytic streptococci| 3 drainage operations yet he developed meningitis and his condition deteriorated | Death after complications |
| Absence       | NO                            | Nonhemolytic streptococci        |                | Craniectomy and radical mastoidectomy | Recovery and discharge |
| Absence       | NO                            | Beta hemolytic streptococci of Lancefield group C | 4 weeks | 2 craniotomies | Full recovery and no recurrence |
| Absence       | NO                            | *Fusobacterium varium, F. mortiferum and Propionibacterium propionicum* | 1.5 years | Cranectomy | Full recovery after physical therapy |
| Absence       | NO                            | *Streptococcus constellatus*     |                | Cranectomy       | Recovery and patient discharge |
| Absence       | No                             | *Proteus, E. coli and Bacteroides* | 48 months     | Burrhole catheter drainage | Recovery and patient discharge |
| Absence       | No                             | *Salmonella Type C*              | 45 months      | Burrhole catheter drainage | Recovery and patient discharge |
| Absence       | No                             | Group D *Streptococcus, Bacteroides melaninogenicus* | 38 months | Craniotomy and ethmoidectomy | Recovery and patient discharge |
| Absence       | No                             | No organisms on culture          | 2 years        | Craniectomy       | Recovery and patient discharge |

(Continues)
In some cases, when the diagnosis by CT and MRI is unclear, hollow screws have a diagnostic value. Road spectrum antibiotics are usually the first-line management, and they may be enough to control the infection. However, the surgical intervention must be considered if the antibiotics fail to maintain or other surgery indications. The most common surgical procedures are craniotomy and burr holes. If the surgical intervention has been done within 72 h, the chance for disability is 10% compared to 70% when done after 72 h.

Because of its rarity, many doctors may not have seen a case in recent years. The topic should be re-visited to remind them to be aware of it. Also, it is difficult to distinguish from meningitis; hence, the attending clinician must have a high suspicion index.

In this report, we presented a SDE case successfully treated by medical treatment in our hospital. Also, we systematically summarized the previously published case reports about SDE.

### 2 | LITERATURE REVIEW

We searched for published case reports in four electronic databases: PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) in October 2020 using the following query: (“Empyema, Subdural” [Mesh]). We included all English case reports about SDE in adolescent patients (10–19 years).

Since 1990, approximately 35 studies with 53 patients have reported similar cases in this age group; almost all were males (86.7%). The observed pattern of predisposing events is sinusitis, otitis media, or an upper airway infection. Patients have usually suffered from fever, headache, and drowsiness. The neurological manifestations started with nuchal rigidity (17% of cases), hemiplegia (11.3% of cases), or seizures (18.8% of cases).

Details of each case and the organism isolated from the culture and the outcome are shown in **Table 1**.

### 3 | CASE REPORT

A 17-year-old male patient was referred to our hospital. He had no history of co-morbid illnesses. At first sight, he seemed distracted, and an altered conscious level was noted. By history, 7 days ago, the condition was started with a headache and low-grade fever without apparent septic focus; no tonsillitis or upper respiratory tract infection. The patient came to our hospital with his family member (from whom the history had been taken). They complained that the patient had a fever, which was not improved by analgesics associated with malaise and disturbing consciousness level in drowsiness and confusion; the patient was inattentive and disoriented to time, place, and persons. On examination, the patient was feverish (38.5), drowsy, confused, and had no focal neurological deficit with positive meningeal irritation signs, neck
Stiffness, positive Kerning’s, and stretch leg signs. CT brain at once showed mild diffuse brain edema of the right cerebral hemisphere with a suspected thin rim of overlying extra-axial fluid collection (Figure 1). We asked for a lumbar puncture (after taking consent from the family) to obtain a CSF sample for analysis. Septic screen samples, urine analysis and cultures, nasal swab, axillary culture, throat culture, blood culture, and sputum culture were also withdrawn. Routine laboratories were withdrawn as well, including complete blood count with differential, kidney and liver functions, and electrolyte levels.

Few days later, the results of CSF analysis showed that CSF was clear colorless fluid, RBCs 400 cells/cm, WBCs 66 cells/cm (neutrophils 30%, lymphocytes 65%, mononuclear cells 5%), CSF glucose was 4.8 mmol/L which is high (normal range 2.2–3.9 mmol/L), CSF protein was 52.7 mg/dl which is also high (normal range 15–45 mg/dl). Also, CSF cultures were negative for any bacterial growth, including gram bacteria and acid-fast bacilli. Acid-fast bacilli PCR is also negative.

Septic screen results also were negative for any bacterial growth. The rest of the tests were normal except for an increased W.B.C.s count of $14 \times 10^3$ with increased neutrophils 87.9.

Low-grade fever at first, high glucose level, and predominance of lymphocytes in CSF are evidence of viral infection. In addition, mucocele and the presence of sinusitis are bacterial infections, so a treatment that covers possible causes of C.N.S. infection was initiated: acyclovir (10 mg/kg IV ter in die [tid]; three times a day), ceftriaxone (2 g IV bis in die [bid]; twice a day), vancomycin (750 mg IV bid), and dexamethasone (4 mg IV quarter in die [qid]; four times a day).

The following day, an MRI brain with contrast was conducted and showed mild diffuse thickening of the pachy/leptomeninges overlying the right cerebral hemisphere with mild intervening fluid collection seen eliciting low signal on t1 and high signal on t2-weighted images with evidence of diffusion restriction, features suggestive right-side meningoitis with mild SDE. Evidence of right-sided mild mass effects that was manifested by effacement of the underlying cortical sulci with mild compression on the right lateral ventricle. In addition to that, there was obliteration and mildly expansion of the frontal sinus, showing a high signal on both t1- and t2-weighted images, likely representing mucocele formation. Also, the sphenoid, right ethmoid sinuses, and suitable mastoid air cells have been destroyed (Figure 2).

At the end of the second day after admission, the patient developed serial attacks of generalized tonic colonic fits, controlled by giving loading phenytoin (15 mg/kg); after that, we kept him on levetiracetam (500 mg F.O. B.I.D.). Also, E.E.G. was done, which showed slowness in activity (Figure 3). The patient’s condition improved on the 5th day regarding consciousness level, and no more fits had occurred. The patient was continued on the same treatment measures. A follow-up MRI brain with contrast was done after 1 week (Figure 4) and

| Medline Shift | Intra-axial component (yes/no) | CNS infection (causative organism) | Follow-up period | Intervention used | Outcome |
|---------------|-------------------------------|---------------------------------|-----------------|------------------|---------|
| Absence       | Yes                           | *Pasteurella multocida*         | 4.5 years       | Empyema evacuation | Recovery and the patient is kept on antiepileptic therapy |
| Absence       | No                            | 4 Negative cultures -1          | 3–60 months     | Craniotomy       | Recovery and discharge |
| Absence       | No                            | *Mycobacterium fortuitum*      | 6 weeks         | Craniotomy       | Full recovery and no recurrence |
| Absence       | No                            | *Streptococcus anginosus*      | Craniotomy      | Recovery and no recurrence |
| Absence       | No                            | *Fusobacterium species*        | Craniotomy      | Recovery and no recurrence |
| Absence       | No                            | Group F streptococci           | 2 months        | Craniotomy       | Recovery and discharge |
| Absence       | No                            | *Streptococcus species*        | 7 weeks         | Conservative treatment after tonsillectomy | Recovery and discharge |
3 weeks (Figure 5), which showed significant regression of the meningeal thickening and enhancement for the right SDE.

The patient was discharged with marked improvement up to his normal state with no complaints.

4 | DISCUSSION

This case report presents a patient with SDE resulting from a mixed bacterial and viral infection. The patient suffered from sinusitis 7 days before our investigation. The CSF analysis showed an increasing number of WBCs (66 cells/cmm) and 30% neutrophils. The CT scan showed mild diffuse brain edema of the right cerebral hemisphere with suspected mucocele formation, which is considered evidence of bacterial infection. Also, CSF analysis showed an increase in the number of lymphocytes 65% and glucose 4.8 mmol/L, which is evidence of viral infection. Our case showed a thin rim in CT and no significant midline shift in MRI, so it is considered a mild case. Although surgery is the first line in the treatment of SDE, there is a widely unutilized option to use antibiotics in mild cases. 18,54 So we treated our patient medically with acyclovir (10 mg/kg IV tid) for viral infection; ceftriaxone (2 g IV bid) and vancomycin (750 mg IV bid) for bacterial infection and dexamethasone (4 mg qid). The treatment was effective, and the patient had recovered with no severe side effects or disability.

What makes this case unique is a mixed infection; the patient was also treated medically, while a limitation was no PCR analysis for causative organisms. The case was diagnosed as SDE depending on the clinical history (fever, disturbed conscious level, meningeal irritation signs, fits, and preceding infection), CSF findings (which showed the proof of mixed infection), and MRI brain findings. Also, there was evidence of EEG changes in the form of slowness activity, which is going with Mauser H.W et al. They found multiple EEG changes that may occur with SDE cases, including diffuse slowness. 54 Thus, diagnosis depends only on clinical history, signs, laboratories, EEG, and radiology findings.

Ruth et al. concluded that a nonsurgical strategy might be considered for patients with a good clinical condition with a minor shift from the midline on radiology results. 19,55 For 4 weeks, Musa et al. reported evidence of pre-surgical treatment with I.V chloramphenicol and metronidazole. They increased a Glasgow coma scale from 8/15 to 15/15 with no seizures. 21 SDE had reported getting negative in culture test; a case series by Madhugiri et al. consisting of 27 patients with a mean age of 10 years reported that 26% of patients get negative in culture test. 20

Based on our case, physicians should consider the treatment of viral and bacterial infections in similar circumstances. Medical treatment of mild SDE patients can be effective and safe. Future research is needed to investigate the merits and limitations of using medical therapy alone in SDE with mild and moderate cases. In conclusion, as there were multiple conflicts in differentiation...
between SDE and meningitis, all attending doctors must suspect it. Start medical treatment as soon as possible for all suspected cases depending on the clinical, radiological, and laboratory findings. According to the case degree, early intervention in those cases, whether medical or surgical, can improve patient outcomes and good prognosis. In spite, our case showed marked improvement only on using medical treatments. Multiple researches should be conducted for clarification and putting criteria for either medical or surgical therapies for SDE patients.

**AUTHOR CONTRIBUTIONS**
All authors have contributed in writing and reviewing the manuscript.

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**CONFLICT OF INTEREST**
There is no conflict of interest.
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