

Bacterial sinusitis and its frightening complications: subdural empyema and Lemierre syndrome

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ABSTRACT

The symptoms of a previously healthy 14-year-old female with an initial history of tooth pain and swelling of the left maxillary evolved to a progressive headache and altered neurological findings characterized by auditory hallucinations, sleep disturbances, and aggressiveness. She was brought to the emergency department after 21 days of the initial symptoms. An initial computed tomography (CT) scan showed frontal subdural empyema with bone erosion. The symptoms continued to evolve to brain herniation 24 hours after admission. A second CT scan showed a left internal jugular vein thrombosis. The outcome was unfavorable and the patient died on the second day after admission. The autopsy findings depicted rarefaction of the cranial bone at the left side of the frontal sinus, and overt meningitis. The severe infection was further complicated by thrombophlebitis of the left internal jugular vein up to the superior vena cava with septic embolization to the lungs, pneumonia, and sepsis. This case report highlights the degree of severity that a trivial infection can reach. The unusual presentation of the sinusitis may have wrongly guided the approach of this unfortunate case.

Keywords

Sinusitis; Empyema; Subdural; Meningoencephalitis; Adolescent.

CASE REPORT

A 14-year-old girl complaining of upper left teeth pain and bulging of the maxillary region sought odontological assistance and was prescribed a 7-day course of cephalexin. At the end of the antibiotic regimen, she started presenting behavioral alterations characterized by auditory hallucination, sleep disturbances, aggression, and frontal headache. With the 14-day history of headache, she was brought to the pediatric emergency care unit presenting alternating periods of agitation, aggressiveness,

somnolence, and mental confusion, besides vomiting. A paranasal sinuses and brain computed tomography (CT) scan showed right maxillary and frontal sinuses opacification, frontal sinus osseous erosion associated with a subdural empyema, and slight cerebral edema (Figure 1). The initial laboratory work-up showed inflammatory alterations without acid-base or electrolytes imbalance (Table 1).

She was referred to the pediatric intensive care unit and was empirically started on ceftriaxone,

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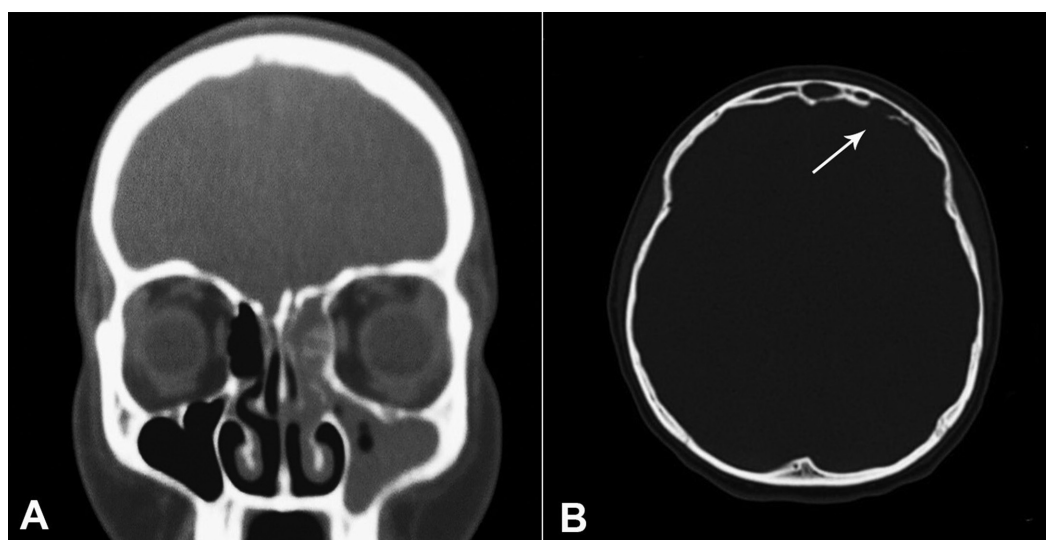


Figure 1. Multidetector CT scan of the brain and paranasal sinuses. **A** – Opacification of the left maxillary and frontal sinuses **B** – Left frontal sinus bone erosion.

Table 1. Admission day laboratory work-up

Exam	Result	RV	Exam	Result	RV
Hemoglobin	10.9	12.3-15.3 g/dL	Monocytes	10.5	2-9%
Hematocrit	33.6	36.0-45.0%	Platelets	363,000	150-400 × 10 ³ /mm ³
Leukocytes	20,400	4.4-11.3 × 10 ³ /mm ³	Urea	18	13-49 mg/dL
Bands	0	1-5%	Creatinin	0.55	0.6-1.1 mg/dL
Segmented	82.8	45-70%	CRP	174	<5 mg/L
Lymphocyte	6.7	18-40%	Blood Culture	Negative	Negative

CRP = C-reactive protein.

levofloxacin, vancomycin, and acyclovir, based on the suspicion of meningoencephalitis. On the same day, her neurologic parameters progressively deteriorated and she had a sudden cardiopulmonary arrest, and recovered the sinus rhythm after 4 minutes of resuscitation maneuvers. After cardiopulmonary resuscitation, the Glasgow Coma Scale (GCS) remained at 3. A new CT scan showed diffuse cerebral edema, signs of brain herniation, and left internal jugular vein thrombosis (Figure 2). She died 48 hours after admission. Analysis of the cerebrospinal fluid (CSF) collected after death is shown in Table 2. Serology and polymerase chain reaction analysis of the CSF showed negative results for cytomegalovirus, Epstein Barr virus, herpes simplex virus types 1 and 2, varicella-zoster virus, and human enteroviruses. An autopsy was performed.

AUTOPSY FINDINGS

A craniotomy revealed intense meningeal purulent exudate (Figure 3A) and frontal bone erosion at the inner aspect of the left side of the frontal sinus (Figure 3B). Typical acute inflammation with neutrophils surrounded the meninges upon microscopic analysis (Figure 3C). Acute osteomyelitis of frontal and mastoid bones was also detected upon histology (Figure 3D). Other areas of the brain, cerebellum, and brainstem showed neuronal and glial necrosis consistent with diffuse encephalic ischemia.

Cross- and sequential sections of the neck and mediastinum organs revealed left internal jugular vein thrombosis, which extended downwards to the superior vena cava and the left brachiocephalic vein. Histopathological analysis revealed thrombophlebitis involving the entire left internal jugular vein until the superior vena cava (Figure 4).

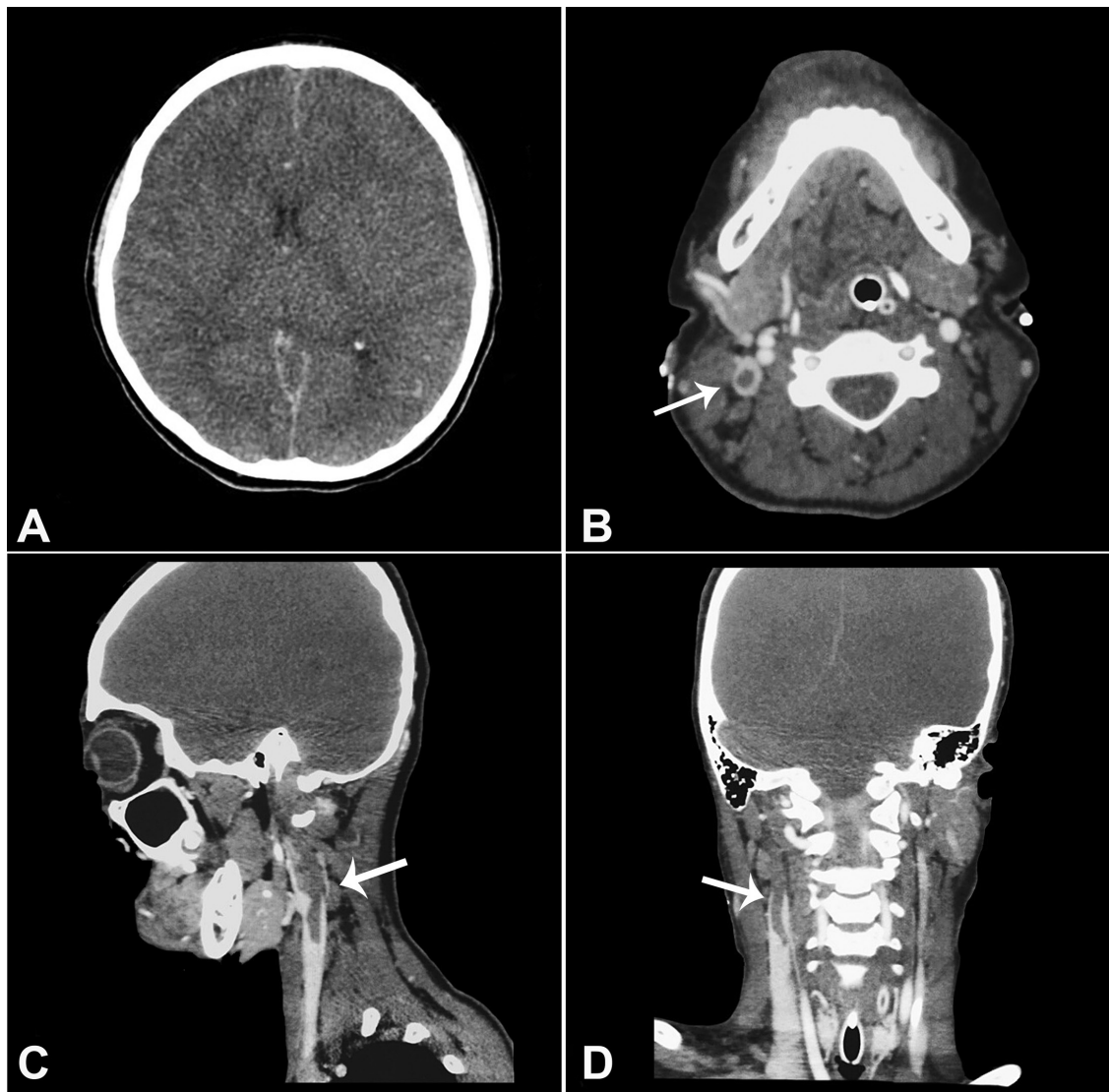


Figure 2. Contrast-enhanced multidetector CT scan. **A** – Diffuse cerebral edema; **B**, **C**, and **D** – Left internal vein thrombosis (arrows).

Table 2. Cerebrospinal fluid analysis

Exam	Result	RV	Exam	Result	RV
Appearance	Clear	Clear	Protein	385.7	15-45 mg/dL
WBC count	250	0-5/mm ³	Glucose	54	40-70 mg/dL ³
Erythrocytes	50	0/mm ³	Lactate	82.7	9-26 mg/dL
Neutrophils	49	0%	Pandy	Positive	Negative
Lymphocytes	30	0%	CSF culture	Negative	Negative
Monocytes	21	0%			

WBC = white blood cell.

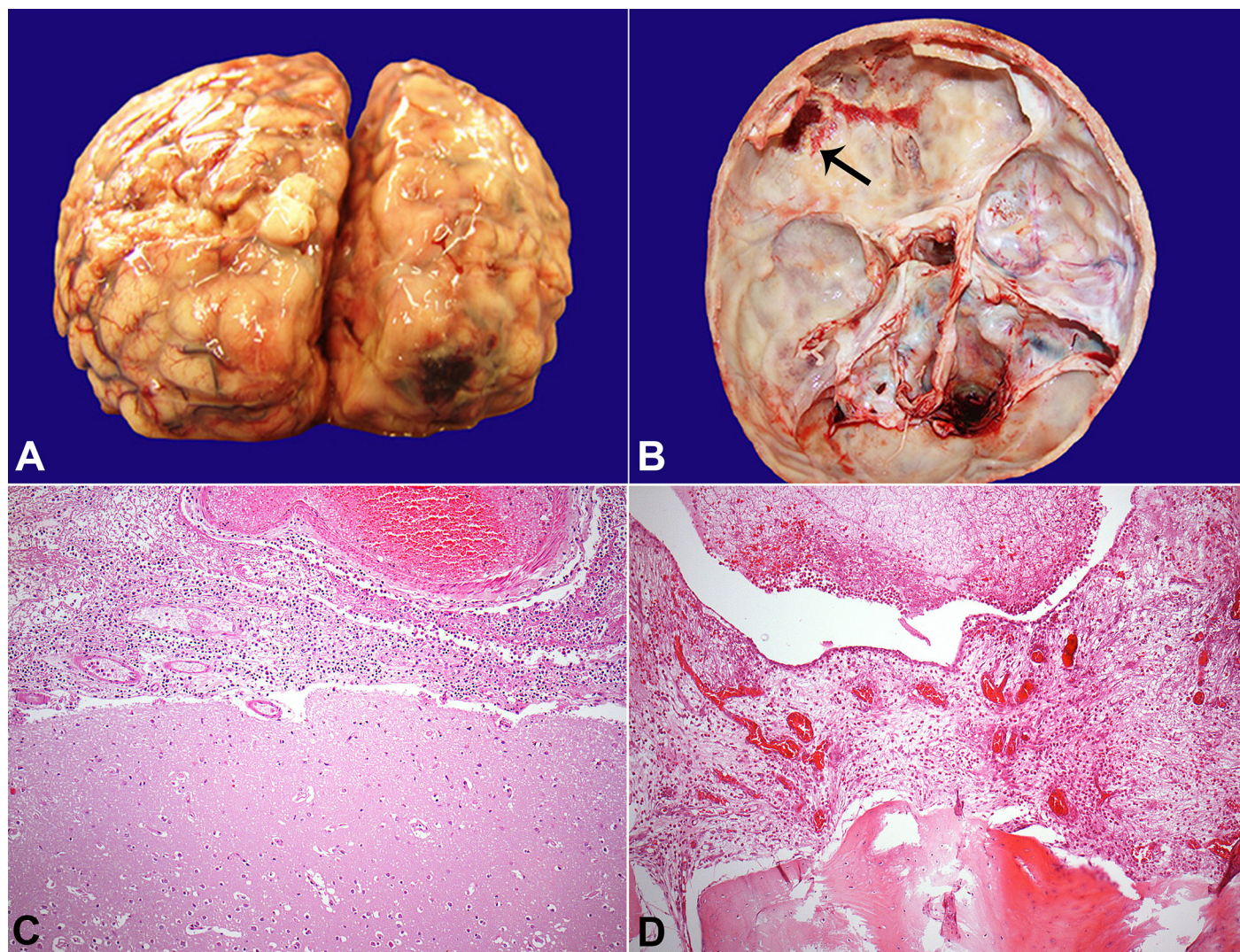


Figure 3. **A** – Anterior view of brain, frontal lobes. Note purulent exudate around the hemorrhagic spot on the left frontal lobe; **B** – Bone erosion on the left inner aspect of the frontal bone with hemorrhage (black arrow); **C** – Photomicrography of the meninges showing acute meningitis with numerous neutrophils (H&E, 200X); **D** – Photomicrography of the mastoid bone showing acute inflammation (mastoiditis) (H&E, 200X).

The lungs showed multiple areas of pneumonia and alveolar edema. Liver, spleen, heart, lymph nodes, and bone marrow showed multiple foci of neutrophilic infiltration, which were consistent with sepsis. The kidneys showed acute tubular necrosis.

DISCUSSION

Acute rhinosinusitis (or sinusitis) is a common condition defined as the inflammation of the mucosal lining of the nasal passage and paranasal sinuses lasting up to 4 weeks.¹ In pediatric patients, these upper respiratory infections (URI) occur with an incidence of 5 to 5.5 cases per child per year, and are mostly due to viral infections.^{2,3} URI is commonly complicated with

bacterial infections, mostly with acute otitis media (29% of the cases in children) or followed by acute bacterial sinusitis (ABS) (5-8% of the cases in children and 0.5-2% in adults).⁴⁻⁶

According to the last guideline of the Infectious Disease Society of America, ABS is defined only by clinical findings (persistent, severe, or worsening symptoms) rather than by imaging techniques, as the latter cannot differentiate between viral and bacterial etiology.^{1,7} ABS complications mostly involve local tissue and the orbit, while intracranial involvement is the least affected.^{8,9} Subdural empyema, as observed in our patient, is the most common intracranial complication of ABS (33-56% among all intracranial complications); however, other intracranial complications may occur:

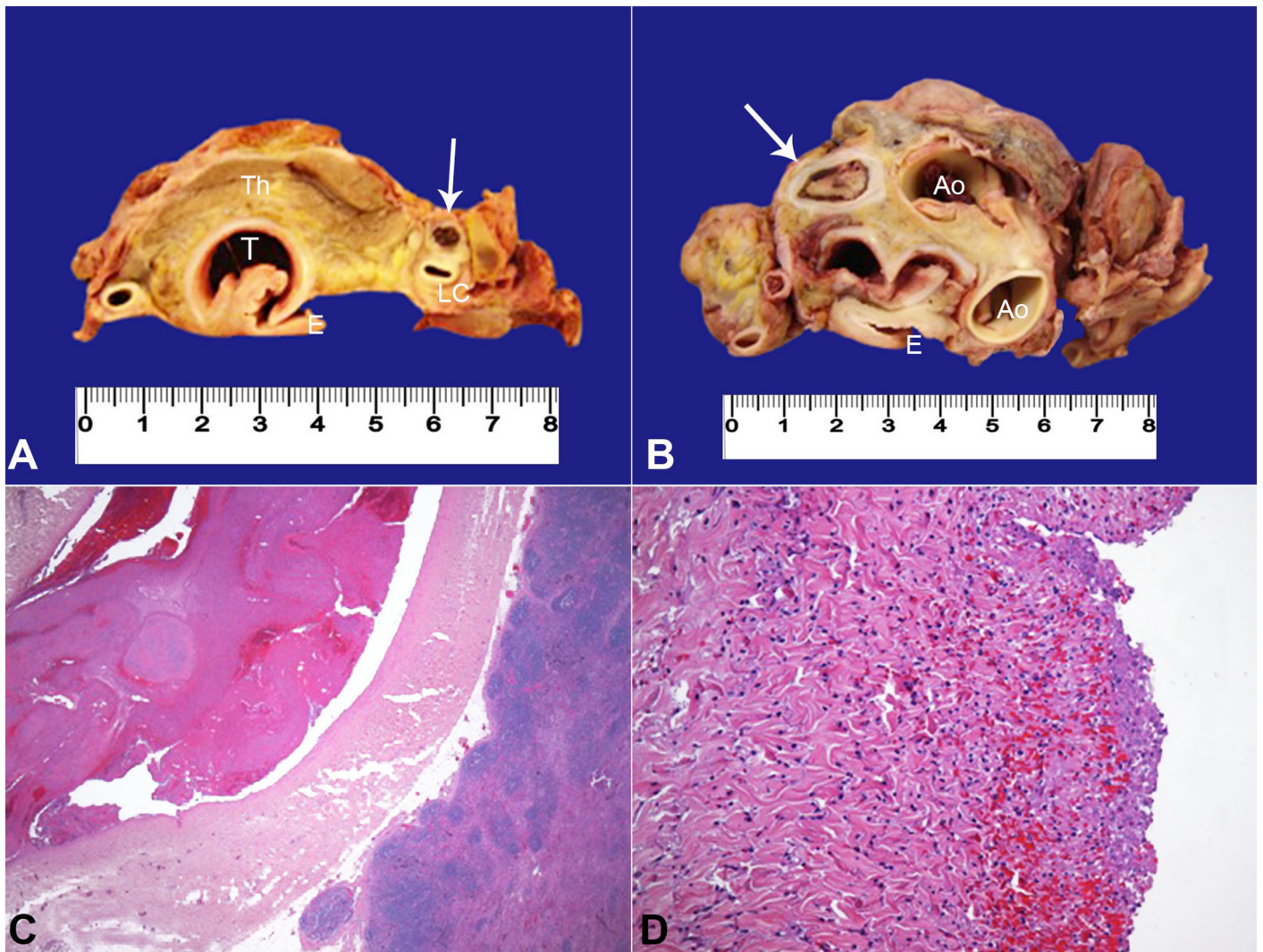


Figure 4. **A** – Gross section showing thrombosis of the left internal jugular vein (arrow); **B** – Gross section showing thrombophlebitis of the superior vena cava (arrow); **C** – Photomicrography of the internal jugular vein showing acute thrombophlebitis (H&E, 25X); **D** – Photomicrography of the internal jugular vein showing acute inflammation with numerous neutrophils and endothelial erosion (H&E, 400X). Ao = aorta; E = esophagus; LC = left internal carotid artery; T = trachea; Th = thyroid gland.

extradural empyema, brain abscess, meningitis, cavernous sinus thrombophlebitis, and sphenoid osteomyelitis, or any combination of these.^{8,10-13}

Subdural empyema is defined as “a collection of pus in the virtual space between the dura mater and the arachnoid membrane”¹⁴, occurring between 1 and 5.8 cases per million inhabitants, accounting for two hospitalizations per year in a tertiary center.^{9,10,12,15} The usual source of infection is by contiguity with paranasal sinuses, mostly the frontal sinus, or with otologic infection. However, a neurosurgical source of infection has been increasingly reported.^{10,11,15-17} Teenagers (mean age between 11 and 15 years old) and males are predominantly afflicted.^{11-13,16-18} Headache, lasting over 1 week, is the most common presenting symptom, but

neurological signs—including altered mental status, seizures, or focal deficits—vomiting, and swelling of the forehead are also common features.^{9,10,12,13,16-18} The GCS was altered in 67% of the admissions.¹⁵ On physical examination, only 38% had normal neurological findings.¹⁷ Fever, rhinorrhea, and nasal obstructions were frequently present, as most of the cases had previous URI symptoms.^{10,12,17} The triad of headache, fever, and altered sensorium was present in 53% of the patients.¹⁵ There was a mean delay of 10 days (range 1-30 days) from the initial symptoms until the diagnosis, and nearly 60% of the patients had previously sought medical attention.^{12,17} The clinical features of our case were typical: a 14-year-old

teenager with a 21-day history of headache, swelling of the maxillary region, and behavioral alterations.

CT is the imaging exam of choice for diagnosing intracranial complications of ABS.^{1,15,19} A laboratory work-up presents the usual findings of any bacterial infection as: (i) elevated C-reactive protein; and (ii) neutrophilia with a shift to the left.¹⁷ Streptococcus spp. are the most common bacteria found in a subdural empyema, especially *Streptococcus milleri*, followed by *Fusobacterium necrophorum*, *Staphylococcus* spp., and anaerobes. Polymicrobial cultures, as well as culture-negative secretions, are also commonly reported.^{9,10,12,13,15,16,18} Intracranial involvement represents the ABS's complication of poorer prognosis, which is usually associated with neurological sequelae (motor deficits, dysphagia, and seizures). Depending on the case series, the mortality ranges from 0% in developed countries to 23% in undeveloped countries.^{8-10,13,15,16} When sinusitis evolves with a persistent headache of a biphasic pattern (localized and then diffuse), altered mental status or focal neurological signs, failure of a former treatment, orbital cellulitis, or persisting fever, a CT scan should be performed to investigate intracranial complications.¹⁰ The treatment of subdural empyema requires broad-spectrum antibiotics—third generation cephalosporin, vancomycin, and metronidazole—and surgery: usually a craniotomy with drainage.^{10,16,17,20,21}

The case presented herein had some peculiarities of challenging interpretation. The history started with apparent toothache, which, unfortunately, remained without a precise diagnosis, but surely required antibiotic therapy. One could suppose that it could be a pulpitis with extension, by contiguity, to the maxillary sinus, which spread to other ipsilateral sinuses, and then to the nervous system by contiguity of the frontal sinus infection. However, the diagnosis of odontogenic sinusitis requires some evidence of dental involvement, such as the history of previous dental procedures, alterations in the examination of the oral cavity, CT scan or magnetic resonance imaging, or autopsy findings diagnosing dental involvement,^{21,22-25} which lacked in this report. Therefore, we cannot be sure that the dental involvement did occur, or if sinusitis was the primary infection since the beginning.

Moreover, the maxillary sinusitis, observed in our case, spread to the neurovascular bundle of the neck causing phlebitis of the ipsilateral internal

jugular vein. These signs resemble those of Lemierre syndrome (LS). This syndrome was first diagnosed by Lemierre²⁶ in 1936 as a local suppuration that evolved with thrombophlebitis and then with multiple septic abscess, mainly in the lung, with *Fusobacterium necrophorum* being the most common involved bacteria.²⁷ The neurological involvement of our case could be due to septic embolization from the infected jugular thrombophlebitis characterizing an atypical LS,²⁸ but the spreading of the sinus infection to the central nervous system by contiguity with bone perforation seems to be more reasonable. However, the mastoid involvement may also be explained by septic embolization. The lack of symptoms of neck pain and the absence of inflammatory signs along the jugular path in the neck do not rule out the LS diagnosis, since similar cases have been reported.²⁹ In our case, septic thrombi were not identified in the autopsy. However, the diffuse pneumonia indeed could be the result of septic embolization from the jugular-vein-infected thrombosis characterizing LS. Intriguingly, *Fusobacterium necrophorum* is one of the most frequent pathogens identified in both subdural empyema and in LS.

The isolation of such pathogens requires special culture media and laboratory techniques, which quite often are responsible for negative results.

Intracranial complications of ABS are uncommon, but if unsuspected they can lead to dangerous consequences with regard to neurological sequelae or death, as exemplified by our case. Any sinusitis with altered neurological findings, biphasic headache, failure of a former treatment, or orbital cellulitis should have a CT done as soon as possible.¹⁰

Unfortunately, the patient reported herein could not be fully treated due to the advanced stage of the disease by the time she came to the hospital.

REFERENCES

1. Chow AW, Benninger MS, Brook I, et al. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis*. 2012;54(8):e72-e112. <http://dx.doi.org/10.1093/cid/cir1043>. PMID:22438350.
2. Zaman K, Baqui AH, Yunus M, et al. Acute respiratory infections in children: a community-based longitudinal study in rural Bangladesh. *J Trop Pediatr*. 1997;43(3):133-

7. <http://dx.doi.org/10.1093/tropej/43.3.133>. PMID:9231631.
3. Chonmaitree T, Revai K, Grady JJ, et al. Viral upper respiratory tract infection and otitis media complication in young children. *Clin Infect Dis*. 2008;46(6):815-23. <http://dx.doi.org/10.1086/528685>. PMID: 18279042.
4. Wald R, Guerra N, Byers C. Upper respiratory children: duration complications. *Pediatrics*. 1991;87(2):129-33. PMID:1987522.
5. Gwaltney JM Jr, Wiesinger BA, Patrie JT. Acute community-acquired bacterial sinusitis: the value of antimicrobial treatment and the natural history. *Clin Infect Dis*. 2004;38(2):227-33. <http://dx.doi.org/10.1086/380641>. PMID:14699455.
6. Marom T, Alvarez-Fernandez PE, Jennings K, Patel JA, McCormick DP, Chonmaitree T. Acute bacterial sinusitis complicating viral upper respiratory tract infection in young children. *Pediatr Infect Dis J*. 2014;33(8):803-8. <http://dx.doi.org/10.1097/INF.0000000000000278>. PMID:24717966.
7. Dankbaar JW, van Bommel AJM, Pameijer FA. Imaging findings of the orbital and intracranial complications of acute bacterial rhinosinusitis. *Insights Imaging*. 2015;6(5):509-18. <http://dx.doi.org/10.1007/s13244-015-0424-y>. PMID:26253983.
8. Chaiyasate S, Fooanant S, Navacharoen N, Roongrotwattanasiri K, Tantilipikorn P, Patumanond J. The complications of sinusitis in a tertiary care hospital: types, patient characteristics, and outcomes. *Int J Otolaryngol*. 2015;1-5. <http://dx.doi.org/10.1155/2015/709302>.
9. Schlemmer KD, Naidoo SK. Complicated sinusitis in a developing country, a retrospective review. *Int J Pediatr Otorhinolaryngol*. 2013;77(7):1174-8. <http://dx.doi.org/10.1016/j.ijporl.2013.04.031>. PMID: 23688379.
10. Bayonne E, Kania R, Tran P, Huy B, Herman P. Intracranial complications of rhinosinusitis. a review, typical imaging data and algorithm of management. *Rhinology*. 2009;47(1):59-65. PMID:19382497.
11. Hakim H El, Malik AC, Aronyk K, Ledi E, Bhargava R. The prevalence of intracranial complications in pediatric frontal sinusitis. *Int J Pediatr Otorhinolaryngol*. 2006;70(8):1383-7. PMID: 16530852.
12. Herrmann BW, Chung JC, Eisenbeis JF, Forsen JW Jr. Intracranial complications of pediatric frontal rhinosinusitis. *Otolaryngol Head Neck Surg*. 2006;20(3):320-5. PMID:16871937.
13. Quraishi H, Zevallos JP. Subdural empyema as a complication of sinusitis in the pediatric population. *Int J Pediatr Otorhinolaryngol*. 2006;70(9):1581-6. <http://dx.doi.org/10.1016/j.ijporl.2006.04.007>. PMID:16777239.
14. Calik M, Iscan A, Abuhandan M, Yetkin I, Bozkuş F, Torun MF. Masked subdural empyema secondary to frontal sinusitis. *Am J Emerg Med*. 2012;30(8):1657.e1-4. <http://dx.doi.org/10.1016/j.ajem.2011.08.003>. PMID: 22030191.
15. French H, Schaefer N, Keijzers G, Barison D, Olson S. Intracranial subdural empyema: a 10-year case series. *Ochsner J*. 2014;14(2):188-94. PMID:24940128.
16. Kombogiorgas D, Seth R, Athwal R, Modha J, Singh J. Suppurative intracranial complications of sinusitis in adolescence. Single institute experience and review of literature. *Br J Neurosurg*. 2007;21(6):603-9. <http://dx.doi.org/10.1080/02688690701552856>. PMID:18071989.
17. Hicks CW, Weber JG, Reid JR, Moodley M. Identifying and managing intracranial complications of sinusitis in children: a retrospective series. *Pediatr Infect Dis J*. 2011;30(3):222-6. <http://dx.doi.org/10.1097/INF.0b013e3181f86398>. PMID:21416657.
18. Skelton R, Maixner W, Isaacs D, Skelton R. Sinusitis-induced subdural. *Arch Dis Child*. 1992;67(12):1478-80.
19. Triulzi F, Zirpoli S. Imaging techniques in the diagnosis and management of rhinosinusitis in children. *Pediatr Allergy Immunol*. 2007;18(Suppl 18):46-9. <http://dx.doi.org/10.1111/j.1399-3038.2007.00633.x>. PMID:17767608.
20. DeMuri GP, Wald ER. Clinical practice. Acute bacterial sinusitis in children. *N Engl J Med*. 2012;367(12):1128-34. PMID:22992076.
21. Derin S, Sahan M, Hazer DB, Sahan L. Subdural empyema and unilateral pansinusitis due to a tooth infection. *BMJ Case Rep*. 2015; pii: bcr2014207666. <http://dx.doi.org/10.1136/bcr-2014-207666>. PMID:26123452.
22. Simuntis R, Kubilius R, Vaitkus S. Odontogenic maxillary sinusitis: a review. *Stomatologija*. 2014;16(2):39-43. PMID:25209225.
23. Martines F, Salvago P, Ferrara S, Mucia M, Gambino A, Sireci F. Parietal subdural empyema as complication of acute odontogenic sinusitis: a case report. *J Med Case Rep*. 2014;8(1):282. <http://dx.doi.org/10.1186/1752-1947-8-282>. PMID:25146384.
24. Kastner J. Orbital and intracranial complications after acute rhinosinusitis. *Neuroimaging Clin N Am*. 2010;20(4):511-26. <http://dx.doi.org/10.1016/j.nic.2010.07.004>.
25. Hoskison E, Daniel M, Rowson JE, Jones NS. Evidence of an increase in the incidence of odontogenic sinusitis over the last decade in the UK. *J Laryngol Otol*. 2012;126(1):43-6. <http://dx.doi.org/10.1017/S0022215111002568>. PMID:21933468.
26. Lemierre A. On certain septicæmias due to anaerobic organisms. *Lancet*. 1936;227(5874):701-3. [http://dx.doi.org/10.1016/S0140-6736\(00\)57035-4](http://dx.doi.org/10.1016/S0140-6736(00)57035-4).

27. Riordan T. Human infection with *Fusobacterium necrophorum* (Necrobacillosis), with a focus on Lemierre's syndrome. *Clin Microbiol Rev.* 2007;20(4):622-59. <http://dx.doi.org/10.1128/CMR.00011-07>. PMID:17934077.
28. Bouziri A, Douira W, Khaldi A, et al. Neurological variant of Lemierre's Syndrome with purulent meningitis: a case report and literature review. *Fetal Pediatr Pathol.* 2013;31(1):1-6. <http://dx.doi.org/10.3109/15513815.2011.618868>. PMID: 22506968.
29. Rahhal H, Campos FPF, Ferreira CR, Felipe-Silva A. Lemierre's syndrome due to intratumoral abscess of the uvula. *Autops Case Rep.* 2015;5(3):11-20. <http://dx.doi.org/10.4322/acr.2015.015>.

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