
Type A Immunoglobulin Deficiency Presenting as a Mixed Polymicrobial Brain Abscess: Case Report

Catherine A. Ruebenacker, M.D., Robert F. Heary, M.D.,
Soly Baredes, M.D.

Divisions of Neurological Surgery (CAR, RFH) and Otolaryngology (SB), University of
Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, New Jersey

OBJECTIVE AND IMPORTANCE: We present a case report of a patient with a left frontal brain abscess. Cultures obtained from the abscess at the time of surgery were identified as dental flora known to establish a synergistic relationship in polymicrobial infections. This type of synergistic relationship makes the clearance of an infection more difficult for an intact immune system. A serum immunoglobulin (Ig) Type A deficiency was identified postoperatively. This immunodeficiency may have contributed to the development of the abscess.

CLINICAL PRESENTATION: The patient presented with headaches and photophobia. Computed tomography of the head performed with intravenously administered contrast demonstrated a left frontal brain abscess.

INTERVENTION: The patient was operated on through a left frontal approach, carefully avoiding the frontal sinus. The abscess was aspirated, and the patient was treated with intravenous antibiotics for several weeks. Postoperatively, the patient did well. There were no signs of enhancement on follow-up computed tomographic scans at 7 and 12 months postoperatively.

CONCLUSION: Through a comprehensive immunological workup, an IgA deficiency was identified postoperatively. Although the deficiency of a single type of Ig may be asymptomatic, complications from recurrent or chronic bacterial infections may occur. The deficiency of IgA, combined with a synergistic polymicrobial infection, contributed to the development of an intracranial abscess. A patient presenting with a brain abscess without any predisposing medical history should be evaluated for an underlying immune deficiency. (*Neurosurgery* 44:411-414, 1999)

Key words: Abscess, Brain, Dysgammaglobulinemia, Immunodeficiency, Immunoglobulin, Phenytoin, Polymicrobial

Advances in the diagnosis and treatment of brain abscesses have successfully reduced the mortality rate to

5 to 20% (8, 15). Most patients have a known predisposing risk factor contributing to intracranial abscess formation

(8). Infections, congenital heart disease, endocarditis, pulmonary abscesses, and skin infections provide sources of direct or indirect infection. The diagnosis of a brain abscess in an apparently immunocompetent young adult with no known risk factors commands a thorough workup.

CASE REPORT

A 27-year-old right-handed Caucasian woman presented with a 1-month history of headaches and photophobia. The patient denied any fever, nausea, emesis, weakness, paresthesias, or change in coordination. She did not notice any changes in vision, hearing, or speech. There was no history of seizure. There was no history of recent dental work, although the patient had chronic poor dentition. The patient had last seen a dentist 6 months before presentation for acute odontalgia. Her medications at the time of presentation included oral cefuroxime and a beclomethasone inhaler, which had been prescribed for the treatment of acute rhinitis. Her medical and surgical histories were unremarkable. The patient smoked one pack of cigarettes per day. She denied any drug or alcohol abuse. She had been recently married and denied any other recent sexual contacts. The patient initially presented to another institution and was transferred to our service for further management.

A physical examination revealed that the patient was a thin Caucasian woman who was slightly lethargic but was easily aroused by both voice and physical stimuli. She was afebrile with normal vital signs. Her neurological examination demonstrated a normal mental status. Comprehension and thought processes were intact. No cranial nerve deficits were present. There was no motor

weakness and no pronator drift. The results of a sensory examination were normal. Deep tendon reflexes were brisk and symmetric. Toes were downgoing bilaterally. The remaining results of her physical examination were unremarkable except for bifrontal sinus tenderness.

Laboratory tests conducted at the time of admission revealed a white blood cell count of 23,300 cells/ml (normal = 4,500-11,000 cells/ml). An erythrocyte sedimentation rate (ESR) was 59 mm per hour (normal = 0-20 mm/h). The remaining results of the patient's admission profile tests were within normal limits.

Computed tomography (CT) performed with and without intravenously administered contrast medium showed a large ring-enhancing lesion of the left frontal lobe. There was a hypodense region within the abscess cavity consistent with gas. Significant perilesional vasogenic edema with midline shift was noted. Significant sinusitis of the frontal and maxillary air sinuses was present (Fig. 1).

Intravenous administration of antibiotics, steroids, and phenytoin was initiated. The patient was taken to surgery for a combined neurosurgical and otolaryngological procedure. A left frontal craniotomy was performed, with care taken to avoid the left paranasal frontal



FIGURE 1. Axial computed tomographic scan enhanced with intravenously administered contrast medium. A ring-enhancing lesion in the left frontal lobe has significant mass effect. A left-to-right shift of midline is appreciated. Note the fluid level and evidence of gas formation from within the abscess.

air sinus. The posterior wall of the frontal sinus was avoided because it was demonstrated to be intact on preoperative computed tomographic scans with fine cuts on the bone window settings. The abscess was accessed through a small craniotomy, at a depth of 1 cm. An incision of the capsule was made. Immediately, samples of green, foul smelling, purulent exudate were obtained and were sent for gram stain, aerobic and anaerobic culture, sensitivity testing, and fungal and mycobacterial stains and cultures. The purulent exudate was suctioned from within the capsule. An intraoperative gram stain revealed many gram-positive cocci in chains as well as many gram-negative rods. The abscess cavity was gently dissected free from the surrounding brain parenchyma. There was no attempt made to free any adherent capsule from the perilesional edematous brain tissue. The abscess cavity was then copiously irrigated with a bacitracin and vancomycin solution. Closure of the craniotomy was accomplished cosmetically, using miniplates (Leibinger Corporation, Dallas, TX).

Immediately after the craniotomy, through a separate skin incision below the left eyebrow, a left frontal trephination with bilateral endoscopic anterior ethmoidectomies and maxillary antrostomies was performed. Purulent fluid was obtained and was sent for gram stain and cultures. Postoperatively, the patient was transferred to the Neurosurgical Intensive Care Unit.

Cultures of the intracranial abscess grew *Pseudomonas buccae*, *Streptococcus milleri* viridans group, *Wolinella* species, and *Bacteroides thetaiotamicron*. Cultures sent from samples taken from both the frontal and maxillary sinuses were also positive for these same bacteria. The patient was treated with metronidazole, ceftriaxone, and nafcillin. When the final sensitivity results were obtained, nafcillin was discontinued and administration of high-dose penicillin was instituted. An intravenous access catheter for long-term antibiotic therapy was placed 6 days later.

Postoperatively, the patient did well. She had transient nausea, and her headache steadily decreased in severity. She was transferred from the Neurosurgical Intensive Care Unit on the 4th postop-

erative day and was discharged to home on the 7th postoperative day. Long-term intravenous antibiotic therapy was administered at her home with penicillin, ceftriaxone, and metronidazole.

A detailed immunological workup was instituted. Lymphocyte subset studies, complement analyses, and immunoglobulin (Ig) electrophoresis were performed. The immunological testing revealed an isolated deficiency of IgA.

The patient received intravenous antibiotics at home for 16 weeks. Her antibiotics were continued until follow-up CT with intravenously administered contrast medium demonstrated resolution of the abscess. The patient underwent monthly CT, with and without intravenously administered contrast medium, for the first 6 months postoperatively. At her 1-year follow-up evaluation, laboratory tests revealed a white blood cell count of 4.5 K cells/ml and an ESR of 3 mm per hour. Follow-up CT demonstrated resolution of the abscess, with no signs of contrast enhancement. Phenytoin was discontinued at 3 months postoperatively because of the patient's complaints of persistent lethargy. At 12 months postoperatively, the patient experienced a generalized seizure. The patient was then treated with carbamazepine. At 30 months postoperatively, the patient was asymptomatic. At the time of this writing, the patient had not received any antibiotic therapy for 26 months. A physical examination revealed that she was neurologically intact. Her serum IgA level remained abnormally low at less than 13 mg/dl (normal = 81-463 mg/dl). At the time of this writing, she had not received phenytoin for more than 2 years.

DISCUSSION

Brain abscesses are associated with significant morbidity and mortality. Intracerebral abscesses, which develop in young adults, are commonly associated with predisposing factors, such as otolaryngological infections, congenital or infectious cardiac disease, upper or lower respiratory tract infections, meningitis, osteomyelitis, previous neurosurgery, or skin infections (15, 22). Infections of the paranasal sinuses account for 1.6% of brain abscesses (22). Colonization of these sinuses with aerobic and anaerobic bacte-

ria may be limited to a single sinus or may present as a pansinusitis. Most cases of sinusitis are managed without complication. Complications are associated with untreated or inadequately treated sinusitis. Orbital complications are frequently encountered because of the proximity to the paranasal sinuses. Mucocele and osteomyelitis may also be associated with complicated sinusitis (19). Intracranial complications, such as cavernous sinus thrombosis, meningitis, epidural or subdural abscesses, venous sinus thrombosis, and brain abscess, may also occur as complications of paranasal sinus infections (17). These complications may represent intracranial extension from either direct or indirect spread.

Sinogenic intracranial abscesses are commonly localized to the frontal lobes. If an abscess develops in an area of noneloquent brain tissue, the abscess may remain clinically silent for an extended period of time (17). When symptomatic from an intracranial abscess, the patient often presents with generalized complaints of headache and fever. The patient presenting with a coexistent sinusitis may not have even noticed symptoms relating to the sinus infection. There have been cases in which the workup of a brain abscess led to the diagnosis of sinusitis (4).

Microorganisms commonly cultured from paranasal sinus mucosa include *Streptococci* species and *Staphylococcus aureus*. Because of the fastidiousness of some bacteria and suboptimal culture techniques, up to 20% of cultures are reported as negative (5). The patient in this case report represents the first reported case of isolation and identification of the combination of *Prevotella buccae*, *Bacteroides thetaiotamicron*, *Wolinella* species, and *Streptococcus milleri* from a brain abscess. *Prevotella buccae*, an obligate anaerobic, gram-negative rod bacteria, is commonly associated with purulent infections in the oropharynx (7). Usually dependent on a polymicrobial infection to provide a low-oxygen environment, *Prevotella* species establish a synergistic relationship with the *Streptococcus milleri* group bacteria (16). *Prevotella* species inhibit the bacteriocidal activity of human neutrophils, which hinders the clearance of the *Streptococci milleri* infection. They are both encapsulated bacteria. *Wolinella* species are

oral nonpathogenic bacteria that are easily cleared by a competent immune system unless found in a deep-seated polymicrobial infection (11). *Bacteroides* species are commonly encountered in both oral and sinogenic infections.

A comprehensive immunological workup showed an isolated deficiency in IgA. Low serum IgA can represent a primary or a secondary immunological deficiency. A primary IgA immunodeficiency would contribute to both local and systemic symptoms of immune dysfunction. IgA deficiency, coupled with both a sinus infection and poor dentition, created a perfect milieu for the development of an intracerebral brain abscess. Patients with isolated IgA deficiency are at an increased risk of developing upper respiratory tract infections (4, 12, 13). Often, these infections present with increased frequency, severity, prolonged duration, and unexpected complications (4). The use of inhaled corticosteroids may also have contributed to local, mucosal immunosuppression in our patient. The use of inhaled steroids has been shown to reduce mucosal inflammation but also may have local immunosuppressive side effects (10).

Secondary IgA depression can occur with the use of certain medications. Phenytoin has been associated with IgA depression, low IgM levels, imbalances of IgG subclasses, and both B- and T-cell dysfunction. Comparative studies have not found a significant difference in the incidence of severely depressed IgA levels in patients treated with phenytoin (2). In patients who developed low IgA levels in response to phenytoin, there was no evidence of recurrent upper respiratory infection.

In IgA deficiency, there is an absence of mature IgA-producing B cells (13). IgA deficiency is the most common dysgammaglobulinemia, known to affect 1 in 700 Caucasians (12). Patients with isolated IgA deficiency are clearly susceptible to recurrent infections, especially when caused by encapsulated bacteria (4, 12, 13). Normal cellular immunity and IgG responses are present (14). A genetic defect in the transcription or translation of the alpha chains of IgA is thought to be the cause of primary IgA deficiency (20).

Patients with signs and symptoms of brain abscess are evaluated using CT of

the brain, with and without intravenously administered contrast medium. The sensitivity of CT for the detection of brain abscesses approaches 100% (21). Follow-up CT with intravenously administered contrast medium and serial white blood cell counts provide accurate assessment of the regression or progression of infection. ESRs are also helpful. Our patient had an initial ESR of 59 mm per hour, which decreased to 10 mm per hour in only 6 weeks after surgery.

Treatment modalities include both surgical and nonsurgical approaches (1, 3, 6). In cases of multiple small abscesses, conservative management with intravenous antibiotics may be warranted. Surgical techniques involve percutaneous or stereotactic drainage of the abscess as well as standard open craniotomy to remove the abscess. Closure of the craniotomy with metal miniplates can be controversial in the face of a contaminated wound. Studies involving the placement of rigid instrumentation into infected mandibular fractures have demonstrated that bony union can occur along with the successful clearance of infection (9). Microplating provided cosmetically satisfying results to the patient in our case and was not associated with any postoperative complications.

Long-term antibiotic therapy is required in the treatment of brain abscesses (8, 15, 19, 22). Often, multidrug regimens are used to ensure adequate coverage or to adequately treat polymicrobial infections, as was the circumstance in our case. The combination of a second or third generation cephalosporin and metronidazole provides good coverage (18). Intravenous antibiotic therapy at home is feasible and appealing to the patient.

CONCLUSION

Cerebral abscess in a patient with no identifiable comorbidity requires aggressive treatment and an evaluation of the immunological profile. Primary Ig deficiencies of the IgA type are the most common dysgammaglobulinemias present in Caucasian populations. Often, asymptomatic IgA deficiencies may not be diagnosed unless the patient develops symptoms of chronic or recurrent infection. Patients with IgA deficiency are predisposed to developing complications from

bacterial infection. Polymicrobial abscesses may be found in cases in which synergistic bacterial infections exist. These abscesses are especially difficult to eradicate. A patient presenting with a brain abscess should receive an immunological workup, especially when there are no other identifiable risk factors.

Received, February 20, 1998.

Accepted, October 1, 1998.

Reprint requests: Robert F. Heary, M.D., Division of Neurological Surgery, University of Medicine and Dentistry of New Jersey, New Jersey Medical School, 90 Bergen Street, Doctor's Office Complex, Suite 7300, Newark, New Jersey 07103-2499.

REFERENCES

- Alderson D, Strong AJ, Ingham HR, Selkon J: Fifteen-year review of the mortality of brain abscess. *Neurosurgery* 8:1-6, 1981.
- Burks AW, Charlton R, Casey P, Poindexter A, Steele R: Immune function in patients treated with phenytoin. *J Child Neurol* 4:25-29, 1989.
- Chun CH, Johnson JD, Hofstetter M, Raff MJ: Brain abscess: A study of 45 consecutive cases. *Medicine* 65:415-431, 1986.
- Dahlen G, Bjorkander J, Gahnberg I, Slots J, Hansson LA: Periodontal disease and dental caries in relation to primary IgG subclass and other humoral immunodeficiencies. *J Clin Periodontol* 20:7-13, 1993.
- Dolan RW, Chowdhury K: Diagnosis and treatment of intracranial complications of paranasal sinus infections. *J Oral Maxillofac Surg* 53:1080-1087, 1995.
- Garvey G: Current concepts of bacterial infections of the central nervous system. *J Neurosurg* 59:735-744, 1986.
- Gomes BP, Drucker DB, Lilley JD: Associations of specific bacteria with some endodontic signs and symptoms. *Int Endod J* 27:291-298, 1994.
- Kaplan K: Brain abscess. *Med Clin North Am* 69:345-360, 1985.
- Koury M, Ellis E III: Rigid internal fixation for the treatment of infected mandibular fractures. *J Oral Maxillofac Surg* 50:434-443, 1992.
- Kumar A, Busse WW: Clinical aspects of anti-inflammatory therapy in asthma. *Curr Opin Pulm Med* 2:40-47, 1996.
- Lai CH, Oshima K, Slots J, Listgarten MA: *Wolinella recta* in adult gingivitis and periodontitis. *J Periodontol Res* 27:8-14, 1992.
- Roitt I, Brostoff J, Male D: Immunodeficiency, in *Immunology*. London, Mosby, 1996, ed 4, pp 21.1-21.4.
- Sell S: Immune deficiency diseases, in *Immunopathology, Immunology, and Immunity*. New York, Elsevier, 1987, ed 4, pp 617-650.
- Sethi DS, Winkelstein JA, Lederman H, Loury MC: Immunologic defects in patients with chronic recurrent sinusitis: Diagnosis and management. *Otolaryngol Head Neck Surg* 13:242-247, 1995.
- Seydoux C, Francioli P: Bacterial brain abscesses: Factors influencing mortality and sequelae. *Clin Infect Dis* 15:394-401, 1992.
- Shirayato T, Saito A: A mechanism of pathogenicity of *Streptococcus milleri* group in pulmonary infection: Synergy with an aerobic. *J Med Microbiol* 40:118-123, 1994.
- Singh B, Van Dellen J, Ramjetan S, Maharaj TJ: Sinusogenic intracranial complications. *J Laryngol Otol* 109:945-950, 1995.
- Sjolin J, Liija A, Eriksson N, Arneborn P, Cars O: Treatment of brain abscess with cefotaxime and metronidazole: Prospective study on 15 consecutive patients. *Clin Infect Dis* 17:857-863, 1993.
- Stankiewicz JA, Newell DJ, Park AH: Complications of inflammatory diseases of the sinuses. *Otolaryngol Clin North Am* 26:639-653, 1993.
- Truedsson L, Baskin B, Pan Q, Rabbani H, Vorechovsky I, Smith CI, Hammarstrom L: Genetics of IgA deficiency. *APMIS* 103:833-842, 1995.
- Yang SY: Brain abscess: A review of 400 cases. *J Neurosurg* 55:794-799, 1981.
- Yen PT, Chan ST, Huang TS: Brain abscess: With special reference to otolaryngologic sources of infection. *Otolaryngol Head Neck Surg* 113:15-22, 1995.

COMMENTS

The authors report an interesting finding of chronically depressed levels of immunoglobulin IgA in a patient with sinusitis and brain abscess. As a result of this finding, it is recommended that patients without risk factors for the development of brain abscess should be evaluated for immunodeficiencies. The discussion is relevant and informative. Two issues require comment. This pa-

tient had a significant sinusitis, which by most accounts would constitute a major predisposing factor even if computed tomography did not discover the communication. It is to their credit that the authors looked so carefully for a communication because I am not certain that this investigation would generally be undertaken. In addition, although the workup disclosed the IgA deficiency, it is not readily apparent that this deficiency was an underlying factor in the development of the brain abscess; deficiencies of IgA have been noted in association with many chronic and recurrent infections, and it is not clear whether this occurrence may be causal or epiphenomenal. Nevertheless, the author's main recommendation to immunologically evaluate patients with brain abscesses in whom no predisposing factors are apparent is well taken and worthy of note.

Jack P. Rock
Detroit, Michigan

Ruebenacker et al. present a patient with a brain abscess caused by a polymicrobial infection of normally nonpathogenic organisms because of an inadequately treated sinus infection and a previously undiagnosed IgA deficiency. It is interesting to note that this deficiency is the most common of the dysgammaglobulinemias and that it is known to affect 1 in 700 Caucasians. I add that cigarette smoking was probably another risk factor in this patient, certainly contributing to the presence of the sinusitis. This is an excellent case report that well summarizes the contemporary management of brain abscesses caused by unusual organisms.

Michael Salzman
Baltimore, Maryland