INTRACRANIAL VENOUS THROMBOSIS IN A PATIENT WITH MULTIPLE SCLEROSIS

A Case Report and Review of Contraceptive Alternatives in Patients with Disabilities[1]

Gerard A. Malanga,[2] MD and Edwin Gangemi, MD

ABSTRACT **Malanga GA, Gangemi E: Intracranial venous thrombosis in a patient with multiple sclerosis: a case report and review of contraceptive alternatives in patients with disabilities. *Am J Phys Med Rehabil* 1994;73:283–285**

Intracranial thrombosis is a rare complication of oral contraceptive use. A case is presented of a 35-yr-old woman with multiple sclerosis who took oral contraceptives and, subsequently, experienced intracranial transverse and sigmoid sinus thromboses and, later, deep venous thrombosis of the calf. A review of the relationship between oral contraceptives and venous thrombosis is presented. In addition, the diagnostic work-up and treatment options for intracranial venous thrombosis are discussed, and appropriate birth control alternatives for disabled patients, that is, diaphragm, sponges, condoms and levonorgestrel, are reviewed.

KEY WORDS: Intracranial Thrombosis, Oral Contraceptives, Multiple Sclerosis, Deep Venous Thrombosis

It is important for physiatrists to be aware of the complications of oral contraceptive use and provide appropriate birth control counseling to female patients who have disabilities. First documented in the early 1900s, intracranial thrombosis has been found to occur as a result of trauma, infection and hypercoagulable states. In young females, its occurrence is associated with pregnancy and the use of oral contraceptives,[1] which have both been implicated in an increased occurrence of deep venous thrombosis. Physiatrists should be aware of these complications when caring for female patients with disabilities that result in decreased mobility or a hypercoagulable state.

CASE REPORT

A 35-yr-old, right-handed white woman, gravida II, para II, with a history of multiple sclerosis for 3 yr, was in her usual state of health, independent in all activities of daily living (ADLs), when her husband noticed the sudden onset of lateral deviation of her left eye. After an evaluation by her physician, prednisone, 90 mg/day, was prescribed. In the ensuing 10 days, the patient's symptoms escalated, with increased weakness in all four extremities. Eventually, the patient became nonambulatory, and she was seen at the local hospital emergency room unconscious and with generalized seizures. She was treated with intravenous diazepam (Valium) and phenytoin (Dilantin) and had no further seizure activity. An emergency computed tomography scan revealed infarcts in the right parietal lobe deep within the white matter and possible small, punctate hemorrhages in the right occipital lobe. Magnetic resonance imaging (MRI) of the head revealed multiple high-signal areas in the centrum semiovale and thrombosis of the right transverse and sigmoid sinuses with associated cortical vein infarction. The patient had been taking oral contraceptives for birth control for approximately 8 yr. She denied a history of cigarette smoking.

The patient was transferred to a tertiary-care hospital approximately 1 wk after this episode. Upon physical examination, her vital signs were normal and she was awake, alert and oriented as to person, time and place. She had an apathetic appearance. Head and neck examination revealed no nystagmus, and a normal funduscopic examination revealed no papilledema and visual acuity of 20/20 bilaterally. She had full range of motion of her cervical spine and no rigidity. The musculoskeletal examination demonstrated increased tone, with 4/5 muscle strength in both upper extremities, 3/5 strength in the right lower extremity and 4/5 strength in the left lower extremity. Active and passive range of motion were normal in all four extremities. Neurologic examination revealed hyperactive reflexes throughout the upper and lower extremities but no clonus. Toes were down-going bilaterally on Babinski examination. Sensory exam-

0894-9115/94/7304-0283$03.00/0
AMERICAN JOURNAL OF PHYSICAL MEDICINE & REHABILITATION
Copyright © 1994 by Williams & Wilkins

[1] From the University of Medicine and Dentistry of New Jersey, Newark, New Jersey and the Kessler Institute of Rehabilitation, West Orange, New Jersey

[2] All correspondence and requests for reprints should be addressed to: Mayo Clinic, 200 First Street SW, Rochester, MN 55905.

ination was normal, with the exception of a mildly decreased vibratory sensation in the distal lower extremities. Cerebellar testing demonstrated significant dysmetria in the upper and lower extremities, with difficulty in fine motor movements of her hands and digits bilaterally. Cranial nerves II–XII were intact, except for a decreased gag reflex bilaterally. Functionally, she required maximal assistance for all transfers and ADLs and was nonambulatory.

During her hospital course, she experienced visual hallucinations, which were attributed to phenytoin toxicity. The phenytoin was tapered, and the hallucinations ceased. An MRI angiogram confirmed the diagnosis of thromboses in both the sigmoid and the transverse sinuses. Laboratory work-up consisted of serum chemistries, complete blood cell count with differential, prothrombin time, partial thromboplastin time and erythrocyte sedimentation rate. All were normal. Serum protein electrophoresis revealed an increase in total immunoglobulin. Laboratory evaluation for systemic lupus erythematosus was negative. A lumbar puncture showed an increase in total protein with a normal cell count. The prednisone dose was tapered, but the patient did not receive anticoagulant therapy.

One month after admission, the patient was transferred to our rehabilitation hospital. Upon admission, she was febrile and had a sinus tachycardia of 136 beats/min, a blood pressure of 102/80 mm Hg, and a respiratory rate of 16/min. Upon physical examination, she was found to have a swollen left calf and suprapubic tenderness. A urine culture revealed a urinary tract infection. Deep venous thrombosis of her left calf was confirmed by impedance plethysmography. She was transferred to an acute-care hospital, where she was treated with antibiotics and anticoagulation therapy.

Two weeks later, the patient was transferred back to our rehabilitation hospital for resumption of therapy. She underwent a 5-wk course of physical therapy and was dismissed, ambulatory, with a walker with distant supervision for 100–200 feet. She was independent in all ADLs except transfers, which required distant supervision. The patient was dismissed to her home with her husband and two children, and she has continued to improve with physical therapy on an outpatient basis.

DISCUSSION

Although the relationship between oral contraceptives and peripheral venous thrombosis has been well documented, there is limited literature on oral contraceptives as a cause of cranial thrombosis.[2–4] Hypercoagulable states appear to be more common in women who are taking oral contraceptives and during pregnancy or peripartum states.[5] Hypercoagulability has been associated with such disease states as disseminated intravascular coagulation, systemic lupus erythematosus, migratory thrombophlebitis (Trousseau's syndrome), nonbacterial thrombotic endocarditis, congestive heart failure, diabetes and sickle cell disease.[6, 7] Other associated causes are tuberculosis, leukemia, malnutrition and regional enteritis.

In 1967, 1 in 63 patients was found to have cerebral venous thrombosis caused by the use of oral contraceptives.[6] That study concluded that functional impairment depended upon the location and extension of the venous thrombosis and the rate of its development. Symptoms cited by Krayenbuhl[8] include unilateral headaches, vomiting, convulsions, hemiplegia and various changes in mental status. Further work-up after diagnosis may consist of electroencephalogram and lumbar puncture. A lumbar puncture may demonstrate xanthochromia and a total increase in protein, along with elevated cerebrospinal fluid pressure. Until the advent of MRI, which offers a noninvasive diagnostic approach, cerebral angiography was the gold standard for the diagnosis of this disease. In some institutions, these tests are now combined to increase the diagnostic accuracy of each. Computed tomography scan and radionuclide scanning have also been the diagnostic tests of choice in certain institutions; however, these have been replaced by MRI techniques.

Histopathologically, pregnancy or the use of oral contraceptives causes a decrease in vessel elasticity, loss of venous tone and endothelial proliferation with fibrosis and hyperplasia of vessel walls.[6] In the cerebral vascular system, these findings are most prominent in the superior sagittal sinus, which is the most commonly affected drainage area involved in hypercoagulable states.

Treatment options are somewhat limited. Medical management includes hydration, administration of mannitol and serial lumbar punctures to control intracranial pressure. Seizures are treated with routine anticonvulsants, and prophylaxis is a common practice. Heparin has been used in some centers and has been shown to reduce extension of the thrombosis, but its use remains controversial. Fibrinolytics have been shown to be effective but are not widely used. Infection-related clots should be treated vigorously with intravenous antibiotics. Surgical management carries with it a high mortality, probably as a result of difficulty in clot retrieval from common deep locations and of secondary infections that increase morbidity. When surgery is performed, thrombectomy is the procedure of choice. Krayenbuhl[8] concluded that surgery might be indicated for drainage of large cerebral hemorrhages and abscesses and for the relief of increased intracranial pressure.

Deep venous thrombosis is a much more common occurrence in patients with disabilities. Although there is little information on the incidence of deep venous thrombosis in patients with multiple sclerosis, there is literature on patients who have

other causes of lower extremity weakness. In spinal cord-injured patients with paraplegia, the incidence ranges from 14% to 40%,[9, 10] based upon clinical examination, and up to 100% if patients are screened with ^{125}I-labeled fibrinogen scan.[11] The thrombosis occurs primarily within the first 3 mo after injury. Myllynen et al.[12] found that deep venous thrombosis in patients with spinal fractures was primarily related to paralysis rather than to immobilization. Patients who have had a cerebrovascular accident have an incidence of lower extremity venous thrombosis of 30–53%. The incidence is 5 times more frequent in nonambulatory patients and 10 times more frequent on the paretic extremity.[13]

Oral contraceptive use has been associated with increased risk of deep venous thrombosis, especially in women over the age of 35 yr and in smokers. Helmrich et al.[14] found an age-adjusted relative risk of 8.1 times when comparing recent users with "never-users." No information is available on the risk of deep venous thrombosis in patients with lower extremity paraparesis or paraplegia who are also using oral contraceptives.

Because multiple sclerosis does not affect fertility, sexual counseling for women must include discussion of birth control with both the physiatrist and the gynecologist. To date, no research is available on methods of birth control that are appropriate for women with multiple sclerosis and decreased mobility. Use of oral contraceptive preparations should be discouraged in patients with decreased mobility, because of the increased incidence of deep venous thrombosis in these patients. Diaphragms and contraceptive sponges are reasonable alternatives to oral contraceptives but may be difficult to manipulate in patients with concomitant spasticity. Intrauterine devices may be contraindicated in patients who lack sensation, because migration of these devices may go unnoticed. Condoms appear to be the safest means of preventing pregnancy in patients with multiple sclerosis. In the future, contraceptive implants may prove to be a convenient and safe alternative for women with multiple sclerosis who seek birth control.[15] Levonorgestrel implants have undergone large clinical trials and have not shown any increased risk for cerebrovascular accidents or deep vein thrombosis.

CONCLUSIONS

This case of intracranial thrombosis caused by oral contraceptive use is of importance to the physiatrist. Although cranial thromboses are rare complications of oral contraceptive use, deep venous thromboses are not uncommon, especially in patients with decreased mobility. Our patient also had a lower-extremity deep venous thrombosis in addition to cranial thrombosis. This lower-extremity lesion was most likely because of diminished mobility and prolonged bed rest, although an underlying hypercoagulable state may have been a contributing factor. Multiple sclerosis has not been associated with hypercoagulable states, and this patient is the first reported case of cranial thrombosis in a patient with multiple sclerosis. For physiatrists caring for women with disabilities it is important to be aware of these complications and discuss alternative methods of birth control with the patients and their gynecologists.

ACKNOWLEDGMENTS

We thank Aynsley Smith and Edward Laskowski, M.D., for assistance in the preparation of this article.

REFERENCES

1. Buchanan DS, Brazinsky JH: Dural sinus and cerebral venous thrombosis: incidence in young women receiving oral contraceptives. *Arch Neurol* 1970;22:440–444.

2. Gettelfinger DM, Kokmen E: Superior sagittal sinus thrombosis. *Arch Neurol* 1977;34:2–6.

3. Scott EB: Intracerebral thrombosis: case report and brief clinical review. *Am J Phys Med Rehabil* 1992;71:119–121.

4. Shende MC, Lourie H: Sagittal sinus thrombosis related to oral contraceptives: case report. *J Neurosurg* 1970;33:714–717.

5. Poltera AA: The pathology of intracranial venous thrombosis in oral contraception. *J Pathol* 1972;106:209–219.

6. Imai WK, Everhart FR Jr, Sanders JM Jr: Cerebral venous sinus thrombosis: report of a case and review of the literature. *Pediatrics* 1982;70:965–970.

7. Bitran JD, Ultmann JE: The paraneoplastic syndromes, in Kelley WN, DeVita VT Jr, DuPont HL, Harris ED Jr, Hazzard WR, Holmes EW, Hudson LD, Humes HD, Paty DW, Watanabe AM, Yamada T (eds): *Textbook of Internal Medicine*. Philadelphia, JB Lippincott Company, 1989, p 1355.

8. Krayenbuhl HA: Cerebral venous and sinus thrombosis. *Clin Neurosurg* 1967;14:1–24.

9. Walsh JJ, Tribe CR: Phlebo-thrombosis and pulmonary embolism in paraplegia. *Int J Paraplegia* 1965;3:209–213.

10. Van Hove E: Prevention of thrombophlebitis in spinal injury patients. *Paraplegia* 1978/1979;16:332–335.

11. Todd JW, Frisbie JH, Rossier AB: Deep venous thrombosis in acute spinal cord injury: a comparison of ^{125}I fibrinogen leg scanning, impedance plethysmography and venography. *Paraplegia* 1976;14:50–55.

12. Myllynen P, Kammonen M, Rokkanen P, Böstman O, Lalla M, Laasonen E: Deep venous thrombosis and pulmonary embolism in patients with acute spinal cord injury: a comparison with nonparalyzed patients immobilized due to spinal fractures. *J Trauma* 1985;25:541–543.

13. Garrison SJ, Rolak LA: Rehabilitation of the stroke patient, in DeLisa JA, Gans BM (eds): *Rehabilitation Medicine: Principles and Practice*, ed. 2. Philadelphia, JB Lippincott Company, 1993, pp 801–824.

14. Helmrich SP, Rosenberg L, Kaufman DW, Strom B, Shapiro S: Venous thromboembolism in relation to oral contraceptive use. *Obstet Gynecol* 1987;69:91–95.

15. Sipski ML: The impact of spinal cord injury on female sexuality, menstruation and pregnancy: a review of the literature. *J Am Paraplegia Soc* 1991;14:122–126.