Spinal Epidural Hematoma during Anticoagulant Therapy

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Spinal epidural hematoma complicated the course of anticoagulant therapy of cerebrovascular disease in a patient in whom observations of multiple aspects of coagulation had been obtained. Examination of this case and a review of the literature allow delineation of a syndrome that should aid in early diagnosis of spinal epidural hematoma. It is clear that coumarin derivatives induce multiple coagulation defects, which vary quantitatively and qualitatively with time. Contemporary evaluation of the benefits and risks of long-term anticoagulants is beset by many problems that have not been fully resolved.

Spinal epidural hematoma in the absence of trauma or malformation of spinal vessels is an exceedingly rare disorder. However, in recent years, at least 3, and possibly 4, instances have been reported as complications of anticoagulant therapy.1-4

The purposes of this paper are 4-fold: (1) to report an additional occurrence of spinal epidural hematoma in a patient on long-term anticoagulant therapy for cerebral vascular disease; (2) to delineate a syndrome that should aid in the prompt recognition of spinal epidural hematoma when it is still amenable to therapy; (3) to consider the coagulation defects induced by a coumarin derivative; and (4) to discuss the problem of evaluation of the benefits and risks of anticoagulants in cerebral vascular disease.

Case Report

A 70-year-old woman was admitted to the Beth Israel Hospital in May 1954 because of the sudden onset of nausea, vomiting, and vertigo. A right lateral medullary tegmental syndrome evolved, as evidenced by crossed dissociated hypalgesia involving the right face and the left side of the body, rhythmic ataxia of the right upper extremity, and a right Horner’s syndrome. The vertigo gradually subsided but the other neurologic abnormalities persisted. Additional findings included mild diabetes mellitus and labile hypertension.

In September 1956, the patient experienced a transient episode of confusion, slurred speech, right facial weakness, and urinary incontinence.

In the following week she developed lethargy, anorexia, defective memory, and blurred vision. Physical examination revealed the neurologic residuals of the previous illness but no new abnormalities. The cerebral spinal fluid was normal. An electroencephalogram was diffusely abnormal. Routine hemogram, urinalysis, blood nonprotein nitrogen, and 1-hour postprandial blood sugar were normal. Chest roentgenogram revealed a large left pulmonary artery; the left ventricle and thoracic aorta were dilated.

Three weeks later nausea, irritability, and visual hallucinosis appeared. Neurologic examination at this time disclosed a relative left superior quadrantanopia. The tendon reflexes had become increased on the right and a left extensor plantar response was present. Over the next week she recovered from her confusion, ophthalmic palsy, and visual field defect.

Dicumarol was thereupon administered by mouth (fig. 1). A rapid fall in prothrombin activity was obtained as measured by a modified Quick 1-stage prothrombin method.5 Beginning with the third week determinations6 of proconvertin activity,6 and prothrombin (Owren method)7 were obtained at intervals of 1 to 2 weeks for the following 7 months. In the last 6 months of this period prothrombin activity by the Quick 1-stage method ranged from 8 to 15 per cent of normal (20 to 30 seconds). Proconvertin was reduced to approximately the same percentage levels and correlated well with the prothrombin activity found by the Quick method. However, the prothrombin levels were for months much less depressed, but gradually fell to the 10 per cent level. In the last 4 months of therapy only a Quick prothrombin time was obtained and this was done in a different laboratory. The patient received 25 mg. of Dicumarol daily during the last 8 months of ther-

*Kindly performed by Miss Angelina DiFrancesco, technician in the laboratory of Dr. Benjamin Alexander, Beth Israel Hospital.
apy. Her clinical state remained stable through this interval.

On September 28, 1957, she arose to void and defecate. While returning to bed she experienced sudden severe pain between her shoulder blades. Six hours later she was unable to move her legs and was incontinent of urine. Thirty hours after the onset of the pain she was readmitted to the hospital. Examination now revealed drowsiness, moderate ataxia of the right upper extremity, and a right Horner's syndrome, but no other neurologic abnormality above the costal margin. The thoracic spine was tender between the sixth and eleventh vertebrae, maximally at the eighth. There was flaccid paralysis of both lower extremities. The tendon reflexes were absent. The plantar reflexes were bilaterally extensor with a crossed extensor response. Position sense was lost in both lower extremities below the hip. Vibration sense was absent below the iliac crest. Pinprick sensation was completely lost below the inguinal ligament bilaterally including the lower sacral segment. There was a shading loss of pinprick below the costal margin on each side. Thermal sensation and touch were similarly affected.

Lumbar puncture between the fourth and fifth interspaces revealed clear, acellular, yellow-brown fluid with a pressure of 35 mm. of cerebrospinal fluid. Intentionally, only a few drops of cerebrospinal fluid were collected. There was a complete dynamic block both to manual compression of the jugular veins and to jugular compression by means of a blood pressure cuff inflated to 40 mm. Hg. There was prompt response upon abdominal compression. One milliliter of pantopaque was then introduced into the subarachnoid space. The myelogram demonstrated a complete block between thoracic vertebrae 11 and 12 (figs. 2 and 3). At this time prothrombic activity was 18 per cent of normal, as measured by the Quick 1-stage prothrombin method.

Fifty milligrams of vitamin K₁ were administered intravenously. Three hours later, 45 hours after the onset of symptoms, a laminectomy was performed between the seventh and twelfth thoracic vertebrae under local anesthesia with no
unusual bleeding. The ligamentum flavum was bluish in color. Upon incision a blood clot extending from the sixth to eleventh thoracic spines was found in the dorsal epidural space. It was not adherent to the dura. The original site of bleeding was not identified. The spinal cord pulsed upon removal of the hematoma. The dura mater was not opened.

Postoperatively there was no recovery of the neurologic defects. Cerebral spinal fluid dynamics were normal 1 week after the operation. Brownish pigmentation was still evident in the spinal fluid. In the ensuing 6 months, there was return of pain sensation in the right lower extremity, but no other improvement in function. The paraplegia has persisted.

DISCUSSION

The evolution of spinal epidural hematoma as observed in our patient and in those reviewed presents a pattern that can be recognized with ease. Acute back pain, rapidly progressive spinal cord and nerve root deficit, usually with complete spinal block, accompanied by a brownish pigment in cerebrospinal fluid are characteristic. Critical determinants are the location of the bleeding point, the volume of the vertebral canal relative to that of the spinal cord in the affected area, the proximity of intervertebral foramina, the presence of coagulation defects, and the final volume of the hematoma. These factors determine the degree of embarrassment of spinal cord circulation as well as the amount of pressure necrosis. The long vertical extent of the lesion, particularly if located in the lumbar or cervical enlargement of spinal cord, may in addition produce severe atonic flaccidity segmentally and a myelographic block several segments below the upper edge of function disturbance. In our case the myelographic block was between T11 and T12 and the upper border of hypalgesia was at T8. The brown pigment observed in the cerebrospinal fluid in subdural, epidural, and intracerebral hematoma has been identified as methemoglobin. In subarachnoid bleeding the golden-yellow pigment in the cerebrospinal fluid is bilirubin.

In a review of 10 cases of acute nontraumatic spinal epidural hematoma straining effort was found to be a common precipitating event. Back pain was the first symptom in 6 of the patients. The interval from the onset of the first symptoms to the development of complete paraplegia varied from 20 minutes to 10 days; however, 50 per cent of the patients were completely paralyzed below the level of their lesion within 3 hours of the onset.
of complaints. The shortest time interval from the development of paraplegia to surgical intervention was 4 days. Three of the 10 cases were fatal before surgical intervention. The location of the hematoma in 2 of these cases was in the upper cervical region. Recovery after surgery has varied from complete to none. Epidural hematoma in some cases does not cause complete spinal block and may not pursue a rapid course; in 1 patient, who had back pain for months after an injury, the syndrome of a ruptured intervertebral disk was simulated.14

Spontaneous spinal epidural hematoma is a rare disease. Of the 27 cases found in the literature, 1 patient had leukemia, 1 hemophilia, and including our case, 4 and possibly 5 had coumarin-induced coagulation defects. Thus, approximately one fourth of patients with this disease have had coagulation defects.

In the case presented, recurrent and progressive vertebral artery disease was the indication for anticoagulant therapy. There were no changes in dose during the last 8 months of therapy. The Quick prothrombin time was steadily in the "therapeutic" range except for 1 determination. In this setting an epidural hemorrhage developed in the absence of obvious trauma or localized disease. The only evident antecedent event was a possible Valsalva maneuver accompanying defecation. It is conceivable that as a result of increased venous pressure during this effort, one of the small valveless venules in the epidural space ruptured and that in the presence of her induced clotting defects the bleeding was not arrested.

In the last few years anticoagulant therapy has been used on a long-term basis in the prophylaxis of recurrent myocardial infarction15-18 and the syndromes of insufficiency of the internal carotid, basilar or vertebral arteries.19, 20 In these states the value of long-term anticoagulant therapy has been difficult to establish. The disease processes demonstrate marked, spontaneous variability. New clot formation, propagation, and dissemination play a variable role in the production of symptoms. Brief hypotension and transiently reduced cardiac output have been recognized as common triggers of ischemic symptoms with and without newly added vascular pathology.21, 22 Clinical evaluation of the extent of vascular disease and clinical determination of progression are difficult. Unconscious bias and nonspecific effects have not been easily eliminated in studies of morbidity.23 Double-blind technics, which might indeed be helpful, are impractical.

The hazards of coumarin-induced coagulation defects include bleeding into the skin and subcutaneous tissue, mucous membranes, kidney, gastrointestinal and respiratory tracts, eye, pericardium, brain, and the coverings of the nervous system. In patients treated for weeks the incidence of major bleeding has been reported generally as 1 per cent, the incidence of any bleeding as 9 per cent.24 The incidence of hemorrhage in patients maintained on anticoagulants for months to years is not as well established. In one series of more than 100 patients treated for 5 years the incidence was 42.1 per cent.17 In other large series the incidence of hemorrhage has varied from 3 to 19 per cent.15, 18 The possibility clearly exists that an increased incidence of bleeding after long-term administration may be due not only to the quantitative factor of the increased time of reduced Quick prothrombin activity but to the qualitative factor of the development of newly developing defects in coagulation after many weeks of administration.25, 26

The degree of hypoprothrombinemia necessary for clinically significant and safe interference with coagulation has been difficult to define. In clinical practice the "therapeutic" level has been accepted as that represented by a Quick 1-stage prothrombin time of approximately 2 to 3 times normal in seconds, roughly equivalent to 10 to 30 per cent of prothrombin activity. The Quick 1-stage prothrombin method reflects multiple factors influencing the rate of elaboration of thrombin and fibrin.27 Coumarin derivatives have been shown to induce multiple coagulation defects.25, 26, 28 Proconvertin, a factor stimu-
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lating the conversion of prothrombin to thrombin, falls rapidly, as was observed in this case. The induced decrease of proconvertin is almost invariably greater in degree and earlier in time than that of prothrombin itself. A large fall in prothrombin may not be obtained for weeks. Deficiencies in plasma thromboplastin component (PTC) and Stuart factor are also induced. There is some evidence that there may be little antithrombotic effect from isolated proconvertin deficiency unless the deficiency is extreme, that the anti-thrombotic effect of Dicumarol may correlate with prothrombin deficiency, and that low levels of prothrombin and of PTC may favor hemorrhage.26 A clear-cut distinction has been demonstrated between the coagulation defect and the antithrombotic effect of Dicumarol.29 Further studies of factors influencing antithrombotic and hemorrhagic effects of anticoagulants are required. It is clear that the commonly used Quick prothrombin time yields information of a general nature, which has been helpful but may not be adequate. At “therapeutic” levels, a defect in coagulation is desired, which can interfere with gross intravascular thrombus formation and propagation and which nonetheless will not produce excessive bleeding from normal trauma.

The qualitative risks of anticoagulant therapy are clear. The occurrence of major bleeding appears unpredictable in an individual. Evaluation of the benefits and risks of long-term anticoagulants requires further studies on both sides of the question.

SUMMARY

The occurrence of spinal epidural hematoma in a patient on long-term anticoagulant therapy of cerebral vascular disease has been reported.

The salient features of spinal epidural hematoma have been described.

Coumarin-induced defects in coagulation have been discussed.

Problems in the evaluation of long-term anticoagulant therapy have been raised.

SUMMARIO IN INTERLINGUA

Es reportate le occurrentia de hematoma spino-epidural in un patiente sub tractamento anticoagulatori a longe vista pro morbo cerebro-vascular.

Es describite le saliente características de hematoma spino-epidural.

Es discutite defectos coagulatori inducite per coumarina.

Es sublevate problemas in le evaluation de therapia anticoagulatori a longe vista.

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Spinal Epidural Hematoma during Anticoagulant Therapy
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Circulation. 1959;19:735-740
doi: 10.1161/01.CIR.19.5.735
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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