Spinal Epidural Hematoma during Anticoagulant Therapy

By Bertram M. Winer, M.D., Simon Horestein, M.D., and Albert M. Starr, M.D.

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.\(^1\)\(^2\)

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 quadrant anopia. 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 determinations\(^6\) 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-

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\(*\) 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...
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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\(^1\)\(^-\)\(^4\),\(^8\)\(^-\)\(^12\) 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 a cellular 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 T\(_{11}\) and T\(_{12}\) and the upper border of hemiplegia was at T\(_8\). 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.\(^13\)

In a review of 10 cases\(^8\) 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 in-
tervention 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 hem-
ophilia, 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 de-
fects.

In the case presented, recurrent and pro-
gressive vertebral artery disease was the in-
dication 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 ab-
sence of obvious trauma or localized disease.
The only evident antecedent event was a pos-
sible Valsalva maneuver accompanying de-
fection. It is conceivable that as a result of
increased venous pressure during this effort,
one of the small valveless venules in the epi-
dural space ruptured and that in the pres-
ence 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 pro-
phylaxis of recurrent myocardial infarc-
tion15-18 and the syndromes of insufficiency of
the internal carotid, basilar or vertebral ar-
teries.19, 20 In these states the value of long-
term anticoagulant therapy has been difficult
to establish. The disease processes demon-
strate 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 pa-
thology.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 coagula-
tion defects include bleeding into the skin
and subcutaneous tissue, mucous membranes,
kidney, gastrointestinal and respiratory
tracts, eye, pericardium, brain, and the cov-
ings 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 pa-
ients 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 4.21 per cent.17
In other large series the incidence of hemor-
rhage has varied from 3 to 19 per cent.15, 18
The possibility clearly exists that an increased
incidence of bleeding after long-term admin-
istration may be due not only to the quanti-
tative factor of the increased time of reduced
Quick prothrombin activity but to the quali-
tative factor of the development of newly
developing defects in coagulation after many
weeks of administration.25, 26

The degree of hypoprothrombinemia neces-
sary for clinically significant and safe inter-
ference 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 approxi-
mately 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 fi-
brin.27 Coumarin derivatives have been shown
to induce multiple coagulation de-
fects.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 antithrombotic effect of Dicumarol may correlate with prothrombin deficiency, and that low levels of prothrombin and of PTC may favor hemorrhage.29 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 hematomaspinino-epidural in un patiente sub tractamento anticoagulatori a longe vista pro morbo cerebro-vascular.

Es describite le saliente caracteristicas de hematoma spinino-epidural.

Es discutite defectos coagulatori inducite per coumarina.

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

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BERTRAM M. WINER, SIMON HORENSTEIN and ALBERT M. STARR

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