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Fever and Thromboembolic Disease in Acute Spinal Cord Injury

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Summary

Thromboembolic Disease (T.E.D.) is a major cause of morbidity and mortality in the first few months following spinal cord injury. The purpose of this three year retrospective study is to delineate the previously poorly described role of fever as both a common component of T.E.D. manifestation and, on occasion, the sole presenting sign of an otherwise occult T.E.D. process.

We reviewed 148 consecutive admissions to the Southeastern Michigan Spinal Cord Injury System (1982–1985). Ten patients with documented T.E.D. were found and extensively reviewed; 3 had inadequate documentaton of clinical manifestations and 1 patient was found from venography to have a non-acute thrombosis. Of the remaining 6 cases, all had fever as a sign, and 4 of these patients had fever as the sole presenting sign. Full fever work-ups were performed in each case and no other source for fever could be found. Fever spikes occurred most commonly at night, with a maximum temperature of 100.2°F (oral) to a high in one case of 103.0°F (oral). All fevers resolved within the first week of adequate anticoagulation therapy.

These findings indicate that fever may be the earliest and, possibly, only clinical sign of an otherwise occult T.E.D. process.
Key words: *Spinal cord injuries; Fever; Thrombophlebitis; Thromboembolism.*

Deep venous thrombosis (D.V.T.) and pulmonary embolism (P.E.) are complications of spinal cord injury that occur predominantly during the first 2 to 3 months after the injury, and are major causes of morbidity and mortality.

The incidence of clinically apparent thromboembolic disease in the acute spinal cord injured without chemical prophylaxis has been reported to range from 12.5% for D.V.T. and 5% for P.E. (Watson, 1968) to 40% for D.V.T. and 13% for P.E. (Van Hove, 1978).

The preliminary diagnosis of D.V.T. in most clinical settings has been based upon the detection of clinical signs of increased deep venous resistance, or by

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inference after the occurrence of pulmonary emboli. The clinical signs most closely watched for include asymmetric swelling of the legs (> 1·5 cm difference), asymmetric warmth of the legs, 'Homans' sign', any evidence of increased irritability/spasticity (Homans, 1944), engorged superficial veins, cyanosis, palpable cord, shortness of breath, sudden onset of confusion, and/or chest pain. Confirmatory studies such as impedance plethysmography, venography, electrocardiogram, arterial blood gases (ABG) analysis, ventilation and perfusion scan (V/P scan), chest X-ray and pulmonary angiography are often performed only after clinical suspicion has arisen.

A preliminary diagnosis of D.V.T. based on clinical criteria has been shown to have a sensitivity of only about 50% (Haeger, 1969; Kakkar, 1969; Nicolaides, 1971, 1975). All too often, the first clinical sign of D.V.T. in a closely watched patient is the occurrence of a massive, sometimes fatal, pulmonary embolus (Walsh, 1965; Watson 1964, 1978).

It has been our experience over the years that fever of questionable origin in the acute spinal cord patient is an important early clinical sign of venous thrombosis. After the recent occurrence of four cases of Thromboembolic Disease (T.E.D.), two of whom presented solely with fever of questionable origin, we undertook an extensive review of all previous cases at our institution of D.V.T., with and without pulmonary embolus.

Materials and methods

All 148 patients hospitalised at the Southeastern Michigan Spinal Cord Injury System acute and/or rehabilitative care units from October 1982 through March 1985 were reviewed. In this series of patients, 80 (54%) had been admitted to our system within 14 days, and 59 (40%) in between 15 and 90 days. Thus, the majority had been admitted by the time of the greatest reported incidence of T.E.D., 2 to 3 months after injury. The detailed hospital case summaries were reviewed and revealed ten cases of deep vein thrombosis and/or pulmonary embolus (preliminary diagnosis were made on a clinical basis). These ten charts were reviewed in detail; relevant data are presented in Table I.

Out of 6 patients with adequately detailed accounts of presentation, 4 had a spiking fever as the only presenting sign of T.E.D. One of these cases is presented in detail.

Case report

On August 3, 1984 a 28-year-old male fell off a ladder while at work, striking his back and neck. He suffered immediate paralysis and loss of sensation from his hands and trunk below his nipples. The patient was transported via ambulance to a local community hospital where he was immediately placed in Crutchfield Tongs for stabilisation. Physical examination revealed C7 complete quadriplegia. On an extensive work-up including tomography, myelogram and CT scan, the only significant abnormality noted was marked cervical cord swelling with passage of dye.

On August 9, 1984 the patient was switched to a Philadelphia collar and

Table I Prophylaxis, symptoms and outcome of thromboembolic disease in 10 spinal cord injured patients

	Case	Days from injury	P.E.	Prophylaxis	Presenting symptoms	Temperature spikes	Swelling/ Warmth	Resolution of fever	Initial (+) culture
1	(L.T.)	35	–	Jobst stockings	Fever	Night ≤ 100.2°	+	3rd Day Heparin	–
2	(J.K.)	72	–	Minidose Heparin	None	None	–	——	——
3	(J.T.)	31	–	Minidose Heparin and Jobst stockings	Fever, swelling and warmth of limb	Night ≤ 101.4° oral	–	7th Day Heparin	–
4	(P.K.)	75	–	Minidose Heparin	Fever	None	–	——	——
5	(S.M.)	27	–	Minidose Heparin and Jobst stockings	Fever	Night ≤ 101.6°	+	1st Day Heparin	+
6	(D.H.)	46	–	None	——	——	–	——	——
7	(R.I.)	44	–	Minidose Heparin and Jobst stockings	Fever, swelling and warmth of limb	Night ≤ 100.6° oral	–	7th Day Heparin	——
8	(F.M.)	26	+	Minidose Heparin and Jobst stockings	Fever	Night ≤ 101.5° oral	–	3rd Day Heparin	–
9	(T.I.)	17	+	Jobst stockings	Fever	Night ≤ 103.0°	–	7th Day Heparin	+
10	(I.J.)	?	–	Minidose Heparin and Jobst stockings	—— OLD D.V.T. FOUND ——		NA	NA	NA

transferred to the Southeastern Michigan Spinal Cord Injury System rehabilitation unit. Spinal X-rays were repeated, a C.T. metrizamide myelogram was performed and a fracture of the body of C7 was found. The patient was switched to a SOMI brace for immobilisation.

On August 30, 1984 the patient spiked a 101.6°F (oral) temperature. The room temperature and type of clothing were unchanged from previous weeks. The patient denied any symptoms of a cold, anorexia, S.O.B., sore gums or chest pain. Vital signs, bowel patterns, and medications given were unchanged. Physical examination was negative. A urine analysis and C&S were positive for a Klebsiella pneumoniae UTI and appropriate antibiotics were given for a 10 day course. The patient remained febrile, however, but a repeat urine analysis and C&S were negative, as were blood cultures. Nightly temperature with spikes of up to 101.6°F (oral) continued unabated for weeks. Multiple physical examinations, chest X-rays, blood cultures and urine cultures were all negative.

An infectious disease specialist was consulted; additional studies including PPD and candida control skin tests, Hepatitis screen, ANA, CMG virus titers and a bone scan were all negative.

On September 24, 1984 a minor asymmetry of calf and thigh measurements was detected (left greater than right) and a subsequent venogram revealed left peroneal, tibial and proximal superficial femoral venous thrombi, with normal appearance of the left iliac vein. The right lower extremity was read as normal. No V/Q scan was performed. The patient was immediately anticoagulated with IV Heparin. Within 48 hours of therapeutic anticoagulation, he was switched over to Coumadin, all without further event or temperature.

Results

Incidence. Ten patients out of 148 (6.8%) developed deep vein thrombosis, and 2 patients (1·3%) developed pulmonary emboli. There were no instances of fatal pulmonary emboli.

Time of Greatest Risk. Nine cases first showed symptoms between the second and 11th week after the injury. One case was found on venography to be non-acute with the presence of well developed collaterals.

Prophylaxis. Of the 9 cases of acute D.V.T., 6 were receiving subcutaneous mini dose Heparin, and 6 wore Jobst stockings. Four of the 9 had both stockings and Heparin.

Presenting signs. Of the patients who had adequately detailed accounts of presentation, all 6 had the symptom of fever. Two of the 6 presented with the classic picture of deep vein thrombosis, i.e., concomitant pyrexia, asymmetric lower extremity swelling, warmth, engorged superficial vein and mild cyanosis. While all 6 patients were febrile, 4 of the 6 patients presented solely with fever. All cases underwent extensive investigations.

Fever pattern. Temperature spikes were almost universally nocturnal and ranged in degree from a low grade pyrexia of 100.2°F up to 103.0°F (oral). The fever was usually one of low grade.

Thromboembolic disease course. Of the 4 patients who initially presented with fever alone, 2 later developed the full classical picture (i.e., leg swelling, warmth, cyanosis, etc.), but two did not have these signs. Once heparinised, no

patient had any further incidence of embolic phenomena. All fevers resolved within 3–7 days after the initiation of continuous Heparin infusion.

Discussion

Ochsner and DeBakey (Ochsner, 1939) and later Homans (1944) were the first to describe deep vein thrombosis in two forms: thrombophlebitis and phlebothrombosis. Thrombophlebitis was the term given to an inflammatory thrombotic process which presents with fever, swelling, warmth, tenderness, cyanosis and superficial venous engorgement. The thrombosis was described as a proximally propagating occlusive clot that is relatively fixed to the vessel wall by the inflammatory process. The combination of major vessel occlusion and the inflammatory process would lead to the more obvious 'classic' presentation of edema, warmth, etc.

Phlebothrombosis was the term given to clinically asymptomatic thrombosis. The thrombus was described as a proximally propagating 'soft' clot, that is non-adherent to the vessel wall and has a 'free floating' tail from which thrombus may dislodge and embolise. Due to its relatively non-occlusive nature there is little warning of pain, swelling or warmth, and secondary to its non-adherent quality, it is the most likely form to embolise and to cause embolic fatalities. 'The more silent and less inflammatory the thrombosis in the lower limbs, the likelier is the process to cause pulmonary embolus' (Homans, 1944; Walsh, 1965; Watson, 1968, 1974). The only early clinical sign noted by many authors was one of 'slight rise of temperature and a persistently elevated pulse rate' (DeTakats, 1941). If one could see a four-hour temperature chart of every patient subject to the possibility of venous thrombosis in the legs, there would be evident, as the earliest sign of embolic detachment, a rise of pulse rate and temperature (Allen, 1943; DeTakats, 1941). This concept was further supported by the observation that venous ligation proximal to the thrombus leads to an immediate remission of increased temperature and heart rate (Homans, 1944).

Ochsner, DeBakey and Homans' observation of elevated temperature and pulse rate as often being the earliest clinical sign of T.E.D., has been noted to apply to the general population (Coleman, 1984; Isselbacher, 1980) and in our experience to the spinal cord injured population as well. Surprisingly, in the spinal cord literature, the few papers (Kakkar, 1969; Perkash, 1978; Sugarman, 1982; Walsh, 1965) that do mention fever in relationship to T.E.D. either do so in only vague passing reference (Jarrel, 1983; Walsh, 1965) or do not adequately rule out other possible etiologies (Perkash, 1978; Sugarman, 1982). No paper reviewed specifically addressed this issue, and in light of the near total omission of this crucial fact from the S.C.I. literature, we have presented our findings.

Fever

When an acute S.C.I. patient presents with a fever, a long and difficult differential diagnosis must be worked through in an organised and complete fashion, taking into account the level of the lesion and the clinical setting (see Table II). Thermoregulatory insufficiency in the acute high paraplegic and quadriplegic is perhaps the most common cause of a fever, but it is often the most difficult to

Table II Fever: Differential diagnosis in acute SCI

Thermoregulatory insufficiency
Infections:
a. Upper respiratory tract infection
b. Viral gastroenteritis
c. Pneumonia
d. Specticemia
e. Urinary tract infection
f. Otitis media/external
Abscess:
a. Traumatic (due to initial penetrating injury)
b. Iatrogenic (incisional, tracheal stoma, IV porto, sites)
c. Perirectal
d. Decubitus ulcer
e. Dental
f. Sinusitis
Atelectasis
Pancreatitis
Perforated bowel
Drug fever
Heterotopic ossification
Thromboembolic disease
Autonomic hyperreflexia
Cholecystitis
Associated brain or brainstem damage

prove and usually become a diagnosis of exclusion. It has been clearly shown by Guttmann (Guttmann, 1958, 1976) that humans with spinal cord injuries will behave as partial poikilotherms when exposed to significantly elevated ambient temperatures. However, it has been our experience that in 'sensitive' individuals, a room temperature of 72°F combined with a moderate amount of bedding covering the patient can induce a mild fever.

Pancreatitis and perforation of the bowel are also extremely difficult to diagnose in the acute high paraplegic and quadriplegic (Berlly, 1984; Miller, 1975). With loss of sensation and early loss of autonomic and reflex activity (spinal shock phase), typical signs of the 'acute abdomen' are masked. Fever has been noted to be an uncommon component of autonomic hyperreflexia. Abscesses below the level of the lesion may go unnoticed secondary to the patient's lack of sensation. A not uncommon form of abscess in a patient on a bowel program that is frequently overlooked is a perirectal abscess. In the elderly spinal cord injured patient, dehydrations should as well be included in the differential diagnosis.

In the four cases presented, all pertinent possibilities of the differential diagnosis were excluded. In each case fever was unexplained, venous thrombosis was found and documented by a venogram, and in all patients temperatures resolved after the insertion of anticoagulation therapy.

Our incidences of D.V.T., P.E. and fatal P.E. are substantially lower than those most frequently reported. Due to our comparatively small sample, the significance of our low rates is doubtful. Notably, no deaths occurred as the result of pulmonary emboli.

All nine cases of acute T.E.D. first became symptomatic from 2 to 11 weeks after injury. This seemingly confirms the previously described predominance of T.E.D. in the first 3 months after injury. Because our average length of stay is

only 89 days, we have limited opportunity to observe D.V.T. after the third month.

It is interesting to note that two patients did have positive urine analysis and cultures at the time of onset of their elevated temperature. While this could be coincidental it does raise the possibility of endotoxin induction of thrombosis (Thomas, 1964; Walsh, 1965). Thomas Wessler showed in animal models that microbial endotoxins (especially in areas of retarded blood flow) produced statis thrombi. While this may explain these two cases, the other four cases of D.V.T. were culture negative initially.

All patients with a venogram diagnosis of deep vein thrombosis, were immediately anticoagulated with a continuous infusion IV Heparin, titrated to approximately 1.5 times the control value. Fully anticoagulating levels of Heparin were maintained for 5–7 days and patients were slowly loaded and switched to Coumadin. No patient had repeated episodes of D.V.T. or P.E.

Deep vein thrombosis in the spinal cord injured is relatively common, it occurs at a rate of 12.5% (Watson, 1968) to 40% (Van Hove, 1978) giving any spinal cord injured patient a high index of suspicion. Unexplained fever should be a valuable early warning sign of an otherwise occult thromboembolic process, and therefore should be on the differential diagnosis list for fever of questionable origin in the spinal cord injured.

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