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Cobb Syndrome: New Case and Historical Review

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Abstract

Cobb syndrome is a combination of a skin nevus and a spinal angioma in the same segmental distribution. Although this syndrome originally was thought to be rare, its prevalence has been reported to be as high as 20% of patients with spinal angiomas in some series. We report on a case and provide an historical review of the literature to emphasize the importance of recognizing Cobb syndrome, which can lead to early diagnosis and treatment of spinal angiomas, helping to improve the prognosis.

Key words: Cutaneomeningeal angiomatosis, Cobb syndrome, spinal arteriovenous malformation, skin angiomas.

Cobb syndrome, or cutaneomeningospinal angiomatosis, belongs to the angiomatous phakomatosis. The syndrome is defined as the combination of a skin nevus and a spinal angioma. The vascular skin nevus may vary in size and appearance, but its segmental level must correspond within one or two segments to that of the spinal angioma. The spinal angioma may vary in extent, nature, or appearance, but must not be angioblastic and must be confirmed anatomically, surgically, or radiologically.[1]

Only a few cases of cutaneomeningospinal angiomatosis have been described (1-36). We report one such case as well as provide an updated review in an effort to emphasize the necessity of recognizing this syndrome early to improve the prognosis.

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Case Report

A 35-year-old white male was initially seen by the vascular surgery department at Henry Ford Hospital at age 16 after having had ligation and stripping of the right lower extremity varicose veins at another institution on two occasions. The vascular surgeons determined that this patient had congenital arteriovenous malformation of his lower extremity. Fifteen years later, the patient was noted to have marked worsening of his small varicose veins.

When we first saw him, the patient indicated that for quite some time he had been experiencing lower back discomfort, mainly in the form of stiffness upon awakening in the morning. For the past six months, he started having increased lower back pain and pain along the right flank radiating to the right lower extremity. He also noticed some paresthesia of the right heel and increased urinary frequency. Because of these symptoms, the patient had undergone myelography and was referred to us for further management.

Examination revealed that flexion of the lumbar spine was moderately restricted. The bulk of the gluteal musculature on the right was decreased compared to the left. The patient had marked swelling and superficial varicose veins over the entire right lower extremity and a mild port wine-colored stain over the buttocks and forefoot (Figure 1). Al-

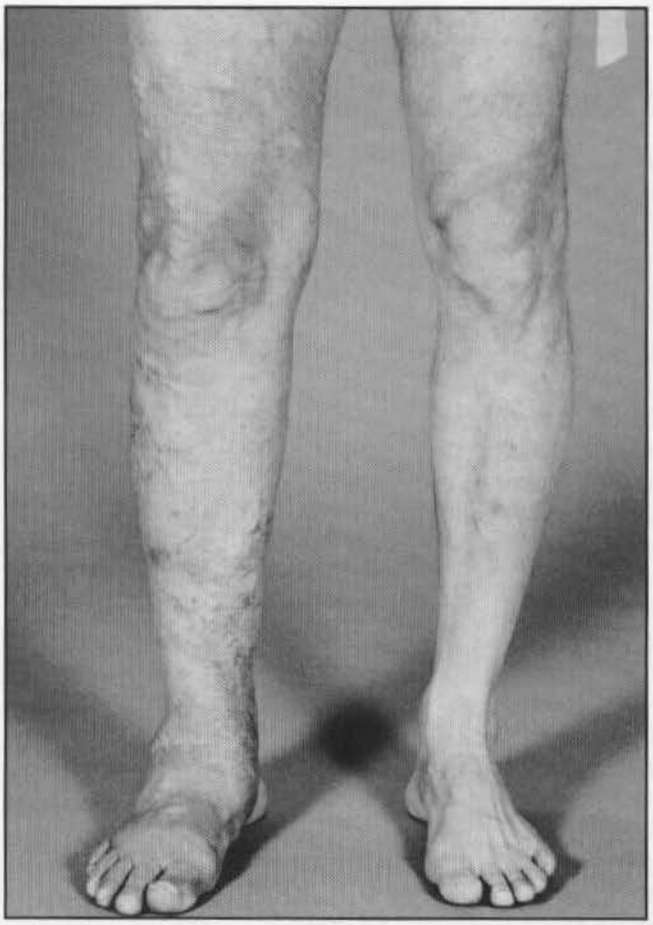

Figure 1. A port wine-colored stain is evident over the forefoot (A) and buttocks (B).

though there was no appreciable weakness, both the Achilles and the patellar reflexes were markedly diminished on the right side. The patient did have decreased pinprick in the L2, L3, and L4 dermatomes. The sensation of the sacral dermatomes was preserved.

The myelogram revealed an almost complete block at the lower level of LI, with a smooth regular margin and a characteristic appearance of an intradural lesion.

The patient was admitted. On the second day he underwent a bilateral laminectomy at T12-L2. Upon opening the dura in the midline, a large dark-red nodule was seen in the middle filling the dural sac (Figure 2). Several nerve roots were seen intimately associated with the mass and stretched coursing over it. The mass was cystic in nature and gave the appearance of a probable hemorrhage within. A large radicular artery on the left came from below and ended on the conus area. Microdissection enabled all the nerve roots to be separated from the tumor capsule. The few nerve filaments considered to be the origin of the mass were sectioned after placing a vascular clip. During the final stages of tumor removal, a small hole was created in the tumor capsule and dark blood drained out, indicating hemorrhage into the capsule.

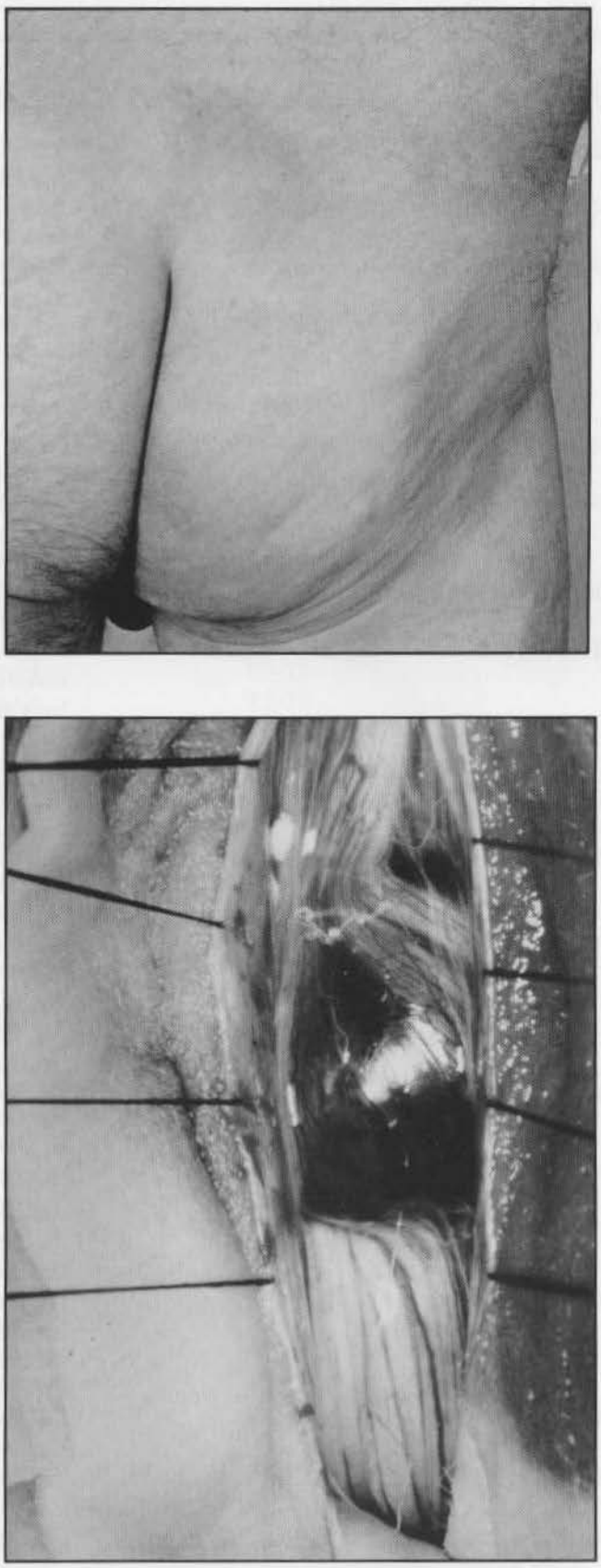

Figure 2. An intraoperative view of the spinal vascular malformation.

Table 1. Reported cases of cutaneomeningospinal angiomatosis

Author/year	Sex/age (years) at Onset of Symptoms	Level of Cutaneous Lesion	Level of Spinal Lesion
Berenbruch/1890 (4)	M/16	3 angiolipomata: left chest, right shoulder, right upper back	C3-T3
Cobb/1915 (5)	M/8	Large port wine nevus on right back (T9)	T6-T10
Rand/1927 (27) Case #2	M/28	Dark pigmented patch 5x3 cm, at the right angle of scapula (T8)	T11-l2
Kaplan/1935 (20)	M/27	Left hemangioma of the spine, 10x15 mm, at T5-T12; cafe au lait spots in the internal aspect of left arm and groin	T3-T8 hemangio-endothelioma
Sterling/1936 (29)	M/?	Nevus planus 10x15 inner aspect of right leg and knee (L4)	L3-L5
Johnston/1938 (19)	M/5	Angiome verruqueux 8 cm in diameter below the left scapula at the level of the 10th rib	T8-T12
Karshner/1939 (22)	M/14	Vascular nevi at T5-T9 and angioma at T7	T6-T8
Ferber/1942 (11)	M/51	Many small hemangiomas mainly at T5-T10 over the back and abdomen	T7 vertebra hemangioma with epidural extension
Wyburn-Mason/1943 (35)			
Case #22	F/10	Telangiectatic nevus in the cervico-occipital region	C2-C6
Case #34	M/6	Diffuse vascular nevus over radial border of left forearm and back of the neck	C3-T1
Silverman/1945 (28)	F/46	Congenital purple discoloration of the skin in the left upper limb and chest (T1-T10)	T6-T10
Cross/1947 (6)	M/19	Angioma of the skin over the left side of the neck	C6 toward posterior fossa
Fracasso/1947 (13)	F/29	Port wine nevus planus over T4-T6 the back between T7 and T10	
Trupp/1948 (32)	F/15	Numerous large nevi over the back in the metamere corresponding to the neurological features	T3-T5
Louis-Bar/1950 (23) Van Bogaert/1950 (34)	F/17	Large angioma in the lumbosacral region down to the calf (L1-L3); nevi over T4-T5 dermatomes around vertebral spine	T12-L5
Henson/1956 (15)	M/13	Left forequarter cutaneous hemangioma	C1-C4
Nielson/1958 (25) Case #2	M/23	T3-T11 left capillary angioma	T10-C3
Ginsbourg/1960 (14) Case #3	M/36	Left iliac crest T11	T11-L2

Table 1 (continued).

Author/year	Sex/age (years) at Onset of Symptoms	Level of Cutaneous Lesion	Level of Spinal Lesion
Fine/1961 (12)	F/15	Vascular nevus over the right arm, another over the right back T2-T4, and a few over left C5-C8 dermatomes	C5-T2
Hurth/1964 (16) Case #6	M/2	Nevus planus over the back (T8-T12)	T2-T7
Strain/1965 (30)	F/28	2 small angiomatous lesions over right scapula and skin nevi in same dermatome	T1 hemangioma
DeSeze/1966 (7)	F/11	Nevus planus in the right lumbar region and buttock (L2-L3) and L2-L3 vertebral angioma	T10-l2
Hurth/1968 (17) Case #10	F/14	Nevus planus T12-L2	T11-T12
Szojchet/1968 (31)	M/38	Hemangioma of the right axilla and chest wall removed in 4 interventions	T2-T4
Doppman/1969 (10)			
Case #1	M/15	Upper midback	C7-T6
Case #2	M/15	Upper midback	T2-T6
Case #3	M/63	Left midback	T6-L2
Case #4	M/49	Right midback	T2-L4
Case #5	F/21	Below right iliac crest	T1-L5
Case #6	M/39	Left upper back	C4-T1
Djindjian/1971 (9) Case #2	M/39	Left lumbogluteal cutaneous angioma	Conus medullaris AVM and vertebral angioma
Kaplan/1976 (21)	F/1.5	Nevi flammi over lips, left arm, left chest, upper back, anterior left thigh (L3-L4)	T12-L5
Jessen/1977 (18)	M/19	Multiple hemangiomas over right trunk, buttocks, and right leg	T8-T10
Zala/1981 (36)	M/17	Cafe au lait spot left paravertebrae, left gluteal, left medial malleoli skin lesion; angioma verrucosum papillokeratoma	AVM T11-T1
Miyatake/1990 (24)	F/15	Skin nevus over back between T6 and T10	T5-T7
Baraitsu/1990 (3)	M/13	10x8 cm vascular nevus over mid-dorsal spine and right posterior chest wall	T3 and above
Bejjani & Malik (present case)	M/35	AVM of the right leg and port-wine stain over forefoot and buttocks	Conus medullaris

Table 2. Series of spinal angiomas reporting cases of cutaneomeningospinal angiomatosis

Series	Number of Cases	Total Patients	Percentage
Turner & Kernohan/1941 (33)	1	46	2
Doppman et al/1969 (10)	6[a]	28	21.5
Adotti et al/1971 (2)	2	25	8
Djindjian et al/1971 (9)	7[b]	54	13
DiChiro et al/1971 (8)	1[c]	23	4
Pia/1973 (26)	1	74	1.5

[a]All 6 cases are reported in Table 1.
[b]One of these cases (case #3) was initially reported by DeSeze (7) (see Table 1), and case #2 is also reported in Table 1.
[c]This case may have been reported by Doppman in 1969.

Histopathological diagnosis confirmed an arteriovenous malformation of the conus medullaris (Figure 3).

Postoperatively, the patient was relieved of the pain in his right leg and the paresthesia of his right heel, and sensory findings started to improve as well.

Discussion

The first report of cutaneomeningospinal angiomatosis was published in 1890 by Berenbruch[4] who described a 16-year-old boy with three huge congenital "angiolipomata" over the right scapula and the latissimus dorsi and left pectoralis muscles. One day after severe exercise, the boy felt weak and tired in his legs and had lancing pain down both legs. Two weeks later, his right leg was fully paralyzed and his left partially paralyzed with increased deep tendon reflexes. A lipoma of the spinal cord was suspected and the boy was operated on. He died four hours later. The autopsy revealed a large plexus of veins along the spinal column connecting outward with an extradural angioma and with the tumors of the back through the intervertebral foramina. There was an angioma in the cord substance itself from C3 to T3.

Twenty-five years later, in 1915, Cobb[5] reported the case of an 8-year-old boy who, over the course of eight days, developed flaccid paraplegia with loss of sphincter control and loss of sensation below the ninth thoracic dermatome. A large port wine-colored mark was on the right side of the back at the upper limit of sensation; there were also similar, but smaller, nevi at the same level on the left side of the back and on the right flank. The paralysis changed from flaccid to spastic in 10 weeks and the diagnosis of spinal cord compression was made. This patient was seen by Harvey Cushing who suggested the presence of a spinal angioma because the skin nevus was on the same metamere as the presumed tumor compressing the cord. This was confirmed during the operation, which revealed a cluster of pulsating vessels extending from the fourth to the ninth dorsal segments of the spinal cord. Cobb concluded that "skin nevi are at times of diagnostic value when segmental phenomena referable to the central nervous system are present."[5]

Several other reports followed these two cases. In 1972, Kissel and Dureux[1] assembled 17 cases, and in 1977, Jessen et al[18] were able to gather 28 cases. Our review of the literature disclosed 36 detailed isolated cases (Table 1) and 10 other undetailed cases cited in other series (Table 2). These cases, plus ours, bring the total to 47 cases of cutaneospinal angiomatosis.

Table 3. Distribution of cutaneomeningospinal angiomatosis cases by age and sex

Age (years)	Male	Female	Total
0-10	4	3	7
11-20	8	5	13
21-30	3	3	6
31-40	6	0	6
41-50	1	1	2
51-60	1	0	1
61-70	1	0	1
71-80	0	0	0
Total	24*	12	36

*The patient's age was unknown in the report by Sterling (29).

Table 4. Initial symptoms in cutaneomeningospinal angiomatosis case

Initial Symptoms	Percentage of Cases
Pain	45
Weakness or paralysis	42
Sensory disturbance	13
Subarachnoid hemorrhage	13
Sphincter dysfunction	7

In reviewing these 47 cases, certain characteristics were determined relating to incidence, age, sex, familial history, clinical symptoms, and level of the spinal angioma.

Incidence: The incidence of cutaneomeningospinal angiomatosis compared to spinal angiomas varies widely

Table 5. Distribution of cutaneomeningospinal angiomatosis case by level

Spinal Angioma Level	Number of patients	Comments
Cervical	3	High located angiomas = 15 cases
Cervicothoracic	5	
Upper thoracic	7	
Upper and lower thoracic	7	7 intermediately located cases
Low thoracic	3	Low located angiomas = 15 cases
Thoracolumbar	9	
Lumbar	3	
Total	37	

and can be as high as 21% of patients with spinal angiomas (Table 2).[10] Kissel and Dureux[1] suggested a figure of 10%, but certainly there are unrecognized cases. Doppman et al[10] reported missing the diagnosis initially in the first three of their six cases; these were only recognized later at follow-up visits.

Age at onset of symptoms: Usually spinal angiomas are symptomatic in late adulthood, between the ages of 40 and 70 years.[37] In cutaneomeningospinal angiomatosis, patients are younger (ranging between 1 and 40 years) with a peak incidence between ages 10 and 20 years for both sexes (Table 3).

Sex: As in spinal angiomas, males with cutaneomeningospinal angiomatosis outnumber females with this condition, but there is a relative increase in the proportion of females with this disease. The ratio of male to female cases is 2:1 for cutaneomeningospinal angiomatosis compared to 4:1 for spinal angiomas (Table 3).[37]

Family history: No positive family history was found in any of the reported cases except in a 16-month-old girl with a maternal history of cutaneous hemangiomas.[21] The familial distribution was compatible with an autosomal dominant inheritance.

Symptomatology: Pain was the most common initial symptom reported by 45% of patients (Table 4). Weakness and paralysis were present in 42% of the patients. These figures are comparable to those seen in simple spinal angiomas.[37] Four patients (13%) had spinal hemorrhage as the initial symptom. In two patients, symptoms of paraparesis or paraplegia appeared during the last trimester of pregnancy, and a third patient had a subarachnoid hemorrhage in the last trimester of pregnancy.[17] The observation that the Valsalva maneuver can highlight the skin changes was reported by Doppman et al.,[10] who noticed this in a 14-year-old boy; according to the boy's mother, he frequently impressed his peers with such a demonstration. Engorgement of the cutaneous angioma was occurring too rapidly to be explained by simple passive venous stasis. Doppman et al. suggested that with sudden alteration of the intraspinal pressure, blood was displaced rapidly from the

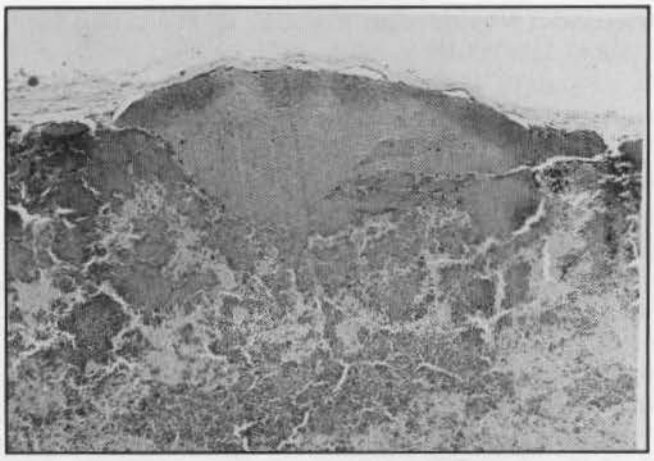

Figure 3. A histopathological section of the vascular malformation.

spinal angioma to adjacent cutaneous vascular spaces, which would presuppose either one continuous vascular malformation or two separate angiomas with large intercommunicating channels.

Level of the spinal angioma: Pure spinal angiomas are situated mainly at the lower thoracic and thoracolumbar levels. In Cobb syndrome, the incidence of high versus low situated angiomas is about equal (Table 5).

We believe that cutaneomeningospinal angiomatosis is not as rare as would appear from the scattered case reports, but that it is frequently unrecognized and its true incidence varies between 5-10% of spinal angiomas, as evident from analyzing previous series (Table 2). The importance of recognizing this association lies in early diagnosis and treatment. By raising the index of suspicion, the clinician may push the studies further in an attempt to make a diagnosis. The emphasis on early diagnosis is based on the fact that patients with spinal angiomas are usually diagnosed late in the course of their disease. In Ommaya's report,[38] 60% of patients were diagnosed two or more years after the onset of symptoms, and the worst outcomes occurred in patients with progressive myelopathy of more than 12 months' duration. With the availability of diagnostic techniques such as mag-

netic resonance imaging and spinal angiography as well as advances in microsurgical techniques, these lesions can be evaluated more precisely and treated before irreversible damage occurs. A high index of suspicion should arise and a vascular malformation should be suspected in any patient who presents with symptoms related to the spine, spinal cord, or spinal roots and a segmentally related cutaneous angioma.

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