Primary Subclavian-Axillary Vein Thrombosis

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SUMMARY
Primary thrombosis of the subclavian-axillary vein is a condition of uncertain origin resulting in proximal arm swelling, discomfort on use, and prominence of engorged collateral veins in the upper arm and chest. The literature is reviewed and the authors' own experience with 23 patients, evaluated from 1950 through 1966, is detailed. This disorder is a clinically distinct venous complication of the neurovascular compression syndrome of the upper extremity. Contrary to the findings recorded by others, spontaneous improvement following conservative management, while initially good, ceases after the first few months. After a mean follow-up period of 8 years, nine patients have major, and 12 have minor, residual symptoms when using the affected arm. Venous collateral patterns persist in all patients. Early venography and thrombectomy are proposed.

Additional Indexing Words:
Stress Effort Pulmonary emboli Thoracic outlet syndrome Neurovascular compression syndrome

Primary deep venous thrombosis of an upper extremity is uncommon, occurring only once or twice for every 100 similar cases of thrombosis in the lower extremity. Approximately 500 cases are now reported in the literature, but an individual physician's experience with this condition is usually limited. While manifestations are characteristic, this venous complication of the thoracic-outlet and shoulder-girdle neurovascular compression syndromes does not clearly emerge as a distinct entity in standard textbooks and monographs of peripheral vascular disease. Like the arterial complications of cervical and first rib deformities, primary subclavian-axillary vein thrombosis, we believe, should be clearly separated from the more benign neurological manifestations of the neurovascular compression syndromes.

Our experience suggests that the prognosis for normal use of the affected limb following conservative management is not as uniformly good as previous reports would indicate.

According to Hughes, Sir James Paget is credited with the first description in 1875 of primary subclavian-axillary vein thrombosis, which he called "gouty phlebitis." Von Schroetter in 1884 was the second author to write on this subject. Hughes, in his monumental review of 320 patients in 1948, originated the eponym, "Paget-Schroetter's syndrome." Primary subclavian-axillary vein thrombosis has also been referred to as spontaneous, idiopathic, traumatic, effort, strain, and stress thrombosis. Sometimes the modifying words, "so called" are used to emphasize the uncertainty of pathogenesis. All these terms are etiologically somewhat unsatisfactory and like most authors, we prefer the term "primary." The major problem in diagnosis is whether the venous obstruction is fixed (thrombus) or intermittent (without thrombus) and whether a causative compression...
Table 1
"Secondary" Subclavian-Axillary Vein Thrombosis

<table>
<thead>
<tr>
<th>1. Direct injury, blunt or penetrating</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Fractures; clavicle, first rib, humerus</td>
</tr>
<tr>
<td>2. Compression by mass</td>
</tr>
<tr>
<td>A. Neoplasm, especially lung, breast</td>
</tr>
<tr>
<td>B. Lymphadenopathy</td>
</tr>
<tr>
<td>C. Subternal thyroid</td>
</tr>
<tr>
<td>D. Aortic arch aneurysm</td>
</tr>
<tr>
<td>3. Thrombophlebitis in distal arm</td>
</tr>
<tr>
<td>A. Chemical</td>
</tr>
<tr>
<td>B. Infectious</td>
</tr>
<tr>
<td>C. Thromboangiitis obliterans</td>
</tr>
<tr>
<td>D. Trousseau syndrome</td>
</tr>
<tr>
<td>4. Intrathoracic infections</td>
</tr>
<tr>
<td>5. Extension of thrombosis of superior vena cava</td>
</tr>
<tr>
<td>6. Generalized stasis disorders</td>
</tr>
<tr>
<td>A. Congestive heart failure</td>
</tr>
<tr>
<td>B. Shock</td>
</tr>
<tr>
<td>C. Extreme dehydraton</td>
</tr>
<tr>
<td>7. &quot;Hypercoagulable&quot; states</td>
</tr>
<tr>
<td>A. Polycythemia vera</td>
</tr>
<tr>
<td>B. Paroxysmal nocturnal hemoglobinuria</td>
</tr>
<tr>
<td>C. Anovulatory drugs (?)</td>
</tr>
</tbody>
</table>

...point by a surrounding structure can be detected. Primary subclavian-axillary vein thrombosis must also be differentiated from the "secondary" types enumerated in table 1.

Methods

The records of 23 patients representing unequivocal examples of primary subclavian-axillary vein thrombosis seen at Walter Reed General Hospital from 1930 through 1966 were reviewed. Many other cases were encountered, especially in the earlier years of this study, but are not included because of incomplete data. The patients were usually transferred from other military hospitals where venography and therapy were initiated. There was no uniform management, and several weeks had frequently elapsed before the patients reached Walter Reed General Hospital. Therefore, this series represents a preponderance of cases with early severity biased by referral considerations. One half of the patients were seen personally by one of the authors (R.H.). A questionnaire emphasizing detailed residual symptomatology was sent to 16 patients seen before 1966. Twelve patients responded to the questionnaire. Three patients were lost to follow-up, and four patients were seen personally by all the authors within the past year. Therefore, the current status is known in 16 of the 23 cases with a mean follow-up period of 8 years.

In the course of this review, enough cases of secondary subclavian-axillary vein thrombosis were found to enable us to construct table 1, with at least one example of each entity. These cases will not be considered further.

Clinical Manifestations

Table 2 summarizes certain features of the patients with primary subclavian-axillary vein thrombosis. All the patients were males except one (case 16). The mean age at the onset of symptoms was 24 years. All were otherwise in excellent health. Symptomatic residual disability was graded on an 0 to 3 scale as follows: 0, arm is asymptomatic during all activities and considered normal by the patient; 1, arm is only mildly and briefly symptomatic during sustained heavy activity and is not considered a disability by the patient; 2, arm is symptomatic during normal activity, but not disabling, and the patient is able to function if activity is restricted, for example, by military profile or minor changes in occupation; 3, arm is severely symptomatic during normal activity, and the patient is unable to perform in a military role or be employed except by major occupational change to sedentary job.

Etiological Factors

In one half of the patients, preceding vigorous activity was mentioned during the initial history. Years later most of these patients did not relate their condition to any unusual activity, indicating its trivial nature. Most of the patients developed symptoms within 24 hours of the mentioned activity. Four patients awoke in the morning with symptoms when stasis and compression during sleep are presumably etiological factors. Eight patients could not relate the onset to anything. In this last group symptoms were somewhat more apt to be intermittent and gradual in development.

The right arm was involved 2.3 times often- er than the left. However, in six of 19 cases in which the dominant hand was known, thrombosis occurred on the opposite side. One right-handed patient (case 5) awoke with right subclavian-axillary vein thrombosis at age 20. Two years later spontaneous
thrombosis developed on the left. Bilateral subclavian-axillary vein thromboses reportedly occur in 2% of all cases of venous obstruction of the upper extremity.

Three of the patients were Negro (cases 8, 10, and 11). One had a hemoglobin C trait proved by electrophoresis (case 11). Another had a peripheral blood smear and hemogram suggesting a hemoglobin C trait (case 10), but electrophoretic study has not been done. As we are not familiar with any coagulation abnormality associated with C hemoglobin, we can only regard this association as coincidence. Complete analyses of individual coagulation factors were normal on several recent patients with subclavian-axillary vein thromboses.

**Table 2**

*Summary of Cases of Primary Thrombosis of the Subclavian-Axillary Vein*

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Affected arm</th>
<th>Dominant hand</th>
<th>Preceding activity</th>
<th>Anticoagulants</th>
<th>Follow-up length (yr)</th>
<th>Residual disability</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21</td>
<td>Right</td>
<td>–</td>
<td>Biceps bruise</td>
<td>+</td>
<td>3 days before 4.5</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>27</td>
<td>Right</td>
<td>Right</td>
<td>Swimming</td>
<td>0</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>Right</td>
<td>Right</td>
<td>Removing</td>
<td>+</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>22</td>
<td>Left</td>
<td>Right</td>
<td>Handball</td>
<td>+</td>
<td>3 wk</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>Right</td>
<td>Right</td>
<td>Sleep</td>
<td>+</td>
<td>16</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>21</td>
<td>Right</td>
<td>Right</td>
<td>Sleep</td>
<td>+</td>
<td>8.5</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>22</td>
<td>Right</td>
<td>Right</td>
<td>Showering</td>
<td>0</td>
<td>20</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>35</td>
<td>Left</td>
<td>–</td>
<td>None</td>
<td>+</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>9</td>
<td>23</td>
<td>Right</td>
<td>Right</td>
<td>Digging</td>
<td>0</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>23</td>
<td>Right</td>
<td>–</td>
<td>None</td>
<td>0</td>
<td>3 mo</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>34</td>
<td>Left</td>
<td>Right</td>
<td>None</td>
<td>0</td>
<td>3.5</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>18</td>
<td>Right</td>
<td>Right</td>
<td>None</td>
<td>0</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>13</td>
<td>20</td>
<td>Right</td>
<td>Right</td>
<td>Sleep</td>
<td>0</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>14</td>
<td>53</td>
<td>Right</td>
<td>Right</td>
<td>Back</td>
<td>+</td>
<td>6.5</td>
<td>1</td>
</tr>
<tr>
<td>15</td>
<td>29</td>
<td>Left</td>
<td>Right</td>
<td>Climbing rope ladder</td>
<td>0</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>16</td>
<td>19</td>
<td>Left</td>
<td>Right</td>
<td>None</td>
<td>0</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>17</td>
<td>28</td>
<td>Right</td>
<td>Right</td>
<td>None</td>
<td>0</td>
<td>2</td>
<td>1</td>
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<tr>
<td>18</td>
<td>17</td>
<td>Left</td>
<td>Right</td>
<td>Lifting bales of hay</td>
<td>0</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>19</td>
<td>20</td>
<td>Left</td>
<td>Right</td>
<td>Weight lifting</td>
<td>0</td>
<td>8 mo</td>
<td>1</td>
</tr>
<tr>
<td>20</td>
<td>21</td>
<td>Right</td>
<td>Right</td>
<td>None</td>
<td>0</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td>21</td>
<td>20</td>
<td>Right</td>
<td>Right</td>
<td>Baseball</td>
<td>0</td>
<td>25</td>
<td>1</td>
</tr>
<tr>
<td>22</td>
<td>25</td>
<td>Right</td>
<td>Right</td>
<td>Axillary trauma</td>
<td>+</td>
<td>5 mo</td>
<td>1</td>
</tr>
<tr>
<td>23</td>
<td>18</td>
<td>Right</td>
<td>–</td>
<td>Sleep</td>
<td>0</td>
<td>1.5</td>
<td>2</td>
</tr>
</tbody>
</table>

*Time in parentheses refers to time from onset of symptoms and institution of anticoagulant therapy.

†Anticoagulant therapy instituted after occurrence of a pulmonary embolus.

Signs and Symptoms

A characteristic triad of swelling, pain, and venous prominence in the affected arm developed within 24 hours in 19 of the patients. In four similar symptoms developed more gradually or were intermittent. Edema of variable degree was present in all 23 cases and was most noticeable in the upper arm and...
shoulder region. The hands became swollen only when massive proximal edema was present. In females, swelling of the breast on the involved side has been reported. The superficial collateral venous pattern was most conspicuous in the inner aspect of the upper arm, in the pectoral region of the chest, and occasionally, laterally in the neck (fig. 1). Discomfort in the same location occurred in most patients, commonly described as a "stiffness" or "dull ache," but occasionally as a "sharp pain." Characteristically, this discomfort, edema, and venous prominence increased with activity, especially if shoulder hyperabduction or bracing positions were involved. With exercise, moderate weakness of the entire arm was frequently noted, despite a normal neurological examination at rest. Resting of the affected arm was uniformly beneficial. Elevation of the arm did not always bring symptomatic relief; the response was probably related to anterior (helpful) or posterior (not helpful) positioning of the arm in relation to the shoulder. During dependency, the hand and fingers on the affected side often became cyanotic; clinical features of vasospasm were not observed. While palpable axillary or less commonly, supraclavicular venous "cords" have been present in one third of the reported cases, only four patients in our series demonstrated this finding.

Six patients demonstrated abnormal arterial thoracic-outlet and shoulder-girdle compression maneuvers. Five of the patients have normal thoracic outlets radiographically, and one showed bilateral cervical ribs. One patient (case 3) obliterated his radial pulse in shoulder hyperabduction, and another (case 23), during shoulder bracing, but the obliterated pulses occurred bilaterally in both and produced no symptoms. We do not regard symmetrical asymptomatic changes in radial pulse during these maneuvers as significant, as this response occurs in many normal individuals. However, perhaps more significantly, the only patient (case 5) who had bilateral venous thromboses readily obliterated his radial pulses on both sides in

**Figure 1**

Infrared photograph of patient (case 5) who has bilateral subclavian-axillary vein thromboses and characteristic venous collateral patterns. Note that the central sternal area is uninvolved, unlike superior vena caval obstruction.

**Figure 2**

Schematic diagram demonstrating effect of exercise on antecubital venous pressure in patient with occluded proximal vein. Each pressure increase represents fist clenching and each plateau, fist relaxation.
of symptoms and with incorrect diagnosis, resection of her left cervical rib and a left scalenotomy were performed without improvement of symptomatology. Patient 19 exhibited a constant discrepancy of 30 mm Hg in the systolic blood pressure in his affected arm and a loud left supraclavicular bruit. Shoulder hyperabduction, bracing, and Adson maneuvers obliterated the bruit and the left radial pulse. An arteriogram showed a constant constructing lesion of the mid-subclavian artery of unknown etiology.

**Diagnosis**

The history and physical findings are usually sufficient for diagnosis. Infrared photography makes a permanent record of the superficial venous collaterals which are otherwise easily seen. The venous pressure can be estimated by raising the straightened arm above the heart and noting the level of collapse of the dorsal hand veins. Venous pressures were determined in an antecubital vein with the arm in neutral position in 14 patients and were clearly abnormal at rest in 11 (above 15 cm saline). If the diagnosis was suspected but the venous pressure was equivocal, rapidly clenching the fist with the manometer open, as advocated by Veal, was found to be a useful maneuver. With proximal venous obstruction, each fist clenching will “milk” up the venous pressure several centimeters (fig. 2); without proximal obstruction, each fist clenching has little effect on the venous pressure. The three patients with borderline values at rest quickly raised their venous pressure about 10 cm of saline by six fist clenches. Several other patients without venous disease angiographically were found to have high venous pressures at rest, presumably due to venospasm about the needle tip; rapid fist clenching exercises in these patients did not significantly change the venous pressure.

Upper extremity venograms were performed in 20 patients at varying times after the thrombosis. The two commonest roentgenographic patterns of obstruction were localized blocks in the subclavian-axillary junction between the first rib and clavicle, and long blocks of the entire axillary vein.

**Figure 3**

Brachial venogram of patient (case 22) shows a short segment of subclavian-axillary vein thrombosis at the junction of the first rib to the clavicle. Note the prominent transverse cervical-jugular collateral pathway.
Lesions in the subclavian vein are difficult to detect due to the great dilution of the contrast medium by the jugular system. Brachial and cephalic venous thrombosis did not occur.

Collateral venous patterns are prominent roentgenographically in all stages. However, these patterns do not seem to bear a uniform relationship to the location and extent of the occlusion in the main vein. In localized subclavian thrombosis, deep collateral venous blood flow is predominantly through the cephalic-transverse, scapular-transverse, cervical-jugular vein route ("first-rib bypass collaterals," fig. 3). The lateral thoracic-intercostal-internal mammary vein route is more apt to be seen in extensive thrombosis involving the axillary vein (fig. 4). Also prominent are numerous small axillary vessels which bridge the length of the thrombosed segment. Recannalization was seen in two of four patients (cases 9 and 23) who had repeat venograms made several months after their initial study.

Phlebography in patients with residual post-thrombotic symptomatology is not without risk. One patient (case 8) developed transient chemical phlebitis and exacerbated symptoms in his affected arm immediately after the study. One patient (case 22) had bilateral upper extremity venograms taken 3 months after onset of his condition and 6 weeks after coumarin anticoagulation had been discontinued. One day following the procedure, severe basilic-cephalic-antecubital chemical phlebitis developed in the normal arm. Three days later, typical symptoms and findings of subclavian-axillary vein obstruction appeared.

Treatment and Results

All patients were treated initially with rest in bed and arm inactivity. Arms were usually kept elevated and warm soaks often applied. On this therapy alone, edema subsided within the first week of hospitalization. Ace bandages and elastic sleeve devices were frequently used to control edema, but not all patients felt more comfortable wearing them. The patients were usually asymptomatic when discharged from the hospital, and symptoms recurred only when normal activities were resumed. Nine patients with subclavian-axillary vein thromboses had a grade 2 or 3 major chronic disability. Usually the degree of disability became manifest within the first few months, and whether mild or severe, did not appreciably change thereafter. Twelve patients continue to have mild discomfort or edema with sustained heavy exercise of the arm; only two are entirely asymptomatic while doing heavy work. The characteristic collateral venous pattern did not disappear in any patient and is a permanent identifying sequela of this disorder. Chronic stasis changes in the skin such as those which occur in the lower extremities did not develop. Fibrinolysin therapy was not used but may offer theoretical advantages in this disorder when a safe, practical preparation is available.

Anticoagulants were administered to eight patients. The days referred to in table 2 are the days between onset of symptomatology and institution of anticoagulation. One patient (case 8), not given anticoagulants, experienced a definite pulmonary embolus on the third day of hospitalization. This case has previously been reported by Aufses. A second patient (case 22), 2 weeks after the onset of his condition and while still receiving heparin, suddenly had an episode of right pleuritic chest pain, dry cough, dyspnea, and tachycardia lasting several hours, but without laboratory confirmation of a pulmonary embolus. Thrombectomy in one patient (case 10) at 10 weeks was unsuccessful, and cervical sympathetic block in two patients (cases 7 and 23) was without benefit.

Discussion

This series of 23 patients shows that the clinical manifestations of primary subclavian-axillary vein thrombosis are so distinctive that this condition should be readily separated from the other upper extremity, neurovascular compression syndromes. This disorder usually affects healthy young adult men who either
in the course of sleep, normal or unaccustomed activity, rather abruptly develop edema and dull pain in the upper arm and shoulder region. Diffuse weakness and cyanotic discoloration of the arm are not uncommon. These symptoms are all greatly exacerbated by activity. While the dominant arm is usually involved, one third of the patients may have the nondominant side affected. Prominent superficial collateral venous patterns in the upper inner arm, shoulder, and pectoral region of the chest are invariably present and are permanent sequelae of the disorder. Increased venous pressure is often obvious on inspection and, when measured with a needle manometer, shows a characteristic stepwise increase with repetitive fist clenching.

That these clinical findings are manifestations of obstructive venous disease is unmistakable. Lack of similar abnormalities in the neck, central thorax, and opposite arm exclude innominate and superior vena caval obstruction. Complete physical and appropriate laboratory examinations, including routine roentgenograms, exclude most secondary causes of subclavian-axillary vein thrombosis. Primary venous thrombosis can be distinguished from the other neurovascular syndromes because vasospastic phenomena and neurological compression rarely occur; in addition, venous thrombosis does not respond to changes in posture or physical conditioning, and shoulder-elevating exercises usually aggravate the symptoms.

Etiologically, we believe that primary subclavian-axillary vein thrombosis is caused by local compression-stasis factors. Anatomic studies and speculations of possible compression points occupy a large part of the literature on this subject. The clavicle,29, 30, 34 subclavious muscle,4, 35 costocoracoid ligament,4, 9, 55 origin of the pectoralis minor muscle,30 and even an aberrant phrenic nerve11, 36 have been incriminated as anterior structures capable of producing a compression action against posterior structures such as the first rib,29, 30, 34 scalenus anticus muscle,37 and subscapularis muscle.38 Adams and associates7 stated that the clavicle, subclavious muscle, and costocoracoid ligament are the major anterior structures that compress the subclavian and axillary vein against the first rib in primary thromboses. Unfortunately, even routine venography rarely delineates the exact point of compression due to propagation of the clot. The subclavian vein, unlike the artery, lies anterior to the scalenus anticus muscle; consequently, venous thrombosis is not a recognized complication of complete cervical ribs.11 During strenuous exercise, Valsalva dynamics increase venous pressure and reduce blood flow, which may constitute a stasis factor at the time of compression. Venospasm has also been postulated as a causative factor.30 Laboratory tests have never shown a systemic state of "hypercoagulability,"11 and complete blood counts and erythrocyte sedimentation rates are usually normal in the acute stages of this disorder.

Intermittent obstruction of the subclavian-axillary vein without thrombosis occurs and may cause permanent superficial collateral venous patterns.36, 40 This entity cannot be differentiated from primary thrombosis without studies of venous pressure or venography. A minimally adequate angiographic study must include serial films—at least two within the first 10 sec of injection and preferably a late film 5 or 10 sec later. The median basilic vein is the injection point of choice.

The chronic disability that may result from conservatively managed primary subclavian-axillary vein thromboses deserves emphasis. Most patients treated only with rest in the acute stage will become asymptomatic and free of edema within a few days of hospitalization. It is perhaps this fact that explains so many favorable prognostic statements in the literature.11 The disability becomes apparent only when the patient returns to normal activities. Of our 23 patients, nine have a major, 12 a minor, and two no disability in using the affected arm. Furthermore, the disability remains unchanged for years, without spontaneous improvement after the initial weeks or few months of the disorder.
Unlike other reports,\textsuperscript{1,15} anticoagulant therapy did not appear to affect to a great extent the symptomatology or long-term prognosis in our cases. We have, however, continued to recommend anticoagulants in the acute stage on the theoretical consideration of preserving collateral vessels and of preventing pulmonary embolism. Examples of pulmonary embolism following upper extremity venous thrombosis are well documented in the literature and occurred in two of our patients. This complication is more frequent and severe in patients with secondary thrombosis, especially if related to malignancy or severe congestive heart failure. None of the pulmonary emboli reported in primary subclavian-axillary vein thromboses has been fatal.\textsuperscript{7,15,19,41–43}

Long-term follow-up in this group of conservatively treated patients does not justify the currently benign opinion regarding the functional recovery from primary subclavian-axillary thrombosis. Preliminary surgical experiences have documented successful thrombectomy in this condition.\textsuperscript{7,44,45} and warrant further consideration. Thrombectomy appears to be most feasible in the acute stage (under 72 hours) if the thrombus length is short, as determined by venographic studies. Routine venography is not totally innocuous, yet is essential if a surgical approach is to be considered. The advocates of a surgical approach stress combining thorough exploration of the outlet spaces with thrombectomy and removal of offending obstructive outlet structures.\textsuperscript{46} Occasionally angiography in chronic stages will reveal external compression of long-standing collateral routes which can be benefited surgically.\textsuperscript{7} While our own experiences cannot be used to support the benefits of thrombectomy, they do serve to draw attention to the poorly appreciated disability following conservative management.

References

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