

FUNCTIONAL ASPECTS ON THE KLIPPEL-TRÉNAUNAY AND RELATED SYNDROMES

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Abstract. Eight patients with two or three symptoms of the Klippel-Trénaunay triad were examined. All patients had varices, increased chloride concentration of sweat and, with one exception, hemangiomas. Four patients showed osteohypertrophy and one patient revealed signs of a-v fistulas. Venous outflow impairment as in deep venous occlusion is known to produce osteohypertrophy in children. The authors are of the opinion that a hemangioma actually is a functional a-v fistula. A hemangioma located in the vicinity of an epiphyseal zone may well cause a localized outflow impairment of the veins draining the epiphyseal zone, leading to an increased growth of the bone. Although patients with the Klippel-Trénaunay triad, Parkes-Weber syndrome and agenesis of the deep veins constitute an etiologically heterogeneous group, they do have some pathophysiological features in common. Treatment would profit by a classification in terms of the pathophysiology rather than the syndrome. The following scheme is therefore suggested:

- I: Infantile varices with a-v shunts. (a) true arterio-venous shunts, (b) functional arterio-venous shunts (hemangioma)
- II: Infantile varices with venous obstruction; (a) venous agenesis, (b) deep venous phlebitis.

Key words: Hemangioma; Varices; Osteohypertrophy; and A-v shunt

In 1869 Trélat and Monod described a condition which they named partial or total unilateral hypertrophy of the body (13). This hemihypertrophy was caused mainly by an increased growth of both osseous, subcutaneous and muscular tissues engaging either an arm or a leg. In the majority of their cases Trélat and Monod found vascular dilatations affecting either the cutaneous capillaries (*taches naeviformes*) or the subcutaneous veins forming proper varices. The authors noted that these naevi almost exclusively engaged just one side of the body. The simultaneous appearance of osteohypertrophy, hemangiomas and varicose veins in one extremity was considered an important finding by Klippel and Trénaunay (K-T) (7). They saw a dis-

tinct connection between these symptoms and proposed that they should be looked upon as a clinical entity.

A similar syndrome but apparently of different origin was reported by Parkes Weber (P-W) (14). The patients described by this author had dilated arteries in the affected region indicating the presence of arterio-venous communications. Ever since this publication, considerable confusion has existed between the triad described by Klippel and Trénaunay, where no indications of a-v communications were presented and the syndrome presented by Parkes Weber in which the a-v communication was the prominent feature (4). Comprehensive reviews of the literature have been made by Koch (8) and Langeron & Vercauteren (10). So far, studies in which a wide spectrum of diagnostic techniques of modern angiology are used have been but rarely presented. In the present study 8 patients with two or three symptoms of the Klippel-Trénaunay triad are described.

On the basis of these observations we believe that the K-T triad, P-W syndrome and agenesis of the deep veins have important pathophysiological similarities. A classification based on the pathophysiological findings is presented.

CLINICAL MATERIAL AND METHODS

Patient material. The patients were seen in the outpatient clinic for vascular surgery at the Seraphimer Hospital in Stockholm. The study comprises 4 men and 4 women (mean age 32 years; range 5-76). Table I.

Measurement of length of extremities. Radiographic measurements of the affected and contralateral extremities were performed. The lengths of the right and left proximal and distal parts of the extremities were compared.

Venogram of the leg. Ascending venograms were performed according to Greitz (5) and retrograde according to Gullmo (6).

Table I. Basic data of the patients

Patient	Sex	Age	Length (cm)	Weight (kg)	Weight at birth (g)	Involved extremity
A. S.	♀	76	154	58	3 100	Left arm
R. J.	♂	19	176	78	4 400	Right leg
S. O.	♂	57	178	66	3 550	Right arm
R. P.	♂	24	191	84	2 900	Left leg
K. L.	♀	23	164	50	3 360	Left leg
A. E.	♂	25	167	61	3 500	Right arm
B. I.	♀	24	180	62	3 650	Right leg
C. C.	♀	5	111	18	3 200	Right leg

Venogram of the arm. With the patient in the supine position a needle was inserted into a superficial dorsal vein of the arm. Some 20–30 ml of contrast medium was injected slowly under TV-fluoroscopic control. If no opacification of the deep veins was then seen, the injection was repeated after the application of a tourniquet above the wrist.

Plethysmography. The technique described by Aschberg (1) for the determination of organic outflow impairment, competence of superficial valves, deep valves and of the calf muscle pump was used.

Oxygen saturation of hemoglobin. The percentage oxygen saturation of venous hemoglobin was measured in the affected and contralateral limbs of all patients. The blood samples were collected from either the common iliac vein or from cutaneous vein of the forearm.

Venous pressure registration. Venous pressure registration was performed using either a 23 gauge scalp vein needle inserted in a dorsal pedal vein or a subcutaneous vein of the forearm. The registrations were effectuated with a pressure transducer connected to a Mingograf 32 graphic recorder (Elema-Schönander). Readings were made with the limb in the vertical position during both rest and exercise and with compression of the superficial veins by an 8 mm plastic tube snugly applied around the extremity.

When a reduction in venous pressure was noted after exercise the restitution time was registered. If an increase in venous pressure after exercise occurred, no restitution time was recorded.

RESULTS

The findings of the Klippel-Trénaunay triad are summarized in Table II. Three patients had the complete triad and 4 patients had a combination of hemangioma and varicose veins, while one had varicose veins and osteohypertrophy.

The differences in length of the affected and contralateral extremities are shown in Table III. In 4 patients the affected limb was longer than its counterpart. In 2 patients the difference in length was reversed and in the remaining 2 patients no dif-

ference was found. The largest circumferences measured at three different levels of the extremities are presented in Table IV. In one patient the affected leg, although shorter, was clearly thicker than its counterpart. This difference was most marked in the lower leg. In 2 patients the affected extremity was not only longer but also slightly thicker than the other. Three other patients had smaller circumferences of their affected legs as compared to their counterparts. These patients also complained of muscular weakness. No notable differences were found in 2 patients; one of these had muscular weakness of the affected arm.

The main venographic findings in 5 patients did not reveal any signs of deep venous occlusion (Table V). In one patient (S. O.) the deep venous system of the arm was only partially visualized and in another patient (A. E.) no deep veins could be seen. Varices were seen in all patients examined and dilated perforators were seen in the four legs but not in the three arms. Patent valves of the deep veins were seen in all extremities examined. Deep reflux was present in one of the three examined legs.

Venous plethysmography was performed in 6 patients (excluding C. C. and K. K.). None of these had any signs of organic outflow impairment. Among these patients were those 2 whose deep veins were partially or totally absent from the venograms.

Four patients had signs of superficial incompetence, while 2 seemed to have intact superficial valvular function. The deep valves were competent in 3 and incompetent in 2 patients. In the patient with no deep veins seen on the venogram (A. E.) the competence could obviously not be tested. The competence of the calf venous pump was found to be impaired in the three examined patient legs.

Measurement of the oxygen saturation of hemo-

Table II. Findings of Klippel-Trénaunay triad

Patient	Hemangioma		Varicose veins	Sto- hyper- trophy (length)
	Capillary	Cavernous		
A. S.	+	-	+	-
R. J.	+	-	+	-
S. O.	+	-	+	+
R. P.	+	-	+	+
K. L.	+	-	+	-
A. E.	-	-	+	+
B. I.	+	+	+	+
C. C.	+	+	+	-

globin of venous blood was normal in all but one patient (A. S.). Her affected arm was shorter than the other but there was no difference in circumference. As this 76-year-old patient had no serious complaints, arteriography of the arm was not performed. Arteriography confirmed the negative findings in all the other patients.

Venous pressure was recorded in 4 patients. In A. S., venous pressure was registered in a dorsal superficial vein of the arm at heart level. On the affected side the pressure varied between 10 and 12 mmHg as compared with the other side where only 6-8 mmHg was recorded. This difference was accentuated after 5 minutes of work. Thus venous pressure on the affected side increased to between 13 and 28 mmHg, while it decreased on the other side to 2-6 mmHg. In A. E. the right arm superficial venous pressure at heart level was 3 mmHg, increasing to 10 mmHg immediately after work. After

Table IV. Differences in largest circumference of extremities (cm)

- = involved extremity thinner than contralateral, + = involved extremity thicker than contralateral

Patient	Proximal part	Distal part	Malleolar level
A. S.	±0	±0	No information
R. J.	±2.0	+5.0	+3.5
S. O.	±0	±0	±0
R. P.	-4.0	-2.0	No information
K. L.	-1.0	-1.5	-0.5
A. E.	+0.5	+0.5	No information
B. I.	+1.5	+1.5	+1.0
C. C.	-0.5	±0	No information

application of a superficial tourniquet the pressure at rest increased to 38 mmHg and after work it reached 130 mmHg.

B. I. was examined with a needle in a dorsal vein in the affected foot in the erect position. The pressure at rest in the erect position was 94 mmHg and the resting pressure immediately after standing on her toes decreased to 58 mmHg. When a superficial tourniquet was applied below the knee the resting pressure after standing on her toes was 62 mmHg.

R. P., who like B. I. had the complete triad, underwent the same type of examination as the previous patient. The resting venous pressure in the erect position was 100 mmHg in both legs. After exercise it decreased in the affected leg to 71 mmHg and to 44 mmHg in the contralateral leg.

DISCUSSION

Certain variations in the symptoms of the K-T triad have been noted by previous workers. Hemangiomas have been of either capillary or cavernous type, simple or multiple, situated especially in the extremities. However, hemangiomas located on the head and trunk have also been described. The atypically localized varices usually appear as soon as the child has learnt to walk. Cutaneous manifestations of deep venous incompetence such as eczema, cellulitis, or ulcerations are seen in some cases and are most probably secondary to phlebitis or absence of deep veins. Hypertrophy of the bones (both in length and thickness) in the extremities has been an almost equally constant finding. However, certain authors have reported atrophy of the affected limb. Hypertrophy of the soft tissues is a

Table III. Radiographic measurement of extremities (cm)

Involved extremity in italics

R = right, L = left

- = involved extremity shorter than contralateral, + = involved extremity longer than contralateral

Patient	Proximal part		Distal part		Total difference
A. S. arm	<i>L</i> 28.0	R 30.0	<i>L</i> 20.5	R 20.0	-1.5
R. J. leg	<i>R</i> 47.0	L 48.0	<i>R</i> 36.5	L 38.0	-2.5
S. O. arm					+1.5
R. P. leg					+3.5
K. L. leg	<i>L</i> 43.5	R 43.5	<i>L</i> 35.0	R 35.0	±0
A. E. arm					+3.0
B. I. leg	<i>R</i> 49.5	L 48.5	<i>R</i> 39.5	L 38.0	+2.5
C. C. leg					±0

Table V. Venographic findings

ne = not examined

Patient	Deep venous occlusion	Varices	Dilated perforators	Presence of valves in deep veins	Deep reflux
A. S.	—	+	—	+	ne
R. J.	—	+	+	+	ne
S. O.	+/-	+	—	+	ne
R. P.	—	+	+	+	+
K. L.	—	+	+	+	—
A. E.	+	+	—	ne	ne
B. I.	—	+	+	+	—
C. C.	ne	ne	ne	ne	ne

common finding ascribed to angiomatous formations in the subcutaneous or muscular tissues.

Some of these formations have been of lymphatic vascular origin. In rare cases localized hypersecretion of sebaceous, sweat, lacrimal and salivary glands has been observed and in some patients ichthyosis of the skin has accompanied the triad (for references, see 8, 10).

Recently an increased chloride concentration in the sweat was described in this category and added to the list of diverse clinical findings (3). The patients included in this study showed two or three symptoms of the K-T triad. All patients had varices and only one lacked hemangiomas. Certain variations were found as regards the osteohypertrophy. However, since all patients had an elevated chloride content in sweat in either the affected or the contralateral limb (or both) their clinical conditions are obviously intimately related (3). There are many similarities in the symptomatology of these patients. Weakness of the affected limb was a common complaint (6/8 patients). In none of these could any sign of muscular weakness be recorded objectively. EMG registrations were normal. Venographic and plethysmographic examination as well as registration of venous pressure are important tools in the evaluation of venous competence in this group of patients. It should be mentioned that plethysmographic examination did not show any outflow impairment in the 2 patients with partly non-visualized deep veins at venography.

A significant arteriovenous admixture was found in one patient (A. S.). No arteriography was done in this patient as her complaints were modest and as she was of advanced age. Despite the fact that neither oxygen saturation nor arteriography showed any arteriovenous communications in B. I., we

found at excision of the hypertrophic subcutaneous tissue four arteries with a diameter of 2–3 mm which supplied the adipose tissue. This tissue was interspersed with cavernous veins.

It seems probable that many hemangiomas act functionally as arteriovenous fistulas, giving varying degrees of arteriovenous admixture. Both arteriovenous fistulas and venous stasis seen in agenesis of deep veins of the extremities are known to be capable of producing an increase in bone growth (2, 12). This acceleration of bone growth could be due to an increase in the mean venous pressure in the epiphyseal zones. However a venous pressure increase can rarely be recorded at rest, but as limb perfusion is multiplied during exercise the pressure rise can readily be noted. Although not all the symptoms of all the 8 patients presented above satisfy the K-T triad as regards osteohypertrophy, they do have some remaining symptoms in common. This might be taken as pointer to a common etiologic denominator. The absence of osteohypertrophy can possibly be explained by a normal mean venous pressure in the epiphyseal zones. A large arteriovenous fistula will probably affect the venous pressure in an entire limb, as also will an obstruction of the deep veins. On the other hand if none of these conditions is present, it is conceivable that even a small hemangioma if located near the epiphyseal region could cause a localized increase in pressure. Hemangiomas located in the skin or subcutaneous tissue would fail to affect venous pressure in this area.

The etiology of the K-T syndrome is still obscure. Larsson et al. produced hemangiomas and skeletal deformities of the extremities in mouse embryos by salicylate injection (11). Laignel-Lavastine located the primary lesion in the spinal ganglia or in

the intermediolateral tract of the medulla in which these authors claim there is a congenital absence of the cell group that ordinarily gives rise to the vasomotor regions (9). We do not know, however, if the chloride concentration of sweat is regulated by post-ganglionic sympathetic fibres.

Patients with K-T triad, P-W syndrome and agenesis of the deep veins constitute an etiological heterogenous group. However, we believe that treatment would benefit from a classification in terms of the physiology rather than of the syndrome. The following schema is therefore suggested:

- I: Infantile varices with a-v shunts; a) true arteriovenous shunts, b) functional arteriovenous shunts (hemangioma)
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