Familial multiple lateral telangiectatic nevi (port-wine stains or nevi flammei)

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Two families with multiple lateral telangiectatic nevi (LTN) (port-wine stains or nevi flammei) in various areas of the body in two and three generations are presented. In the second family, some members in addition to LTN also had superficial (strawberry) hemangiomas and hemangioma-like venous malformations. The pedigrees of these families indicate autosomal dominant inheritance of multiple LTN.

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Key words: familial hemangioma-like venous malformations – familial multiple capillary malformations – familial multiple lateral telangiectatic nevi – familial multiple nevi flammei – familial multiple port-wine stains – familial superficial (strawberry) hemangiomas – vascular birthmarks

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Congenital capillary malformations belong to the group of cellularly adynamic vascular malformations (Pasyk et al. 1984a, Pasyk 1987) and are present at birth in two main types: 1) medial telangiectatic nevus (MTN), also known as salmon patch, angel's kiss, stork bite, etc., and 2) lateral telangiectatic nevus (LTN), more popularly called port-wine stain or nevus flammeus, neither of which are scientific or medical terms.

The MTN appears in 50 to 74% of all newborn infants (Bettley 1940, Jacobs & Walton 1976, Osburn et al. 1987) as pink-red or light violet, irregular maculae or patches primarily on the medial part of glabello-frontal, occipito-nuchal or lumbosacral areas. These vascular discolorations gradually disappear in about 50% of cases during the first years of life (Hurwitz 1981). In adults they were found as persistent MTN, especially in the occipito-nuchal region in 57.5% (van Baar et al. 1989).

The LTN, however, is found in 0.3 to 1% of neonates (Jacobs & Walton 1976, Pratt 1953, Merlob et al. 1981) as a flat pink-red to purple macula, usually on the face in the distribution of the trigeminal nerve. The lesion may very rarely cross the midline (Rook 1972), be located bilaterally and symetrically on the face (Schnyder 1954) and extremities (Rook 1972). The LTN may occur anywhere on the body and is usually asymmetrical and unilateral with a dermatomal pattern, but bilateral nonsymmetric distribution on the trunk has also been reported (Wilkin et al. 1979). The LTN, however, rarely appear in multiple areas of the body. The lateral type of telangiectatic nevi have no tendency to fade, and they persist throughout life.

Both types of congenital telangiectatic nevi exhibit mature, ectatic capillaries with flat endothelium in the dermis, primarily in the superficial plexus. In the case of MTN, however, it appears that a defect in maturation of cutaneous sympathetic innervation occurs (Rosen & Smoller 1987). For LTN, Hasegawa & Yasuhara (1979) have suggested that developmental anomalies of vasomotor nerve cells derived from neural crest give rise to these vascular malformations. Kitamura et al. (1981), on the basis of ultrastructural studies of LTN, concluded that it is the loss of peripheral nervous elements in the perivascular region that is the basis of this disorder. Smoller & Rosen (1986) in their elegant immunohistopathologic studies documented significantly decreased nerve density in the perivascular tissue in the lateral type of telangiectatic nevus. These authors suggest that alterations in innervation, and especially loss of perivascular sympathetic neurons, cause dysfunction in vasoconstriction leading to vasodilatation. This concept was recently confirmed by Lanigan & Cotterill (1990), who observed in LTN reduced vasoactive responses to vasodilating and vasoconstricting stimuli. The cause of these disorders, however, is still unclear.

According to Koblenzer (1970), LTN appears

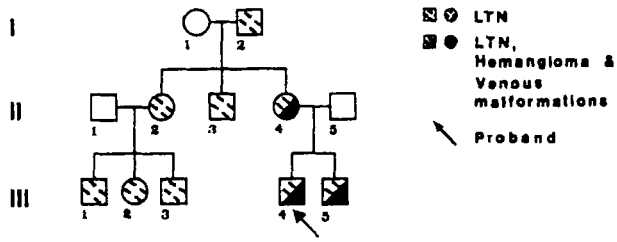

Fig. 1. Pedigree of Family 1 with multiple lateral telangiectatic nevi (port-wine stains).

randomly in the population without convincing evidence that it is inherited. Multiple LTN, however, have been reported in a few families (Shelley & Livingood 1949, Kaplan et al. 1976, Zaremba et al. 1979, Mercer et al. 1978, Shuper et al. 1984).

Two additional families with the lateral type of telangiectatic nevi that appeared in numerous locations on the body are presented here. Some members of the second family also had superficial (strawberry) hemangiomas and hemangioma-like venous malformations. Multiple LTN in these families show an autosomal dominant mode of transmission.

Description of families

Family 1

The proband (I-2 in the pedigree shown in Fig. 1), a 33-year-old female, was referred to the Laser Clinic for treatment of red spots on the left leg. These lesions had not changed in size or color since birth. During examination numerous reddish macules from 0.5×1 cm to 1×2.5 cm in size were seen dispersed on the left leg. The remainder of the physical examination was unremarkable.

The proband's 7-year-old daughter (II-1) was born with a few flat, red patches dispersed on the trunk and one red spot on the neck. All these vascular lesions, approximately 1×2 cm in size, are still visible. The child was otherwise healthy.

The proband's 5-year-old son (II-2), had also had red spots approximately 1 to 2 cm in diameter on the upper left eyelid, the left side of the neck and left thigh since birth. Routine, pediatric examination did not show any other abnormalities.

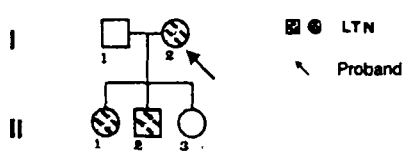

Fig. 2. Pedigree of Family 2 with multiple lateral telangiectatic nevi, superficial (strawberry) hemangiomas, and hemangioma-like venous malformations.

Fig. 3. Proband of Family 2 (III-4), a 7-year-old boy with lateral telangiectatic nevus on his face. Note small pigmented nevus on left side of forehead.

Family 2

The proband was a 7-year-old male (III–4 in the pedigree shown in Fig. 2) delivered by C-section. He was brought by his mother for evaluation of various vascular malformations he has had since birth. During examination, red, macular, well-demarcated areas on the left side of his nasal bridge, the left upper eyelid, and the forehead were seen (Fig. 3). Dilated blood vessels were also present on the medial conjunctiva and sclera of the left eye. Several vascular macules were present on the right

Fig. 4. The same boy (III–4) as in Fig. 3 with lateral telangiectatic nevi and pigmented nevi on right side of neck and back. Arrow indicates involuting superficial (strawberry) hemangioma.

Fig. 5. Lateral telangiectatic nevus on right foot of proband of Family 2 (III-4).

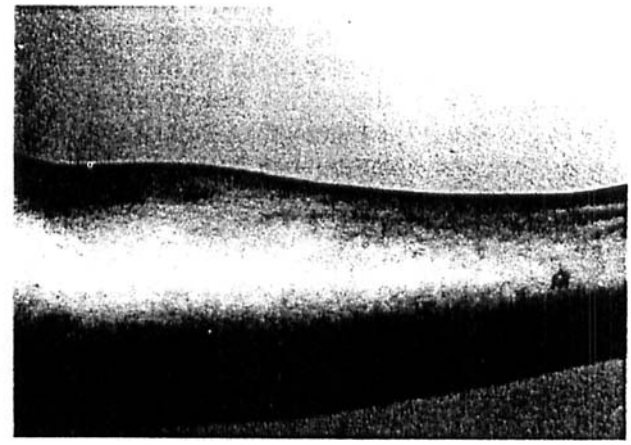

Fig. 7. Case II-4 of Family 2. Mother of above two boys with lateral telangiectatic nevi on right forearm.

side of the neck, the trunk, the left arm and the left thigh, measuring approximately 1×2 cm to 1.5×3 cm. An irregular, raised red area, 4 cm in diameter, with a scar consistent with a resolving superficial (strawberry) hemangioma was present on the mid-back (Fig. 4). On the right foot there was a macular, erythematous patch 2×3.5 cm in size (Fig. 5). Moreover, the child had numerous small pigmented nevi on his body. He had also had a few asthmatic episodes. During periodical ophthalmologic examinations there was no sign of glaucoma.

The proband's 6-year-old brother (III–5) was also born with vascular malformations. During examination he had a 2 to 3 cm soft, compressible mass on the left lower lip (probably a deep hemangioma) and an erythematous mass, 1.8 cm in diameter, on the back with a white scar in the center consistent with an involuting superficial (strawberry) hemangioma. On the left arm, forearm and hand, flat, red spots measuring 0.5×0.7 cm and 1×2 cm were present (Fig. 6).

The proband's mother (II-4) had had red patches and small pigmented nevi on her body since birth. At examination, besides the pigmented nevi, there were a few dispersed small (1 to 2 cm in diameter), flat, red macules on the trunk and extremities (Fig. 7). On the mid-back there was a red spot approximately 5×8 cm in size with a soft mass in the deeper part of this lesion (Fig. 8).

Numerous members of the proband's family (Family 2), i.e., a grandfather (I-2), an aunt (II-2), an uncle (II-3), and three cousins (III–1, III-2, III-3), had also had pink or red patches on various areas of their bodies since birth.

Discussion

The LTN has very rarely been reported as an inherited entity. In 1913, Benedict described a family in which both mother and daughter had LTN on the right chest, arm, shoulder, and neck. I myself

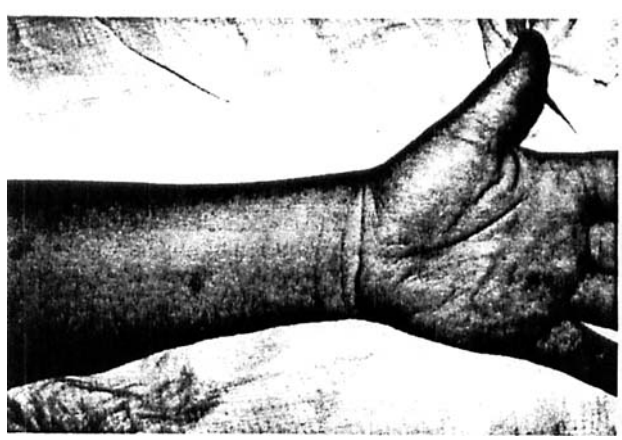

Fig. 6. Six-year-old boy of Family 2 (III-5) with a few lateral telangiectatic nevi on left forearm and hand.

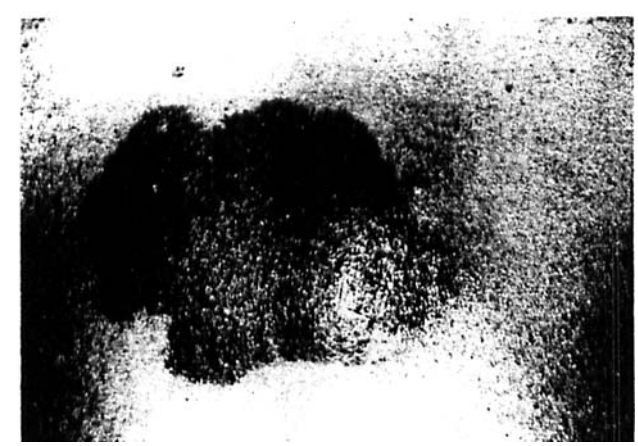

Fig. 8. Case II-4 of Family 2. Lateral telangiectatic nevus on the back and hemangioma-like venous malformations beneath the lateral telangiectatic nevus.

have treated, with the argon laser, a mother with LTN on the left side of the face and her daughter with a similar telangiectatic nevus on the right side of the face (unpublished data). The occurrence of LTN in phacomatosis pigmentovascularis type IVa in a mother and daughter has been described by Hasegawa & Yasuhara (1985). Multiple LTN have been reported by Shelley & Livingood (1949) in a family in which 12 members had numerous vascular malformations on various areas on the skin in four generations. Kaplan et al., in 1976, presented a family with multiple LTN in six members in three generations. Among them were a mother and daughter with multiple LTN; the daughter also had an intraspinal (T12-L5) arteriovenous malformation. A similar family with multiple LTN and arteriovenous malformations of the spinal cord (Cobb syndrome) in one member was described by Mercer et al. (1978). Zaremba et al. (1979) examined a family with multiple LTN in various areas of the body together with intracranial and intraspinal (C6-T1) arteriovenous malformations. There were four affected members in three generations. This condition was transmitted as an autosomal dominant trait. Shuper et al. (1984) described a family with multiple LTN occurring in nine members, including non-identical twins. In this family autosomal dominant inheritance was confirmed.

The coexistence of LTN, cavernous hemangiomas, and intraspinal arteriovenous malformations has also been observed in a few families (Kufs 1928, Nova 1979, Foo et al. 1980a, b).

Our two families, with numerous LTN disseminated on the body, did not show the presence of any vascular malformations in the central nervous system. It is interesting that some affected members of the Family 2 also had superficial (strawberry) hemangiomas in the involuting stage and hemangioma-like venous malformations.

The occurrence of MTN in families has also been reported (Shafer & Doig 1955, Zumkeller 1957, Merlob & Reisner 1985, Selmanowicz 1968, Tan 1972, Nova 1979, Esterly 1987, Mulliken 1988, Pasyk et al. in preparation). Other familial vascular malformations appearing in several generations were described by numerous authors (McIntosh 1957, Riley & Smith 1960, Clark 1970, Tabor & Wyatt 1970, Trell et al. 1972, Ide et al. 1974, Marriott et al. 1975, King et al. 1977, Barre et al. 1978, Goldberg et al. 1979, Snead et al. 1979, Zonana et al. 1976, Hayman et al. 1982, Higginbottom & Schultz 1982, Wertelecki et al. 1982, Pasyk et al. 1984b, Mitchels et al. 1985, Hurst & Baraitser 1988, Battoni et al. 1990, Gangemi et al. 1990, Nakagawa et al. 1990, Watson et al. 1990).

In the vast majority of familial vascular malformations reported in the literature, the pattern of inheritance shows an autosomal dominant mode of transmission with high penetrance. More studies are needed on the familial incidence of vascular malformations. They might give information about the proportion of familial cases, eventual clinical differences between familial and "sporadic" cases and differences in sex expression and transmission. They might also help to find the genetic defect(s) that lead to these disfiguring and very often devastating lesions.

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