CASE REPORT

Port-wine stain as a clue for two rare coexisting entities

Filipa Tavares Almeida, Regina Caldas, Maria da Luz Duarte, Celeste Brito

Department of
Dermatovenereology, Hospital
de Braga, Braga, Portugal

Correspondence to
Dr Filipa Tavares Almeida,
filipa.almeida6@hotmail.com

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SUMMARY

Phakomatosis pigmentovascularis (PPV) is an uncommon dermatosis characterised by the presence of both pigmentary and vascular abnormalities.¹ Its pathogenesis is not elucidated, and the prognosis is mainly determined by the presence of extracutaneous manifestations, such as Klippel-Trenaunay syndrome (KTS), that is defined by the triad of a port-wine stain (PWS), anomalous veins and progressive overgrowth of the affected extremity. Herein, we report a case of an adult patient, who presented with a large PWS, nevus of Ota, ocular melanosis, and limb hypertrophy and varicosities. These findings represented a rare association of PPV type IIb and KTS.

biomicroscopic follow-up was recommended. No other anomalies were found, including glaucoma.

At neurological assessment, no abnormality was found.

TREATMENT

Due to the absence of symptomatic or aesthetic concerns, the patient refused the treatment procedures.

OUTCOME AND FOLLOW-UP

The lesions remained stable for a 1-year period, and the patient was maintained on a multidisciplinary follow-up.

BACKGROUND

It is important to report cases of phakomatosis pigmentovascularis (PPV) combined with overlapping features of Klippel-Trenaunay syndrome (KTS) for its extreme rarity and prognostic implications, and to elucidate its pathogenesis.

CASE PRESENTATION

A 40-year-old man presented with diffuse red-purple aggregated patches, confined to the left half of his body. The patient had these asymptomatic cutaneous lesions since birth. Personal history and family history were unremarkable. His parents were non-consanguineous. Physical examination revealed diffuse and extensive red-purple patches on his left half-body, namely upper chest, shoulder, back and limbs, compatible with a port-wine stain (PWS) (figure 1). He also had a slight periorbital diffuse bluish-grey pigmentation and brownish-grey macules on scleral areas (figure 2). The periorbital and scleral pigmentation was consistent with nevus of Ota. These pigmentary lesions combined with the PWS were clinically considered as PPV type II. Furthermore, varicosities and hypertrophy were found on the left limbs, especially on the thigh (figure 3). These findings combined with PWS conducted to clinical diagnosis of KTS.

INVESTIGATIONS

Laboratory investigation was unremarkable. Chest radiography, abdominal ultrasonography, echocardiogram, venous Doppler ultrasonography and cranial MRI revealed no abnormalities.

At ophthalmological consultation, he was diagnosed with ocular melanosis and annual

DISCUSSION

PPV is a rare condition defined by the presence of both vascular and melanocytic nevi. Its pathogenesis remains elusive, but both abnormal development of blood vessels and migration of melanocytes during embryogenesis are considered.² This is thought to result from dysplasia of the vasomotor nerve cells and melanin cells, both of which are derived from the embryonic neural crest.³ Another theory is a genetic phenomenon characterised by loss of heterozygosity, called twin spotting, that is a specific mechanism of somatic mosaicism.⁴ Twin spots consist of paired patches of mutant tissue that is genetically different from each other and from the heterozygous background tissue.⁵ It results from vascular and melanotic genetic mutations that occur in each of a pair of homologous chromosomes; consequently, stem cells from the mutant pair origin mixed homologous daughter cells from two different mutations.⁶ Recently, frequent somatic mutations of GNAQ, a heterodimeric G protein alpha subunit, have been found, both in blue nevus, uveal melanoma and oculodermal melanocytosis and in PWS.⁷ The findings suggest that clinical manifestations of these conditions can be, in part, caused by activating mutations of GNAQ gene.⁸

PPV has been classified into four main types according to the pigmentary lesion associated with capillary malformation, classically a PWS. In 2003, a fifth group was described, characterised by cutis marmorata telangiectatica and dermal melanocytosis.⁹

Each type is further subdivided according to the presence of the cutaneous-only condition (subtype a) or if associated with systemic disease (subtype b).¹⁰ In all groups of PPV, it is estimated that half of the patients have systemic manifestations associated,

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Figure 1 Port-wine stain localised on the left half-body (upper chest, shoulder and arm).

besides skin lesions, the majority of which are ocular, vascular, musculoskeletal and neurological.¹¹ Ophthalmic alterations in PPV include hyperpigmentation of the corneal stroma, conjunctiva, sclera, episclera, iris, trabecular meshwork and choroid. The presence of oculodermal or fundus melanocytosis encompasses a greater risk to develop melanoma. Iris mammillations can also be found, sometimes mimicking Lisch nodules typical of neurofibromatosis type 1.¹² Congenital or acquired glaucoma is another condition to be aware, since intraocular pressure is increased due to ocular melanocytosis and nevus flammeus, when it appears in the ocular region.¹³

PPV type II, also called *phakomatosis cesioflammea*, consists of PWS and dermal melanocytosis, that in our case was represented by nevus of Ota. Given the additional presence of ocular melanosis and KTS, it was subclassified as PPV type IIb.

KTS is a triad of PWS, venous varicosities and soft tissue or bone hypertrophy. Rarely, concurrence of KTS in PPV has been described in the literature.¹⁴ The anomalous venous network present in KTS may be associated with a chronic intravascular coagulopathy and patients are at risk of developing a

Figure 2 Nevus of Ota and ocular melanosis.

Figure 3 Port-wine stain associated with varicosities and hypertrophy of the left leg.

thromboembolic event.¹⁵ Therefore, the evaluation of a patient with PPV should include an appropriate screening for systemic involvement which greatly determines the prognosis of the disease.¹⁶ In fact, evolution and prognosis of PPV depend on extracutaneous manifestations, since patients without systemic involvement have a benign course and do not require treatment.¹⁷ Regarding ophthalmology, it is important to perform a regular follow-up with a careful fundus examination, due to the higher incidence of choroidal or ciliary body melanoma and glaucoma in patients with PPV.¹⁸

Considering the aesthetic impact of skin lesions and to enhance the quality of life of the patients, pulsed laser light can be considered to treat PWS and Q-switched laser for pigmentary nevi.¹⁹ Concerning KTS, prophylactic anticoagulation should be considered, especially in patients with evidence of hypercoagulability, when they have additional risk factors for venous thromboembolism, such as surgery, trauma or pregnancy.²⁰

To conclude, the occurrence of PPV with concomitant features of KTS is very rare. It is important to perform a complete clinical

Learning points

- ▶ Phakomatosis pigmentovascularis (PPV) is a rare cutaneous disorder characterised by the presence of both pigmentary and vascular abnormalities.
- ▶ Prognosis of PPV depends largely on its extracutaneous features.
- ▶ Klippel-Trenaunay syndrome, which is defined by the triad of a port-wine stain, anomalous veins and progressive overgrowth of the affected limb, can present with PPV and worsens its prognosis.

and imagiological work-up in patients who present with PPV, in order to identify any underlying condition that may determine the outcome of this disorder.²¹

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