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Case Report RADIOLOGY

The lump of the medial canthus as diagnostic clue to cerebro-facial venous metameric syndrome: Report of a case

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ABSTRACT

The Cerebro-Facial Venous Metameric Syndrome is characterized by ipsilateral venous/lymphatic anomalies involving simultaneously the brain and the face with a metameric distribution. This case report to describe a case of Cerebro-Facial Venous Metameric Syndrome presenting with a lump of the medial canthus. This was a case report a 24-year-old woman with a history of a mild headache, complained of a sporadic (at least once a month) serous leakage from the left eye and a small cutaneous protuberance in the left medial canthus, without focal neurological symptoms. The patient underwent brain Magnetic Resonance Imaging and findings were suggestive of a Cerebro-Facial Venous Metameric Syndrome 1-2. When multiple and ipsilateral vascular anomalies are observed, it should be considered the presence of Cerebro-Facial Metameric Syndrome, even without neurological symptoms and port-wine stains. Follow-up is mandatory, especially if there are cavernomas or facial arterio-venous malformations due to the risk of bleeding.

Keywords: Cavernoma; cerebro-facial arterio-venous metameric syndrome; cerebro-facial venous-lymphatic metameric syndrome; magnetic resonance imaging.

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Brain vascular anomalies are often detected for the first time in neuroradiological examinations in both asymptomatic and symptomatic patients.

When vascular anomalies are multiple and ipsilateral, complex clinical conditions should be considered, such as Cerebro-Facial Arterio-Venous Metameric Syndrome (CAMS) or Cerebro-Facial Venous-Lymphatic Metameric Syndrome (CVMS), depending on the portion of the vascular tree involved.

In these latter cases, since mesoderm cells of the neural crest also contribute to blood vessels development simultaneously in specific areas of the face and the brain [1], maxillo-facial malformations should be excluded. Lasjaunias et al. previously categorized these complex cerebrofacial vascular syndromes on the basis of the involved metamers [2, 3]: CAMS/CVMS 1 (median prosencephalic) involve the hypothalamus and pituitary gland in the brain and nose and orbit in the face; CAMS/CVMS 2 (lateral prosencephalic) involve the occipital lobe, thalamus, optic tract, retina and maxillary bone; CAMS/CVMS 3 (lateral rhombencephalic) involve the cerebellum, pons and the mandible.

In this report, we described a case of CVMS 1-2 presenting with a lump of the medial canthus. The case high-

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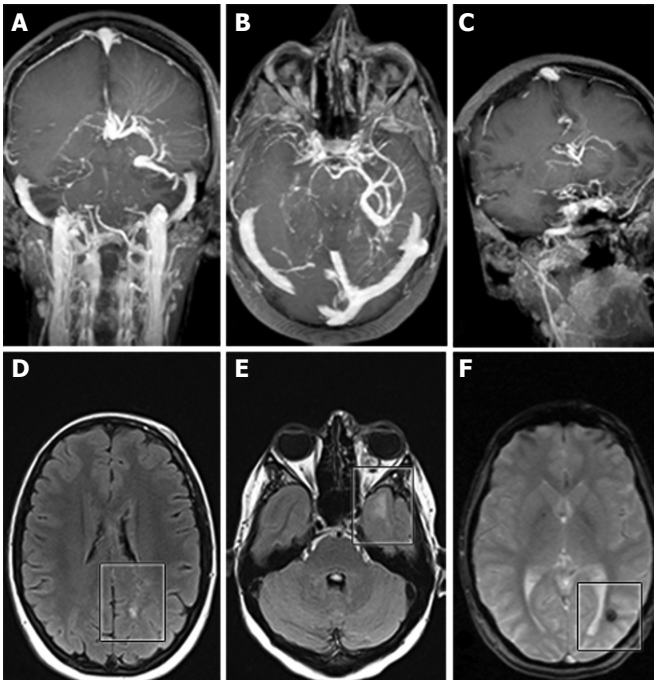

FIGURE 1. MIP reformatted images from contrast-enhanced gadolinium 3D MPRAGE sequences, on coronal **(A)**, axial **(B)** and coronal-oblique **(C)** planes; axial FLAIR **(D, E)** and axial GRE T2* **(F)** images which show three intracranial DVAs of the left hemisphere: a parieto-occipital DVA with deep drainage **(A)**; a DVA with two drainages in the perimesencephalic cistern and in the middle cranial fossa **(B)**, with FLAIR hyperintense signals which suggests gliosis **(D, E)**; a DVA in the fronto-insular region **(C)**, with deep drainage in the vein of Galen; and a cavernous hemangioma in the subcortical occipital lobe.

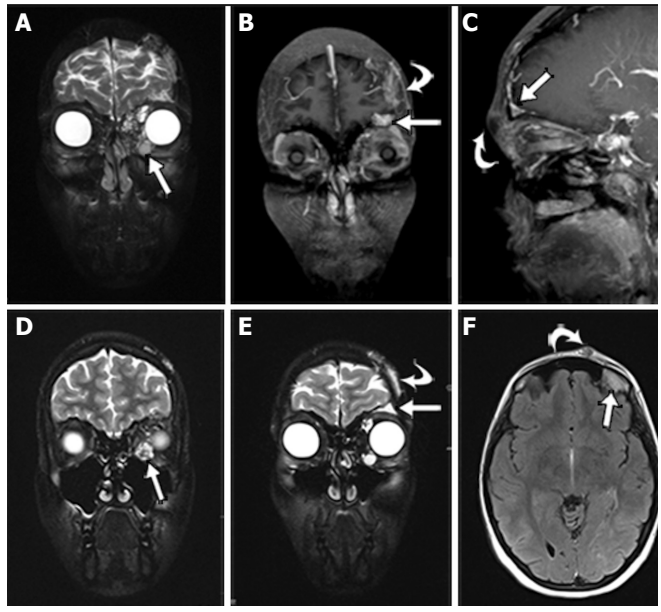

FIGURE 2. MIP coronal T2 fat-suppressed **(A)**, and coronal **(B)** and sagittal **(C)** contrast-enhanced 3D MPRAGE reformatted images. Coronal T2 fat-suppressed **(D, E)** and axial FLAIR **(F)** images. Note a left inhomogeneous T2 hyperintense intra-orbital medial mass, consistent with a slow flow venous-lymphatic congenital anomaly (straight arrow in **A, D)**, that was clinically visible as a lump of the left medial canthus. A bone hemangioma at the roof of the left orbit (straight arrow in **B, C, E, F**), sub-cutaneous fluid retention in the left frontal scalp (curved arrow in **B, E**) and thickening of the subcutaneous tissues in the left fronto-nasal skin (curved arrow in **C, F**).

lights the importance of considering every single little symptom in order to establish an early diagnosis of CVMS.

CASE REPORT

The patient's written, informed consent for publication of MRI data was obtained for the present case report.

A 24-year-old woman with a history of a mild headache, complained a sporadic (at least once a month) serous leakage from the left eye and a small cutaneous protuberance in the left fronto-nasal region, without specific neurological symptoms.

Ophthalmologic examination was negative except for slight conjunctival hyperemia. Three months later, Magnetic Resonance Imaging (MRI) examination of the brain and the orbits, without and with the administration of Gadolinium-Based Contrast Agent (GBCA), showed the presence of three venous developmental abnormalities located in the left hemisphere (Fig. 1).

A sharply hypointense area in the Gradient Echo (GRE) T2* sequence of the subcortical white matter of the left occipital lobe was related to a cavernous hemangioma with haemosiderin deposits (Fig. 1). No dural venous thrombosis was present.

In the left intra-orbital space, at the level of the clinically visible lump of the left medial canthus (Fig. 2, straight arrow in A and D), we observed a T2 hyperintense cystic irregular mass, with peripheral contrast enhancement after gadolinium administration. Moreover, swelling and subcutaneous fluid retention were present in the left frontal side of the scalp (Fig. 2), both findings suggesting a slow-flow mixed venous-lymphatic vascular malformation.

A bone hemangioma was detected in the roof of the left orbit (Fig. 2). MRI findings were in keeping with a CVMS 1-2 syndrome.

The patient was followed-up with an MRI on a yearly basis without relevant changes in the findings. Before each MRI examination, updated information about the safety of GBCA was provided to the patient [4].

DISCUSSION

CVMS and CAMS are complex cranio-facial vascular abnormalities that, in association with other symptoms, may allow to diagnose wider clinical syndromes, respectively, Sturge-Weber and Wiburn-Mason or Bonnet-Dechaume-Blanc [2, 3].

The full expression of Sturge-Weber Syndrome (SWS) is characterized by ipsilateral facial port-wine stains, glaucoma, maxillo-facial and skull base bone hypertrophy, venous and lymphatic malformations and pial cortical venous occlusions. Furthermore, vascular malformations, due to chronic venous stasis, are at increased risk of ischemic damage with consequent atrophy, gliosis and cortical calcifications. Therefore, SWS may clinically manifest as seizures and mental retardation, especially in young patients [5, 6].

The case presented here was not a Sturge Weber Syndrome, but rather a spectrum of CVMS because the facial involvement did not include port-wine stains and brain leptomeningeal venous thrombosis, cortical enhancement, cortical calcifications and enlarged choroid plexus were not present.

Experimentation on avian embryos has shown the metameric genesis of the brain and cranio-facial structures deriving mainly from the neural crest and the neural plate [7].

A somatic mutation in the neural crest region or in the adjacent cephalic mesoderm before migration is expected to produce a metameric pattern of vascular malformations [3, 8].

An incomplete pattern with variable phenotypic expressions is frequent due to different triggers and changing vulnerabilities at different developmental ages [9].

In addition to sharing the territorial distribution, the metameric syndromes have some features typical of angioarchitecture malformations, such as a potential angiogenic trait and progressive expression in time [9].

Among the previously reported paper, Ramli et al. [5] published a case of CVMS 3 with bilateral lymphatic-venous malformation of the mandible, associated with a cutaneous port-wine nevus, consistent with the diagnosis of SWS.

Compared to the case reported by Agid et al. [10], we found a different metameric involvement, CVMS 1-2 instead of CVMS 2-3. Moreover, different from our case, they also observed a very extensive splanchnocranium involvement with a very large orbito-maxillo-facial venous malformation and consequent facial asymmetry. We also noted other several differences, such as that our patient has no mental retardation and seizures, no abnormalities of the dural sinuses, no bilateral cerebellar venous anomalies and no hemiatrophy of the cerebral hemisphere. However, there were some similarities, such as the absence of port-wine stains and the presence of a cavernoma on the same side of all vascular supratentorial anomalies. The last similarity is in contrast with the series of 40 patients with extensive venous malformations of the head and neck, reported by Boukobza et al. [11]. Indeed, they found developmental venous anomalies (DVAs) in eight patients (20%), four of them had multiple intracranial DVAs. One patient (2.5%) had an intracerebral cavernoma but no DVA. None of their patients had both DVAs and cavernomas.

Another type of vascular abnormality potentially involving the association of multiple intracranial and extracranial vascular anomalies is sinus pericranii. This abnormality is characterized by communication between intracranial dural venous sinuses and anomalous epicranial veins. Indeed, Macit et al. [12] described two cases of paediatric patients with the association of sinus pericranii, other cerebrofacial venous anomalies, ocular abnormalities and developmental delay. In the case presented, sinus pericranii was not present.

Among the possible etiological explanations of the syndrome, a non-physiological intracranial venous blood flow, which begins from early embryological stages, may explain the association between CVMS and ipsilateral development of cavernomas, which occurred in our case as well.

Concerning the therapeutic aspects in patients with complete expression of SWS, seizures are present in 55-97% of the cases [13], and the first-line therapy is based on anticonvulsants.

The risk of bleeding in CVMS and CAMS is expected to be significantly low; however, the facial arterio-venous malformations (AVMs) and cavernomas may grow

over time and bleed, as outlined in the case reported by Agid et al. [10].

Treatment is extremely challenging regardless of the technique (surgery, embolization or radiosurgery) and curative attempts often lead to focal neurological deficits since there is normal brain tissue between the abnormal vessels.

In case of haemorrhage, the patient must be treated on an emergency basis, requiring surgical intervention in the most severe cases. Other treatment options are endovascular embolization and radiosurgery [14].

Pre-surgery embolization may allow reducing blood loss, decreasing the size and having access to otherwise surgically inaccessible vessels of the lesion [15]. Most of the cases with this type of brain vascular anomalies do not need surgery or endovascular procedures and the patients should be reassured about the low risk of bleeding. However, if maxillo-facial vascular abnormalities and cavernomas are present, bleeding may occur. Thus, brain MR imaging follow-up with a protocol, including DWI, GRE T2* and MR angiography, is mandatory [16– 18].

According to our experience, in the absence of new symptoms, we suggest a brain MRI follow-up on a yearly basis in such cases.

Conclusion

Here, we have shown a case as a CVMS 1-2. Regarding differential diagnosis, if multiple and ipsilateral vascular anomalies are observed, CVMS and CAMS should be considered, although the phenotypic expression is not characterized by skin port-wine stains and neurological symptoms.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

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