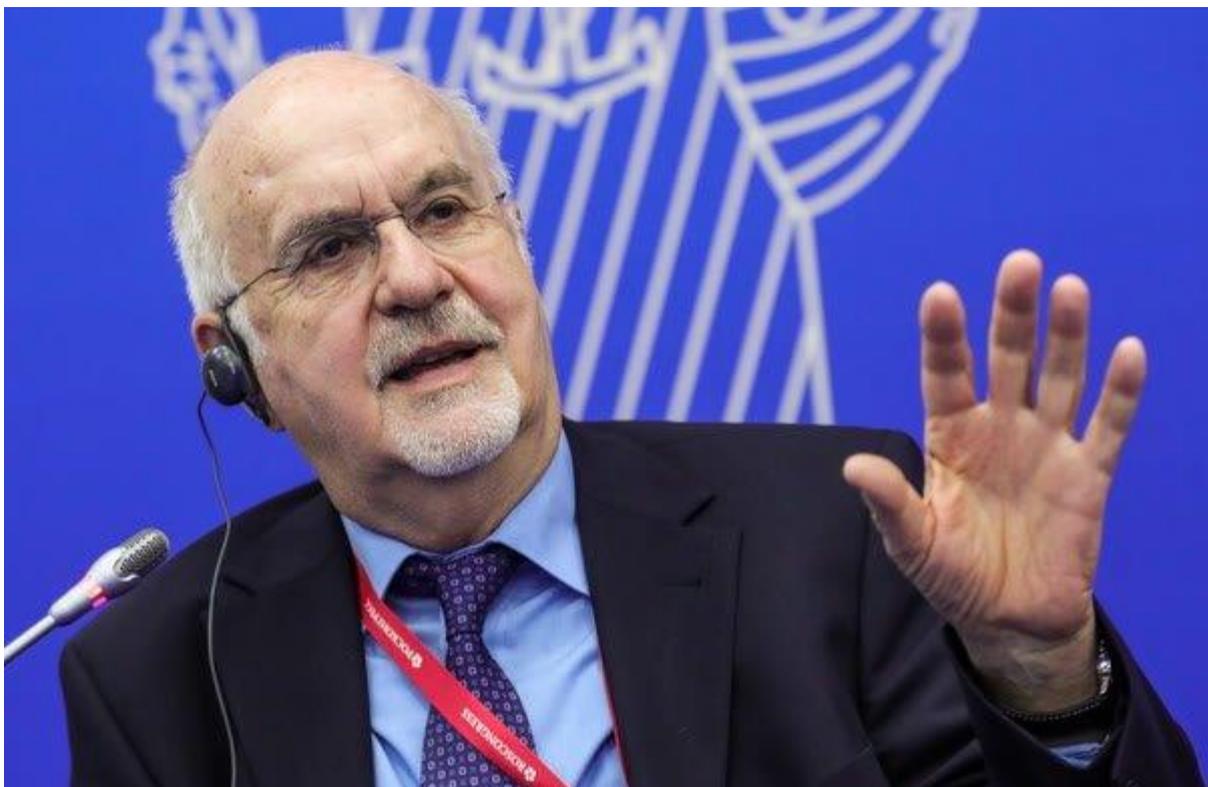


Glaucoma Specialist Blog: The "Glog"

WEDNESDAY, AUGUST 7, 2019

THE FLAMMER SERIES

PART II
FLAMMER SYNDROME



INTRODUCTION

Flammer syndrome (FS) is a cluster of signs and symptoms which can occur in both healthy as well as diseased individuals.

FS is a medical eponym named after Prof Josef Flammer in recognition of his contribution to this field and of his observations leading to the definition of such a phenotype.

FS shows a combination of primary vascular dysregulation tied to characteristic physical and psychological conditions along with some additional signs and symptoms.

PREDISPOSING DISEASES

Although commoner in healthy individuals, FS is associated with certain systemic and ocular diseases. These include:

- Normal tension glaucoma.
- Retinal vein occlusion, in the absence of classical risk factors.

PRIMARY VASCULAR DYSREGULATION

There is often a fluctuation in the demand and supply of blood flow in tissues and organs over time.

The vascular system achieves this through adapting perfusion pressure and by changes in local resistance.

Local resistance is a function of vessel diameter, regulated by the tone of the smooth muscles in these structures.

The contractile cells adapt to changes by receiving crucial inputs from the surrounding tissues, the autonomic nervous system and the vascular endothelium.

The term “vascular dysregulation” encompasses pathological constrictions (spasms), as well as inappropriate vasodilatation (more or less than what is desirable).

Dysregulation in anatomically healthy vessels can also occur secondary to other diseases such as inflammation in other remote organs (Secondary Vascular Dysregulation).

Insufficient or improper adaption of blood flow, despite healthy vessels and in the absence of any causative disease is termed “*primary vascular dysregulation*” (PVD).

The combination of PVD with a cluster of additional signs and symptoms was previously called PVD syndrome. However, to label the entire condition and to avoid confusion, the term Flammer Syndrome was introduced.

In individuals suffering from FS, the blood flow is normal or only mildly altered under baseline conditions, yet it can drastically change in response to stimuli, such as cold or physical/emotional stress.

PHYSICAL AND PSYCHOLOGICAL CONDITION OF PATIENTS SUFFERING FROM FS

FS is commonly seen in the following type of individuals:

- Female sex.
- Slender build.
- Sufferers of systemic hypotension.
- Individuals involved in indoor activities.
- Blue collar workers.
- Asians.
- Persons who are physically and mentally active and successful in their jobs.

The condition manifests itself during puberty and mitigates with age.

Often both parents of the patient also suffer from FS and so an inheritable component is suspected.



SYMPTOMS OF FS

- Cold hands and feet.
- Low blood pressure.

- Prolonged sleep onset time.
- Shifted circadian rhythm.
- Reduced feeling of thirst.
- Increased sensitivity, such as:

Pain sensitivity.

Perception of thunderstorm.

Increased ability to smell.

Increased response to high altitude.

Vibration sensitivity.

Sensitivity to certain drugs is also increased, such as that of:

- Calcium channel blockers.
- Systemic beta blockers.

Subjects suffering from FS can well tolerate these drugs, but only at low doses.

There is often muscular cramps and tinnitus.

Patients with concomitant migraine have increased sense of prodromal symptoms, such as visual aura.

SIGNS OF FS

There is lowered temperature of hands, feet and cornea, while core temperature is normal or even slightly increased.

Blood flow velocity in various organs is either normal or slightly decreased; it often drops significantly when triggered.

On nailfold capillaroscopy, prolonged blood flow cessation after cold provocation is observed.

Blood pressure becomes low on standing or during sleep.

The level of Endothelin-1 in the circulating blood is often slightly increased and endothelin sensitivity is inversely related to BP.

The circadian rhythm is delayed by almost one hour.

Heart rate variability reveals an autonomic imbalance with sympathetic predominance and frequency of silent myocardial ischemia is increased.

Under stress, the skin temperature tends to become more inhomogeneous.

In eyes, the retinal vessels are stiffer, their spatial variability larger and flow mediated vasodilation is reduced.

The autoregulatory responses to increase in IOP or decrease in BP are reduced or absent.

The altered autoregulation explains why in such cases, blood flow correlates with peripheral blood flow.

Patients of FS who also have normal tension glaucoma show increased frequency of:

- Optic disc hemorrhages.
- Increased retinal venous pressure.
- Activation of retinal astrocytes.
- Increased blood flow resistance in retro-ocular vessels.
- Increased oxidative stress.
- Optic nerve compartment syndrome.
- Fluctuating diffuse visual field defects.

DIAGNOSTICS

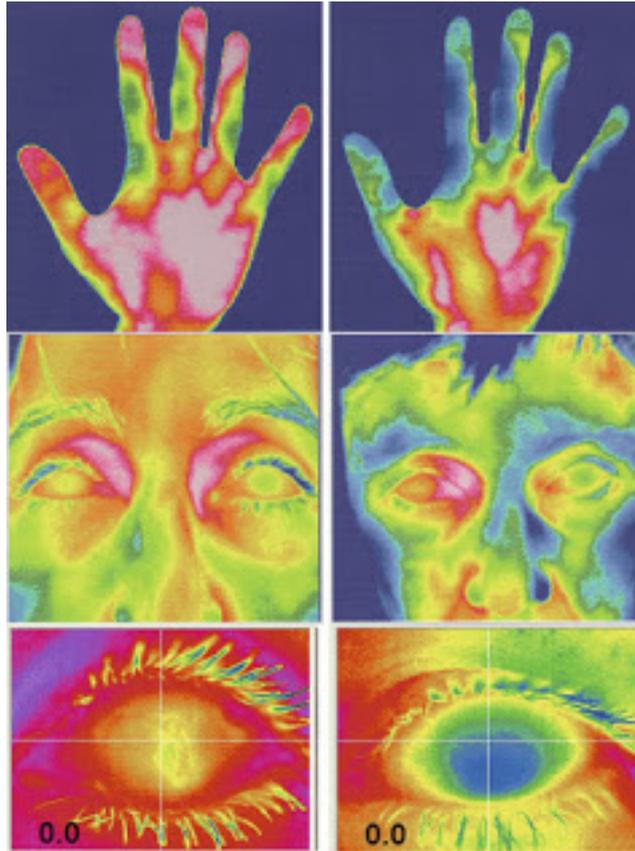
FS is suspected on the basis of classical symptoms such as cold hands or feet.

24-hour BP monitoring is useful to detect systemic hypotension.

Certain special examinations can be performed in selected cases to further aid in diagnosis.

These tests include: dynamic retinal vessel analysis, nailfold capillaroscopy and quantification of gene expression in lymphocytes.

The gold standard for diagnosis is yet to be elucidated.



Thermographic image in FS

TREATMENT

Since FS *per se* is harmless, most subjects do not require any treatment.

However, treatment is necessary if patients develop additional diseases or have annoying symptoms.

The intensity of treatment needs to be individualized.

The management of FS is based on three principles:

- Life-style changes.
- Nutrition.
- Medical therapy.

Life-style changes=

Most subjects with FS are aware of the trigger factors and measures can be taken to avoid those. These include:

- Thermal protection.
- Stress prevention.
- Regular sleep.
- Regular, but not excessive physical activity, including sports.
- Autogenic training or yoga can be tried to improve relaxation.
- While going on high altitude, adequate adaptation time should be given to avoid flaring of the condition.

Nutrition:

- Symptoms of FS inversely correlate with Body Mass Index (BMI).
- Recommend eating enough to avoid extreme slimness.
- Fasting may trigger symptoms and patients should be cautioned.
- In cases where low BP is consistently present, salt and fluid intake can be increased, especially in the evenings to avoid excessive nocturnal dips in BP.
- Supplementation with Omega-3 fatty acids is recommended.
- Mild but repeated decreases in blood flow due to disturbed autoregulation and fluctuation of ocular perfusion pressure leads to an unstable oxygen supply and increased local mitochondrial oxidative stress. Anti-oxidants may counter this stress and help in neuroprotection.

Medical therapy:

Magnesium, a physiological calcium channel blocker, reduces the vasoconstrictive effect of endothelin-1 and improves blood flow regulation.

Recommended dose: 10-20 mmol/day.

Side effects: Diarrhea (which subsides when dose is reduced).

If magnesium alone is insufficient to improve vascular regulation, then a low dose of Calcium channel blockers (nifedipine or amlodipine) can be added.

Low dose of Calcium channel blockers is recommended for the following reasons:

- Low dose has a better effect on regulating blood vessels.
- Subjects with FS have higher sensitivity to drugs.
- In most cases lowering of BP is not advisable.

Oxidative stress to mitochondria can be reduced by addition of ginkgo biloba extract (120 mg per day).

Severe arterial hypotension can be treated with Fludrocortisone (0.1 mg twice per week).

ABOUT THE AUTHOR



Myself **Saleha Hasan** belonging to Samastipur Bihar, India.
I am a final year student of BUMS course at Ajmal Khan Tibbiya College, Aligarh Muslim University, India.

I am mostly interested in searching religious books and correlate with our unani-pathy as natural things are most beneficial for health.

Moreover, I also take interest in creative works like: craft work, poetry, decoration etc. and I also have little bit interest in cooking different kind of dishes.

This is all about me....

This topic, Flammer syndrome, enhanced my knowledge and increased my curiosity to gain and know more about this interesting phenomenon.

Posted by **Syed Shoeb Ahmad**