# TERSON SYNDROME - A REVIEW OF THE CLINICAL, PATHOLOGICAL AND THERAPEUTIC ASPECTS

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***Abstract:*** *The so called "Terson syndrome" is characterized by the association of subarachnoid hemorrhage with its related intraocular bleeding disorder. The authors of this paper aimed at emphasizing the great importance of interdisciplinary collaboration among the medical and surgical specialties in order to improve patient care.*

## INTRODUCTION

The subarachnoid hemorrhage (SAH) implies the presence of blood in the subarachnoid space, caused by traumatic or non-traumatic acute events. The incidence of SAH is estimated to be 10-25 cases/100 000 population.(1,2)

The "Terson syndrome" associates SAH with a related intraocular bleeding disorder.

## PURPOSE

The purpose of this paper is to review the current literature on the clinical, pathological and therapeutic aspects of the Terson syndrome, while emphasizing the importance of multidisciplinary teamwork in patient care.

## MATERIALS AND METHODS

Ophthalmology, neurology and neurosurgery articles and textbooks were consulted with the primary focus based on the Terson syndrome association. The different opinions of these close related specialities were reviewed and a synopsis was formulated.

## RESULTS

The mortality rate in the first 30 days was about 46%. Rebleeding represents the most common complication but also the major cause of morbidity and mortality. About 30% of the patients who survive remain with moderate to severe disabilities.(1,2,3,4)

The SAH can also be primary, or secondary, when the bleeding takes place first in the cerebral parenchyma and later makes way via the pressure gradient to the subarachnoid space. Common non-traumatic SAH etiologies are ruptured cerebral aneurysms, vascular malformations or tumours. 50% of patients with aneurismal SAH have prodromal symptoms usually 6 – 20 days before the acute event. These warning symptoms are headache (97%), hemiparesis, seizures, and cranial nerve palsies (oculomotor nerve palsy, monocular visual loss, quadrantanopsia, facial syndromes affecting the ophthalmic and/or maxillary nerves).(2,3,4,5)

Of all patients with SAH, between 4% to 27% also have intraocular bleeding, usually bilateral. A higher incidence of Terson syndrome is associated with a low Glasgow coma scale, high Hunt and Hess scale.(3,4,5)

**Table no. 1. Common SAH causes (1,2,3,4,5)**

| Common SAH causes | |
|---|---|
| Ruptured aneurysm | 75-80% |
| Traumatic brain injury (TBI) | 15% |
| Vascular malformations | 4-5% |
| Miscellanea (tumours, vasculitis, hematological disorders, drugs) | variable |

This type of bleeding usually develops in 12 days post SAH, although some authors describe the appearance of intraocular hemorrhage after 1 hour. Intraocular hemorrhages can also occur when a rebleeding complication takes place. A correlation between the injured eye and the location of the aneurysm is not well established.(5)

There are many theories which try to explain the pathogenesis of this rare association. One theory holds that blood diffuses through a pressure gradient from the subarachnoid space on way of the optic nerve to the preretinian space. Another possible pathogenic mechanism could be the rupture of the retinal vessels through an acutely increased pressure in the cranial cavity. This makes the outflow of blood from the ocular veins to the cranial cavity difficult, increasing the intraocular pressure and rupturing the retinal blood vessels. The increased pressure in the cranial cavity can damage the peripapilary tissue and the optic nerve structure. There are three types of intraocular bleeding disorders associated with SAH: preretinal – subhyaloid hemorrhage (this type of intraocular hemorrhage is associated with a higher mortality rate), intraretinal hemorrhage and vitreous hemorrhage. The Terson Syndrome causes 5,5% of vitreous hemorrhages. This syndrome regularly develops in adulthood.(5,6)

**Table no. 2. The Glasgow Coma Scale (7,8)**

| Eye opening | Best verbal response | Best motor response |
|---|---|---|
| 4 Spontaneous | 5 Oriented | 6 Obeys commands |
| 3 To Speech | 4 Confused | 5 Localizes pain |
| 2 To pain | 3 Inappropriate words | 4 Withdraws |
| 1 None | 2 Incomprehensible sounds | 3 Abnormal flexion |
| | 1 None | 2 Extension posture |
| | | 1 None |
| **Total GCS: between 3-15** | | |

The usual clinical picture of SAH is a variable

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combination of the following:

- Altered consciousness;
- Very intense headache, the most common symptom (usually the worst headache ever experienced by the patient; 30% of the patients presented ipsilateral headache to the side of the ruptured aneurysm).(2)
- Meningeal irritation signs (photophobia, nuchal rigidity: positive Kernig's or Brudzinski's sign);
- Signs of increased intracranial pressure (projectile vomiting);
- Focal neurological deficits ;
- Seizures;
- Autonomic disturbances.(2)

**Table no. 3. Hunt & Hess grading scale for SAH (7,8)**

| Grade | Signs and symptoms |
|---|---|
| 1 | Asymptomatic or minimal headache and slight nuchal rigidity |
| 2 | Moderate-to-severe headache, nuchal rigidity, no neurological deficit other than cranial nerve palsy |
| 3 | Drowsy, confusion, or mild focal deficit |
| 4 | Stupor, moderate-to-severe hemiparesis, possibly early decerebrate rigidity and vegetative disturbance |
| 5 | Deep coma, decerebrate rigidity |

**Table no. 4. World Federation of Neurosurgical Societies grading system (7,8)**

| Grade | Glasgow Coma Scale | Major focal deficit |
|---|---|---|
| 1 | 15 points | no motor deficit |
| 2 | 13 – 14 points | without deficit |
| 3 | 13 – 14 points | with focal neurological deficit |
| 4 | 7 – 12 points | with or without deficit |
| 5 | <7 points | with or without deficit |

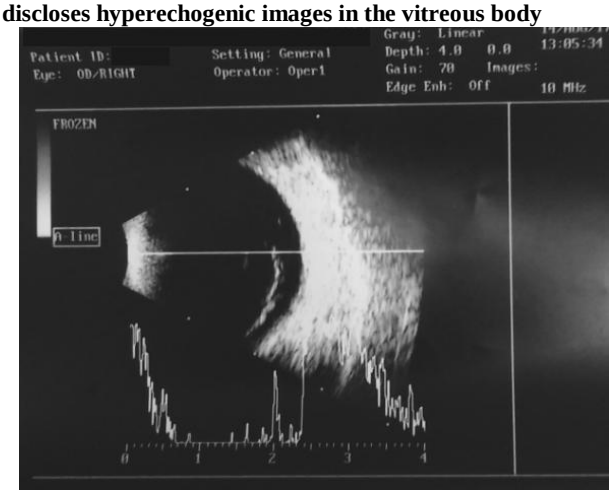
The usual ophthalmologic signs are:

- In the case of a conscious patient, the visual acuity can be decreased unilaterally or bilaterally, with the presence of black spots and/or floaters in the visual field.
- The direct ophthalmoscopy reveals an absent red pupillary reflex, the presence of blood in the vitrous body, and black shadow-like blood clots on a red background.
- Ophthalmoscopically, there are different types of intraocular bleeding patterns: dome-shaped hemorrhages in the macula, or a "double ring" sign in the macula can be seen. The inner ring is caused by the hemorrhage under the inner limiting membrane, while the outer ring is caused by the subhyaloid hemorrhage.(8,9,10)

**Ancillary examinations**

a. Laboratory tests show anemia and possibly coagulation disturbances;
b. Native head tomography (Head-CT) is very sensitive and specific showing spontaneous hyperdense (+40 to +60 Hounsfield units) representing blood in the subarachnoid space, over the convexities or basal and possibly blood in the ventricular system secondary to a rupture of o vessel deep in the cerebral parenchyma;(2,10)
c. The cerebral angiography is the gold standard for detecting the source of bleeding (80-85%) and vasospasm. The Terson syndrome was associated regularly with aneurysms in the anterior circulation of the brain (anterior communicating artery aneurysms).(3,9)
d. The magnetic resonance imaging (MRI) is no more specific than the CT in case of SAH. T1 and T2 sequences reveal isointense signal, while FLAIR sequences show an increased signal in the subarachnoid space. In addition, contrast enhanced MRI can detect the source of bleeding. The most important disadvantage of MRI is the longer scanning time required.
e. The lumbar puncture is of paramount diagnostic value if the native head-CT scan does not reveal the bleeding. The cerebrospinal fluid (CSF) has an intense hemorrhagic appearance in the first hours, followed by an xanthocromic appearance after several hours. Microscopic evaluation of the CSF discloses an increased ratio of erythrocites to leucocytes, similar to the peripheral blood.
f. The cerebral artery transcranian Doppler examinations should be done regularly at 2 day intervals in order to screen for arterial spasm.
g. The ocular ultrasonography using B-mode imaging is useful for ophthalmologists in assessing the presence of hemorrhage in the eye. A hyperechogenic appearance in the vitreous body confirms a bleeding diathesis. By using ocular ultrasound technique, one can evaluate also the integrity of the retina and therefore the prognostication of later visual impairments.(9,10,11,12)

**Figure no. 1. The ocular ultrasound examination in B mode discloses hyperechogenic images in the vitreous body**




The differential diagnosis for the intraocular bleeding disorder can be made with the following:

- Retino-vascular hemorrhages: disruption of the neovascularization in the proliferative type of diabetic retinopathy; central vein occlusion; hypertensive retinopathy;
- Inflammatory and infectious causes of hemorrhages: vasculitis or sarcoidosis.
- Tumoral hemorrhages: choroid tumours (especially melanoma)
- Choroid hemorrhages: choroid neovascularization in the age related degeneration disorder; exudative hemorrhage retinopathy of the choroid.(9,10,11,12)

**Management and treatment options**

The treatment of Terson syndrome is complex. Therefore, interdisciplinary collaboration among ophthalmologists, neurologists, neurosurgeons and general practitioners is vital in order to increase the quality of patient care.

In the acute phase, both medical, supportive and surgical treatment, if indicated, are begun.

The general supportive treatments aim to maintain an optimal cerebral perfusion through adjusting the blood pressure. Body temperature, blood glucose levels, oxygen saturation levels and other vital parameters should be intensely monitored and pathological variations promptly treated. It is still in debate whether prophylactic treatment with antiseizure drugs is efficient and safe, taking into account the higher risk of seizures

in SAH patients. Nimodipine administered in the first 21 days prevents the vasospastic reaction secondary to the SAH.

The neurosurgical treatment aims to repair the primary bleeding site and prevent a secondary hemorrhage. There are two main techniques: endovascular embolization of an aneurysm or vascular malformation and open craniotomy technique with clipping the aneurysm. The factors involved in choosing the optimal technique are: the aneurismal size, morphology and localization, the patient's health status and the general outcome prognosis. Another indication for the neurosurgical intervention is the acute obstructive hydrocephalus, where the surgeon places a shunt in order to drain the CSF out of the ventricles.(13-18)

**The treatment of the associated eye hemorrhage**

As mentioned above, the first step is to evaluate the intravitrean bleeding with the ultrasound examination. Complications like retinal detachment should be operated on upon in order to reduce the risk of blindness.

The general recommendations are to avoid any physical activity, including standing up, coughing or sneezing, for several days, and to maintain the head elevated at 30 degrees. This facilitates the blood sedimentation. Medication that could increase the risk of rebleeding should be interrupted.

The ophthalmologic treatment is begun in parallel with the neurological treatment, while still admitted in the hospital. If no ocular complications occur (such as elevated intraocular pressure, retinal detachment or folds), follow-up consultations should be done weekly, then monthly in the first 6 months. It is also advised to repeat the ocular ultrasound examination in B mode. Most cases (80%) have a good long-term prognosis for vision acuity. They can improve fully in 6 to 12 months time.(1,3,6,9)

Surgical ophthalmological treatment is indicated in retinal detachments, dense intravitrean hemorrhages (which are still present after 3 months from onset), or smaller vitrean hemorrhages in pediatric patients (because of the risk of developing amblyopia), but also in case of secondary glaucoma with iridian neovascularization. The surgical technique implies vitrectomy pars plana, with the excision of the hemorrhagic vitreous, excision of the bridles and the preretinal fibrosis, retinal stabilization, and if retinal detachment is associated, it is recommended to stabilize the retina with perfluoropropane gas injection. Alternatives are hexafluoride sulfurus or silicon gel. The retinal ruptures can be treated using LASER photocoagulation or cryotherapy.(3,9)

**The general complications of SAH**

In the first 24 hours from onset of the SAH, the risk of rebleeding is maximal. About 50% of patients with SAH suffer secondary hemorrhages in the next 6 month. The patients with a high Hunt & Hess severity scale have the bleeding risk increased. The surgical or endovascular treatment can prevent rebleeding.(2)

The obstruction of CSF flow in the ventricular system, secondary to the blood clots, can determine an acute internal hydrocephalus. Factors associated with a high risk of developing acute hydrocephalus are: elderly patients, hypertension at time of admission, posterior circulation aneurysms, low Glasgow Coma Scale and hyponatremia. Ventriculostomy should be taken into consideration for patients with positive CT signs for acute hydrocephalus. It is recommended that the intracranial pressure should be monitored and kept between 15 and 25 mmHg. A study showed improvement in 80% of patients after ventriculostomy.(2)

Blood in the subarachnoid space can determine the presence of vasospastic reaction in the cerebral arteries. If the vasospasm is not immediately treated, ischemia supervenes. It is common practice to screen patients for new neurological deficits and reexamine the cerebral vessels using ultrasound or cerebral angiography. This is important for the early diagnosis and treatment of the vasospastic reaction. High velocities on ultrasound can signify a vasospastic reaction.(2)

The arterial narrowing, or vasospastic reaction, can have an early onset (in the first hours), or can be delayed (between the $4^{th}$ and $14^{th}$ day). 30 to 70% of the angiographies revealed cerebral vasospasm after 7 days of SAH, but only 20-30% of these patients where symptomatic.(2)

As mentioned above, Nimodipine is administered to prevent this reaction. The so called "triple H therapy", hypervolemia, hypertension and hemodilution could be taken into account only after securing neurosurgically the site of hemorrhage.

**Table no. 5. The Fisher Grading System (higher grade means a higher risk for vasospasm) (7)**

| Grade | CT scan |
|---|---|
| 1 | No blood detected in the subarachnoid space |
| 2 | Diffuse or <1 mm of blood |
| 3 | Localized clot or >1 mm of blood |
| 4 | Intracerebral or intraventricular clots with diffuse blood in the subarachnoid space |

Another complication of SAH is the increased secretion of ADH (antidiuretic hormone), which leads to increased water reabsorbtion and hyponatremia**.** Cardiovascular complications with electrocardiogram disturbances cand occur in the acute phase. Cardiac disturbances are associated with a high simpatethic tone, which can cause subendocardial ischaemia or coronar vasospasm. A cardiologic consult is advised.(2,17,18)

To all these possible complications of the SAH, deep vein thrombosis, pulmonary infections, pulmonary edema, decubitus ulcers, urinary infections, and so on can complete the clinical picture.(17)

**The ocular complications**

Hemosiderosis bulbi can occur secondary to the bleeding in the vitreous body. Hemoglobin releases iron, which has a toxic effect on the retinal receptor cells. Massive intraocular bleeding does not reabsorb completely. This is why the so called "Ghost cell glaucoma" can develop later, when distorted cells migrate to the trabecule (4% in Terson syndrome). Another mechanism for glaucoma is the obstruction of the trabecule from the debris of hemolysis.(13,14,15,16)

The retinal detachment is yet another complication which can lead to blindness, approximately 9% of the cases. Detachment occurs when vessel proliferation in the retina occurs.

The most common eye complication of the Terson syndrome is the epiretinal membrane formation, with an incidence of 15-78%.(13,14,15,16)

## DISCUSSIONS

The physician's most important duty is patient care. For this reason, the interdisciplinary collaboration among ophthalmologists, neurologists, neurosurgeons and general practitioners is of paramount importance in order to improve patient care and good outcome.

Even in the face of life threatening SAH, an ophthalmologist's consult is important in order to prevent vision loss if an ocular complication is to accompany the disease.

The Terson syndrome is commonly described as being an association of SAH with a intraocular bleeding disorder. It has been shown that also other intracranial hemorrhages both traumatic and nontraumatic can determine the "Terson duet", although SAH is the most common association with the

intraocular bleeding. The associated intraocular bleeding occurs in 8-19.3% of patients with SAH, 9.1% of patients with intracerebral hemorrhages and 3.1% of patients with traumatic brain injuries.

## CONCLUSIONS

If the Terson syndrome is overlooked, the patient's quality of life is low due to blindness. The complex approach of monitoring and treating the patient with SAH must be individualized for each patient.

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