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Terson sign: from the eponym to emergency neurosurgery – a review

Sinal de Terson: do epônimo à emergência neurocirúrgica- uma revisão

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Abstract

Terson's sign (TS) is classically defined as vitreous hemorrhage associated with subarachnoid hemorrhage of aneurysmal origin, being an important predictor of severity, indicating greater morbidity and mortality when compared to patients without the sign. The objective of this study is to review the relationship of Terson syndrome/Terson sign with the prognosis of aneurysmal subarachnoid hemorrhage. A search for original articles, research and case reports was performed on the PubMed, Scielo, Cochrane and ScienceDirect platform, with the following descriptors: Terson sign and subarachnoid hemorrhage. Retrospective, prospective articles and case reports published in the last 5 years and which were in accordance with the established objective and inclusion criteria were selected. Ten (10) articles were selected, in which the available results show an unfavorable prognostic relationship of TS and subarachnoid hemorrhage, because these patients had a worse clinical status assessed on the Glasgow scales ≤ 8, Hunt & Hess > III, Fisher > 3, in addition to intracranial hypertension and location of the aneurysm in the anterior communicating artery complex. The early recognition of this condition described by Albert Terson in 1900 brought an important contribution to neurosurgery, being recognized until nowadays.

Keywords**:** Terson's sign; Intracranial aneurysm; Vitreous hemorrhage

Resumo

O sinal de Terson (ST) é definido classicamente por hemorragia vítrea associada à hemorragia subaracnóidea de origem aneurismática, sendo um importante preditor de gravidade, indicando maior morbimortalidade quando comparado aos pacientes sem o sinal. O objetivo deste estudo é revisar a relação entre síndrome de Terson/sinal de Terson e o prognóstico da hemorragia subaracnóide aneurismática. Foi realizada uma busca de artigos originais, relatos de casos e revisões na plataforma PubMed, Scielo, Cochrane e ScienceDirect, com os seguintes descritores: sinal de Terson e hemorragia subaracnóidea. Foram selecionados os artigos retrospectivos, prospectivos e relatos de caso publicados nos últimos 5 anos e que estivessem de acordo com o objetivo estabelecido e critérios de inclusão. Foram selecionados 10 artigos, nos quais os resultados disponíveis mostram uma relação prognóstica desfavorável do ST e hemorragia subaracnoide, em razão destes pacientes terem apresentado pior estado clínico quando avaliados nas escalas de Glasgow ≤ 8, Hunt e Hess > III, Fisher > 3, além da hipertensão intracraniana e localização do aneurisma no complexo da artéria comunicante anterior. O reconhecimento precoce desta condição descrita por Albert Terson em 1900 trouxe importante contribuição para a neurocirurgia, sendo reconhecido até hoje.

Palavras-chave**:** Sinal de Terson; Aneurisma intracraniano; Hemorragia vítrea.

Introduction

Albert Terson was born in 1867 in the French city of Toulouse. Since the time of the Lycée School, Terson has demonstrated his intellectual development and relationship with science, being most notorious when he entered the Faculty of Medicine of Toulouse.[1] He was the first to describe in 1900 about vitreous hemorrhage as a consequence of intracranial bleeding in a chapter published in the Ophthalmology clinic: *De l'hémorragie in the corps vitré au cours of l'hémorragie cérébrale*. Later, in 1926, he published in *Annales d'Oculistique*: The syndrome of hematoma of the vitré body and spontaneous intracranial hemorrhage.[2]

Terson's sign or Terson's syndrome (TS) is classically defined by vitreous hemorrhage (retinal, sub-internal limiting membrane and sub-hyaloid) associated with subarachnoid hemorrhage (SAH) of aneurysmal origin, most commonly from the anterior communicating artery or the carotid artery and its branches[3,4], and may be present in up to 40% of patients and is linked to its prognosis. [4]

This important predictor of severity in patients affected by SAH is characterized by vitreous hemorrhage (retinal, sub-internal limiting membrane and sub-hyaloid) associated with subarachnoid hemorrhage.[5] It indicates greater morbidity and mortality when compared to patients without the syndrome. [5]

The objective of this study is to review this relationship of Terson syndrome/Terson Sign with prognosis SAH.

Method

The bibliographic search was carried out on the Scielo and PubMed search platform and on the Cochrane and ScienceDirect database in the period from March to April 2020, using the crossing of the descriptors: terson's sign AND subarachnoid hemorrhage; terson sign AND subarachnoid hemorrhage.

Initially, after the execution of the descriptors, the inclusion criteria were applied: (I) original articles, research and case reports published in the last 5 years; (II) studies on the relationship of Terson syndrome/Terson sign and SAH prognosis; (III) written in Portuguese, English or Spanish.

In a total of 36 articles found, in the PubMed platform 19 articles, in Scielo 2 articles, in ScienceDirect 15 articles and in Cochrane no articles. The manual search resulted in 4 articles. Of the 40 articles found and selected based on the title, abstract and inclusion criteria, 10 studies were chosen.

Results

The results found from the 10 articles are seen in Table 1 demonstrated as follows: author/year, method including the sample and type of study, and results.

Most studies are retrospective. The majority evidenced a correlation of Terson syndrome/Terson sign and the unfavorable prognosis in patients with SAH, because they have unfavorable clinical conditions since admission to their evolution.

Discussion

Approximately 85% of cases of non-traumatic subarachnoid hemorrhage result from an aneurysmal event, with a mortality rate between 8.3% and 66.7%. [6,7] The subarachnoid hemorrhagic event has a variable peak from 50 to 60 years, six times more frequent in women, influenced by hormone estrogen levels, mainly after menopause. There are modifiable risk factors (alcoholism, smoking and hypertension) and non-modifiable risk factors (female sex, oriental origin, increased age and a history of aneurysm) for the development of SAH. Among the factors, hypertension, size, irregularity and location of the aneurysm, oriental origin and age are associated with a higher incidence of ruptured aneurysms. [7]

It is estimated that 13% of patients remain with a significant degree of neurological and cognitive impairment, affecting quality of life. Patients with low Glasgow score or modified Rankin scale, advanced age, hypertension, aneurysm of larger size and present in the posterior circulation and amount of blood in the subarachnoid space, were associated with unfavorable results. In 1900, Terson, when describing his sign of vitreous hemorrhage, made this association with severity and prognosis.[7,8]

Table 1. Result of selected studies.

Citation	Methods	Result
Joswig et al.[9]	Retrospective study with 36 patients.	All with TS showed pathological ICP values > 20 cmH_2O. Patients with aSAH of the anterior cerebral artery complex were ten times more likely to suffer from TS, 45 times higher mortality and significantly higher neurological morbidity over the 3-month period.
Czorlich et al.[10]	Retrospective analysis of 213 patients who suffered SAH and investigation for TS.	The ST rate in this study was 23.9% (51), associated with GCS ≤ 7, HH degree, Fisher's grade IV, initial unconsciousness, intracerebral hemorrhage and an increase in intracranial pressure of ≥ 25mmHg. TS patients had higher mortality and greater risk of worse long-term outcome.
Moteki et al.[11]	Cross-sectional study of 343 patients with non-traumatic SAH.	22 patients had TS (6.4%). The presence of eye movement disorders and ST occurred more frequently in patients with dissection of vertebral artery aneurysm.
Hong et al.[12]	Retrospective with 22,864 patients with treated SAH.	196 cases of TS, of these 93 (47.4%) in males and 103 (52.6%) in females. There was no significant difference in mortality rates between patients with TS and those without (4.08% and 7.30%, respectively) and in the age group, but the incidence was higher in patients < 40 years. The mortality rate was 4.08% over a 5-year period.
Kang et al.[5]	Retrospective and interventionist with 31 patients with aneurysmal SAH.	10 (32.3%) of the patients had TS in the absence of visual symptoms and had a significantly worse grade GCS and HH than those without, with the exception of the Fisher scale. There was no significant difference in mRS at 6 months.
Stewart et al.[13]	Prospective study with 117 patients with aneurysmal SAH	The general incidence of ST was 24.9% (29). Compared to patients without ST, those with ST had the lowest mean GCS score (8.66 ± 4.97 vs 12.09 ± 1.10) and the highest degree of Fisher's hemorrhage. The increasing sign of CT was present in 7 patients (6.0%), 6 (5.1%) of whom had high-risk TS. 88 (75.1%) did not have TS among the 110 patients with no sign of CT.
Lee et al.[14]	Case report of a 45-year-old patient with a history of subarachnoid hemorrhage who suffered from blurred vision.	The patient presented visual acuity of 30 cm in the right eye and 0.6 in the left eye when counting the fingers. CT and MRI did not show changes in the visual pathways. The fundus and ocular ultrasound showed vitreous hemorrhage in the right eye.
Citirik et al.[15]	Case reports.	Patients presented a reduction in visual acuity after 6 to 8 months of SAH and vitreous hemorrhage on examination with an ocular slit lamp.
Ren et al.[16]	Case report, 42-year-old man, coma after aneurysmal rupture of the left posterior communicating artery.	CT showed SAH and bilateral background hemorrhage. Visual evoked potential and ocular ultrasound showed vitreous hemorrhage compatible with TS.
Munteanu et al.[17]	To report a case of a 34-year-old woman with aneurysmal subarachnoid hemorrhage and bilateral Terson syndrome.	Examination of the fundus, reduced visual acuity, and ocular ultrasound revealed vitreous hemorrhage in both eyes.

Subtitle: ICP = intracranial pressure; aSAH = aneurysmal subarachnoid hemorrhage; GCS: Glasgow coma scale; TS= Terson syndrome; HH = Hunt & Hess; CT = computed tomography; mRS = modified Rankin scale; MRI = magnetic resonance imaging.

Terson's syndrome has its pathophysiology uncertain. There are two possible pathophysiological mechanisms for TS. One of them explains that the blood originating from HSA enters the vitreous space through the optic nerve, penetrating the sclera's crusty lamina. [18] The second mechanism is that in the presence of SAH there is a sudden and transient increase in intracranial pressure (ICP), diffused by the sheath of the optic nerve, which is derived from the three layers of meninges. Therefore, the cerebrospinal fluid or blood moves in the intraorbital subarachnoid space, compressing the central retinal vein and reducing drainage by venous hypertension that causes stasis and intraocular hemorrhage.[2,3,5,4,19,20,21]

The evidence of TS is considered a risk factor for higher morbidity and mortality compared to patients with SAH without TS. [12] Such risk is present in patients with severe neurological disease, characterized by widely used scales - Glasgow Coma Scale (GCS) ≤ 8, Fisher ≥ 3 or Hunt & Hess (HH) > III, WFNS score , initial unconsciousness, increased ICP and SAH originating in the left hemisphere. [10,12,22,24]

These scales have the purpose of evaluating and measuring the neurological condition, through clinical or radiological examination, helping in the recognition and prognosis.

Joswig et al retrospectively evaluated 36 patients with TS and all presented intubation and coma at hospital admission and unfavorable clinical evaluation by the World Federation of Neurosurgical Societies (WFNS) and HH scale. Patients with TS were more likely to develop increased ICP (mean initial ICP of 26 ± 6.9 mmHg vs non-TS 15 ± 5.8 mmHg), in some ventriculostomy was performed and all showed unsatisfactory results in the follow-up. [9] 56.9% of the cases analyzed by Czorlich P. et al had an ICP > 25 mmHg. However, some patients had a pathological increase in ICP, favorable results and did not develop TS, a fact reported in both studies. [9,10,16]

In the systemic review carried out by McCarron et al., the number of TS cases in patients with SAH ranged from 3% (retrospective) to 13% (prospective). Most patients have bilateral vitreous hemorrhage, with the most prevalent aneurysms in the anterior circulation. [9,11,22,23] The mean age was 55.2 years in patients with TS compared to 52 years for patients without TS and there was no significant difference regarding sex. The HH scale was higher in patients with TS, with an increased risk of mortality of 4.8 times in patients. [23]

In another prospective clinical study, Fountas et al found a 28.6% mortality rate in patients with TS versus 2% without the syndrome. Again, most patients had GCS < 8, HH > III, WFNS score > III and Fisher > 3 on admission and there was no significant difference between genders. [22,24] As for the location of the aneurysm and the relationship with vitreous hemorrhage, patients generally had aneurysm of anterior communicating artery (Acom), however there was no considerable difference between the occurrence of Terson's hemorrhage and the size of the aneurysm, the incidence was similar in aneurysms various. [9,22,23] Joswig et al, found a higher incidence in segments A1, A2 and Acom in the anterior cerebral artery system. [9] Patients with ruptured aneurysms in this complex were ten times more likely to experience TS compared to patients who had aneurysms in other regions.[9] Furthermore, the presence of bilateral and unilateral hemorrhages was not associated with a worse visual prognosis, with vitreous hemorrhage occurring up to 47 days after the event in patients with SAH. [9,22]

The detection of TS has its limitations due to the low sensitivity of the gold standard method for diagnosis, fundoscopy, which should be performed in all patients with SAH regardless of the clinical state in which they are admitted, especially those with a degree of HH > 3 on admission. [5] Ophthalmic screening for TS is not considered a routine exam, so it remains a devalued disease with a prevalence of 40% in patients with intracranial hemorrhage. [5] Kang et al. observed that 32.3% of patients with TS denied any visual symptoms during diagnosis. [5]

Regarding the early detection of TS, the right time has not yet been characterized, but most cases are identified in the initial 24 hours after SAH[25], and some reports of 72 hours or even weeks after the hemorrhagic event.[2,4,21] Thus, patients must have an ophthalmological evaluation performed and serialized during the hospitalization period and after discharge. [25]

In a secondary evaluation, TS should be confirmed with cranial tomography and ocular ultrasonography.[10] Tomography, according to Fountas et al, presented in most patients with TS increasing retinal hyperdensity and nodularity, however, these findings are often subtle and neglected or misdiagnosed, especially in the most severe patients. [22] In contrast, Stewart et al, in their prospective study, found an increased signal sensitivity (presence of significant sub-internal limiting hemorrhage of the membrane) on CT for the diagnosis of TS in 85.7% high-risk patients and 99.1% specificity. [13] Kang et al, reports that other conditions, such as leukemia, can lead to retinal hemorrhage, suggesting a simultaneous pathogenesis with Terson's syndrome. [5]

Conclusion

Terson's syndrome is a clinical condition that results in higher rates of morbidity and mortality and is related to a worse prognosis when found. Its true prevalence is questionable due to the lack of early identification and thorough eye examination. Early recognition of TS is of paramount importance because vitreous hemorrhage can lead to reduced visual acuity and in the future functional blindness, delaying the rehabilitation process. Furthermore, the finding of TS can help in the prognosis of patients affected by SAH in a coma.

Albert Terson brought an immeasurable contribution to neurosurgery and today we know that the identification of intraocular hemorrhages is not only related to cases of intracerebral hemorrhages, it can also be associated with other neuropathologies such as epidural injections, post-surgery, neuroendoscopic procedures, among others. Attention should be paid to patients with TS due to the clinical severity in which they are and continuously neglected and underdiagnosed. [25]

References

1. Rochon-Duvigneaud A (1935) Albert Terson. Le Progrés Médical. Paris, 91-94.

2. Shaw HE, Landers MB (1975) Vitreous Hemorrhage after Intracranial Hemorrhage. American Journal of Ophthalmology, Durham, 80(2):207-213.

3. Khan SG, Frenkel, Marcel (1975) Intravitreal Hemorrhage Associated with Rapid Increase in Intracranial Pressure (Terson's Syndrome). American Journal Of Ophthalmology, Chicago, 80(1):37-43.

4. Biousse V, Newman NJ (1999) Aneurysms and Subarachnoid Hemorrhage. Neurosurgery Clinics Of North America, Atlanta, 10(4):631-651.

5. Kang HM, Cho JM, Kim SY, Choi JH (2020) Clinical characteristics of asymptomatic Terson syndrome in the patients with aneurysmal subarachnoid hemorrhage. Int J Ophthalmol, 13(2):292-300.

6. Ambrosi PB, Ambrosi CB, Alencar I, Azevedo Filho H (2018) Prejuízos neurocognitivos na hemorragia subaracnóide aneurismática no pré e pós operatório. Jbnc - Jornal Brasileiro de Neurocirurgia, 20(4):425-432.

7. Macdonald RL, A Schweizer T (2017) Spontaneous subarachnoid haemorrhage. The Lancet, Toronto, 389(10069):655-666.

8. Rouanet C, Silva GS (2019) Aneurysmal subarachnoid hemorrhage: current concepts and updates. : current concepts and updates. Arquivos de Neuro-psiquiatria, São Paulo, 77(11):806-814.

9. Joswig H, Epprecht L, Valmaggia C, Leschka S, Hildebrandt G, Fournier JY, Stienen MN (2016) Terson syndrome in aneurysmal subarachnoid hemorrhage-its relation to intracranial pressure, admission factors, and clinical outcome. Acta Neurochir (Wien), 158(6):1027-36.

10. Czorlich P, Skevas C, Knospe V, Vettorazzi E, Westphal M, Regelsberger J (2016) Terson's syndrome - Pathophysiologic considerations of an underestimated concomitant disease in aneurysmal subarachnoid hemorrhage. J Clin Neurosci, 33:182-186

11. Moteki Y, Niimi Y, Okada Y, Kawamata T (2018) Ruptured Vertebral Artery Dissecting Aneurysm as a Risk Factor for Ocular Symptoms Accompanied with Subarachnoid Hemorrhage. World Neurosurg, 116:505-512.

12. Hong EH, Seong M, Yeom H, Choi S, Choi KS, Kang MH, Cho H, Shin YU (2019) Incidence of Terson Syndrome in Treated Subarachnoid Hemorrhage in South Korea: a National Health Insurance Database Study. Sci Rep, 9(1):19048.

13. Stewart MW, Hasan SA, Collins C, Stanko C, Summer J, Braziz PW, Tawk R, Freeman WD (2020) Can Baseline Computed Tomography Scans Be Used to Identify Patients at High Risk of Vision Loss due to Terson Syndrome? American Journal Of Ophthalmology, Jacksonville, 211:217-228.

14. Lee SH, Seo JH, Park SH, Won YH, Ko MH (2015). Terson Syndrome in Aneurysmal Subarachnoid Hemorrhage: A Case Report. Ann Rehabil Med, 39(4):640-4.

15. Citirik M, Tekin K, Teke MY (2019) Terson syndrome with persistent vitreous hemorrhage following traumatic brain injury. Saudi J Ophthalmol, 33(4):392-397.

16. Ren Y, Wu Y, Guo G(2018). Terson syndrome secondary to subarachnoid hemorrhage: a case report and literature review. World Neurosurgery, S1878-8750(18)32907-3.

17. Munteanu M, Rosca C, Stanca H(2019) Sub-inner limiting membrane hemorrhage in a patient with Terson syndrome. Int Ophthalmol, 39(2):461-464.

18. Hanai K, Hashimoto M, Sasaki M, Nakamura H(2020) Microsurgical observation of the posterior vitreous in patients with vitreous hemorrhage caused by Terson syndrome. American Journal Of Ophthalmology Case Reports, Sapporo, 17:100613.

19. Castrén JA (1963) Pathogeneses and treatment of terson-syndrome. Acta Ophthalmologica, Finland, 41(4):430-434.

20. Medele RJ, Stummer W, Mueller AJ, Steiger H, Reulen H(1998) Terson's syndrome in subarachnoid hemorrhage and severe brain injury accompanied by acutely raised intracranial pressure. Journal Of Neurosurgery, Munich, 88(5):851-854.

21. Pfausler B, Belcl R, Metzler R, Mohsenipour I, Schmutzhard E(1996) Terson's syndrome in spontaneous subarachnoid hemorrhage: a prospective study in 60 consecutive patients. Journal Of Neurosurgery, Innsbruck, 85(3):392-394.

22. Fountas KN, Kapsalaki EZ, Lee GP, Machinis TG, Grigorian AA, Robinson JS, Vergados I, Theodosiadis PG(2008) Terson hemorrhage in patients suffering aneurysmal subarachnoid hemorrhage: predisposing factors and prognostic significance. : predisposing factors and prognostic significance. Journal Of Neurosurgery, 109(3):439-444.

23. Mccarron, MO(2004) A systematic review of Terson's syndrome: frequency and prognosis after subarachnoid haemorrhage. : frequency and prognosis after subarachnoid haemorrhage. Journal Of Neurology, Neurosurgery & Psychiatry, Londonderry, 75(3):491-493.

24. Fonseca APA, Rosa Júnior M (2017) Terson's syndrome: an important differential diagnosis of subarachnoid hemorrhage. : an important differential diagnosis of subarachnoid hemorrhage. Radiologia Brasileira, Vitória, 50(5):346-347.

25. Costa BL, Ferreira FM, Barbosa A, Lopes JL, Lopes A (2013) Terson's syndrome: neurosurgical considerations on the subject of a rare case with ophthalmological sequelae. Arquivos Brasileiros de Neurocirurgia: Brazilian Neurosurgery, Coimbra, 32(2):114-117.

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