Comparison of CT and clinical findings of Terson’s syndrome in 121 patients: a 1-year prospective study

Clinical article

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Object. Terson’s syndrome (TS) is a vitreous hemorrhage in association with subarachnoid hemorrhage (SAH). Its diagnosis is often delayed, which may result in vision loss secondary to treatable conditions. Methods to hasten early diagnosis and consequent ophthalmic referral are desirable. The aims of this study were 1) to assess the specificity and sensitivity of conventional head CT for diagnosing TS in patients with aneurysmal SAH (aSAH); and 2) to determine the incidence of TS and its association with age, sex, aSAH severity, and overall mortality.

Methods. Patients admitted to Helsinki University Central Hospital who underwent surgery or endovascular treatment for a ruptured intracranial aneurysm during 2011 were participants in this prospective study. They underwent serial dilated fundoscopic examinations during a 6-month period. Two radiologists independently reviewed ocular findings suggestive of TS on conventional CT head scans obtained in all patients as a routine diagnostic procedure. Associations between TS and relevant clinical, radiological, and demographic data were analyzed with uni- and multivariate logistic regression.

Results. Of 121 participants, 13 (11%) presented with TS, and another 22 (18%) with intraretinal hemorrhages. For reviewing CT head scans, the overall observed agreement between the 2 raters was 96% (116 of 121 cases), with a substantial k of 0.69 (95% CI 0.56–0.82). The sensitivity of the CT findings for TS was 42%, and the specificity was 97%. Associations of the World Federation of Neurosurgical Societies (WFNS) and Hunt and Hess grades on admission, the presence of intracerebral hemorrhage, female sex, and aneurysm length with TS were all statistically significant. Logistic regression demonstrated that sex and WFNS grade were independently associated with TS and provided the best fit to the data.

Conclusions. Routinely looking for TS findings in CT head scans may prove valuable in clinical practice. Terson’s syndrome is associated with female sex and poor clinical condition on admission. (http://thejns.org/doi/abs/10.3171/2014.2.JNS131248)

Key Words • subhyaloid hemorrhage • ruptured intracranial aneurysm • vascular disorders

Terson’s syndrome (TS) is a vitreous hemorrhage in association with subarachnoid hemorrhage (SAH).33 Its incidence in patients with SAH ranges from 5% to 27%,4,7–9,18,22,23,27–29 and TS correlates with worse clinical condition and in some studies with higher mortality rates.1,18,22,28,29 Complications of intraocular hemorrhages are diverse, and in many cases prompt ophthalmic care is necessary to prevent permanent vision loss secondary to treatable conditions, especially proliferative vitreoretinopathy and retinal detachment.31,25,34 Patients with bilateral TS can be functionally blind, and early vitrectomy is often necessary to hasten visual recovery.11 Moreover, impairment of binocular depth perception after vision loss in one eye may slow rehabilitation and increase patients’ risk for accidents.

In cases of aneurysmal SAH (aSAH), referral to an ophthalmologist in most departments is not routine, and only patients complaining of visual disturbances undergo a fundoscopic examination. Patients may, however, suffer from cognitive impairment preventing them from noticing and expressing any visual problems. Radiologists do not systematically seek features of TS on CT head scans and may not even be aware of this phenomenon. A few retrospective case reports or series of subhyaloid hemorrhages detected on CT of the brain do exist, but systematic prospective evaluation of its usefulness is lacking.1,2,15,24,30

The purpose of this prospective study was twofold:

Abbreviations used in this paper: aSAH = aneurysmal SAH; CTA = CT angiography; DSA = digital subtraction angiography; ICH = intracerebral hemorrhage; MRA = MR angiography; mRS = modified Rankin Scale; OR = odds ratio; SAH = subarachnoid hemorrhage; TS = Terson’s syndrome; WFNS = World Federation of Neurosurgical Societies.
CT and Terson’s syndrome

1) to assess the specificity and sensitivity of conventional head CT scans for diagnosing TS in patients with aSAH; and 2) to determine the incidence of TS and its association with age, sex, aSAH severity, and overall mortality in Finland.

Methods

All consecutive patients with a ruptured intracranial aneurysm who were admitted for surgical or endovascular treatment to the Department of Neurosurgery, Helsinki University Central Hospital, during 2011 were participants in this prospective study. All patients with aSAH within our catchment area in southern Finland (population 1.8 million) are treated in our department without selection bias. Foreign-resident patients were excluded from the study because of obvious difficulties in arranging the long-term follow-up. Diagnosis of aSAH was established by CT, MRI, lumbar puncture, or a combination of these, and associated aneurysms were evaluated using CT angiography (CTA), MR angiography (MRA), digital subtraction angiography (DSA), or a combination of these modalities. We did not make any changes to the CT protocol for patients with aSAH at our institute for this study, and all CT scans were medically indicated.

This study was approved by the University of Helsinki ethics committee.

On admission, evaluation from the radiological images (R.K.) included locations and dimensions of the aneurysms, severity of aSAH on the Fisher scale, and presence of any intracerebral hemorrhage (ICH) or hydrocephalus. The clinical severity of aSAH was evaluated based on the World Federation of Neurosurgical Societies (WFNS) and Hunt and Hess scales. We also graded clinical outcomes at 6 months after the aSAH using the modified Rankin Scale (mRS).

Dilated fundoscopy with indirect ophthalmoscopy was performed by an ophthalmologist (E.K.) postoperatively within 3 days of admission or immediately after clinical consent by the attending neurosurgeon. The next follow-up visit for patients cooperating adequately was at the neuro-ophthalmology service at discharge. All patients underwent follow-up assessments 2–4 months and 6 months postoperatively. Best corrected visual acuity testing and dilated fundoscopy took place at every visit.

Intraocular hemorrhages were classified as mild (intra-retinal) or severe (vitreous or major subhyaloid hemorrhage, TS). Additional visits for patients with TS were for ophthalmological reasons.

Indications for vitrectomy in TS at our institution include: retinal detachment (prompt treatment) and dense and bilateral vitreous hemorrhage. We closely follow patients with unilateral TS without retinal detachment and without subretinal or intraretinal hemorrhage in the foveal area for a few months to monitor for spontaneous clearing; earlier vitrectomy is recommended if the hemorrhage markedly slows the patient’s neurological rehabilitation.

Two qualified radiologists (R.K. and J.P.) reviewed ocular findings suggestive of TS on all CT head scans performed within 1 month after onset of symptoms of aSAH, because delayed vitreous hemorrhages have been noted in the literature. The radiologists worked independently, unaware of each other’s evaluations as well as of patients’ ophthalmic findings. Visualization of the globe of the eye in the scan was assessed with a scoring scale of 0–2: Grade 0, no visualization to the level of the optic disc, not sufficient for diagnosis; Grade 1, visualization to the level of the optic disc; and Grade 2, complete visualization of the globe. Further, CT findings were classified as normal or abnormal (suggestive of TS) and subsequently compared with the findings detected on dilated fundoscopy.

The CT brain images were acquired for most studies as a volume acquisition with a 64-row scanner (GE Lightspeed VCT, GE Medical Systems), with creation of reformatted images in axial and coronal planes (reformatted slice thickness 2.5–5 mm). Some of the studies were done at the admitting hospitals with different scanners and imaging parameters.

Statistical Analysis

Statistical analysis was carried out with Stata (Release 10.0; StataCorp LP). All tests were 2-sided. Baseline characteristics—patient age and sex, aneurysm dimensions (height and width), presence of ICH, presence of hydrocephalus, and Fisher, WFNS, and Hunt and Hess grades—and the mRS score at 6 months were compared statistically with the presence of TS. Continuous variables were compared with the Mann-Whitney U-test. Unordered and singly ordered contingency tables were analyzed with Fisher exact test and Kruskal-Wallis test, respectively. The level of significance was set at p < 0.05.

We performed uni- and bivariate logistic regression to model TS as a dependent variable. We first fitted univariate models to identify independent variables significantly associated with TS for multivariate modeling. The WFNS and Hunt and Hess grades were dichotomized into 2 categories: with Group 1 including Grades I–III and Group 2 Grades IV–V. We then considered independent variables with a p value < 0.10 for bivariate models. We compared different bivariate models using the likelihood ratio test.

Interevaluator reliability for the presence of TS in CT scans (level of agreement between the 2 readers) was determined by calculating the κ coefficient (slight agreement, κ = 0.0–0.2; fair agreement, κ = 0.2–0.4; moderate agreement, κ = 0.4–0.6; substantial agreement, κ = 0.6–0.8; almost perfect agreement, κ = 0.8–1.0) and its 95% confidence interval.

Results

Overall Outcome

This study involved 121 participants (55 male, 66 female), which includes 97% of all the non–foreign resident patients undergoing an operation for aSAH during 2011 at our institution: 3 patients with Hunt and Hess Grade V were excluded because they died within 5 days of admission, before dilated fundoscopy was allowed. The mean age of the 121 patients was 55 years (range 20–84 years). Hydrocephalus was the preoperative diagnosis in 63 pa-
tients (52%), and 42 (35%) presented with ICH. Most patients (n = 110) underwent surgical treatment; 11 patients were treated with endovascular coil embolization or stent placement.

Intraocular Hemorrhages on Fundoscopy

TS was observable in 13 patients (11%); 1 of these patients had bilateral TS, and 3 had mild intraocular hemorrhages in the other eye. Another 22 patients (18% of the study group) had mild intraocular hemorrhages, and in 8 of these cases the hemorrhages were bilateral. Characteristics of the patients with and without TS are presented in Tables 1 and 2. TS was more common in women (n = 11 [17%]) than in men (n = 2 [4%]) (p = 0.036, Fisher exact test). During follow-up, 1 patient with TS died of aSAH sequelae, compared with 9 patients without TS. Visual acuity of the eyes with TS ranged from hand movements to 20/20 on the Snellen chart. None of the patients developed retinal detachment. Two patients with TS underwent a standard pars plana vitrectomy. The worst visual acuity at the 6-month visit was 20/63 as a result of disruption of the retinal pigment epithelium in the foveal area (macular scarring) due to TS.

The associations between TS and the WFNS and Hunt and Hess grades on admission were statistically significant (p = 0.0002 and p = 0.0018, respectively, Kruskal-Wallis test). Intracerebral hemorrhage was present in 9 patients with TS as compared with 33 patients without TS (p = 0.011, Fisher exact test). Half of the patients without TS had hydrocephalus, compared with 69% in the TS group (p = 0.25, Fisher exact test). We found no statistically significant differences between these groups in regard to age (p = 0.34, Mann-Whitney U-test), Fisher grade (p = 0.30, Kruskal-Wallis test); or mRS score at 6 months’ follow-up (p = 0.26, Fisher exact test). We detected a statistically significant difference in aneurysm length (p = 0.024, Kruskal-Wallis test) but not in width (p = 0.28, Kruskal-Wallis test) between the groups.

Univariate and Multivariate Analysis of TS in Relation to Clinical and Radiological Findings

Univariate logistic regression confirmed the lack of an association between TS and age, hydrocephalus, and aneurysm width (Table 3). TS was strongly associated with higher WFNS and Hunt and Hess grades (odds ratio [OR] 15.00 and 14.30 for Grades IV–V vs I–III, respectively; p = 0.0010 for both variables). TS was associated with female sex (OR 5.30, p = 0.035), the presence of ICH (OR 5.11, p = 0.010), and increasing aneurysm length (OR 1.11 for each 1-mm change, p = 0.086).

We chose the WFNS grade for bivariate modeling and combined it with the other 3 significant univariate variables: the presence of ICH, aneurysm length, and patient sex (Table 3). The number of patients with TS did not allow a multivariate model that would have included more variables. The final model that best fit our data set—and was the only one of the 3 alternative models in which both variables were independently associated with TS—combined the dichotomized WFNS grade (OR 15.05, p = 0.0010) and sex (OR 5.34, p = 0.043). This model fit the data significantly better than the simpler univariate model that included only the dichotomized WFNS grade (Δ log likelihood, 65.8–60.6 = 5.18, 1 df, p = 0.023, chi-square test).

CT Findings of TS

The ocular CT findings of TS included subhyaloid hyperdense crescents, hyperdense thickening, and nodules within the posterior pole of the eyes (Fig. 1). The findings were visible up to 19 days after the hemorrhage. In the CT images, no vitreous hemorrhage was visible. Among the patients with false-positive CT findings, 3 had mild intraretinal hemorrhages and 1 had marked papill edema.

Within 1 month of aSAH, the patients in the TS group underwent a mean of 5.4 CT head scans (range 1–8 scans), compared with 4.8 (range 2–14 scans) in the non-TS group. All patients with TS had their first CT scan within 3 days after symptoms of aSAH; visualization in the first 2 scans was Grade 2 (complete visualization of the globe) in 9 patients, and Grade 1 (visualization to the level of the optic disc) in 4. Patients in the non-TS group also had Grade 1 or 2 images of the globes available.

Overall, the raters detected findings suggestive of TS in 11 patients, of whom 6 had TS and 3 had intraretinal

| TABLE 1: Locations of 121 ruptured aneurysms in 121 patients treated during 2011* |
|-----------------------------|----------------|----------------|
| Location                     | No TS | TS |
| internal carotid artery      | 24    | 5  |
| medial cerebral artery       | 31    | 6  |
| anterior communicating artery| 32    | 0  |
| anterior cerebral artery     | 5     | 1  |
| posterior inferior cerebellar artery | 6 | 0 |
| basilar artery               | 7     | 1  |
| posterior cerebral artery    | 1     | 0  |
| posterior circulation, other | 2     | 0  |

* Values represent numbers of patients.

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Within 1 month of aSAH, the patients in the TS group underwent a mean of 5.4 CT head scans (range 1–8 scans), compared with 4.8 (range 2–14 scans) in the non-TS group. All patients with TS had their first CT scan within 3 days after symptoms of aSAH; visualization in the first 2 scans was Grade 2 (complete visualization of the globe) in 9 patients, and Grade 1 (visualization to the level of the optic disc) in 4. Patients in the non-TS group also had Grade 1 or 2 images of the globes available.

Overall, the raters detected findings suggestive of TS in 11 patients, of whom 6 had TS and 3 had intraretinal

| TABLE 2: Characteristics of 121 patients with aSAH treated during 2011* |
|-----------------------------|----------------|----------------|
| Characteristic              | No TS | TS |
| clinical condition on admission |      |    |
| Hunt & Hess Grade I–III     | 78    | 2  |
| Hunt & Hess Grade IV–V      | 30    | 11 |
| WFNS Grade I–III            | 79    | 2  |
| WFNS Grade IV–V             | 29    | 11 |
| radiological findings on admission |      |    |
| Fisher Grade 1–2            | 21    | 1  |
| Fisher Grade 3–4            | 87    | 12 |
| clinical outcome at 6 months |      |    |
| mRS Score 0–3               | 86    | 8  |
| mRS Score 4–5               | 12    | 4  |

* Values represent numbers of patients.
hemorrhages on dilated fundoscopy (Table 4). Overall observed agreement between the 2 raters was 96% (116 of 121 cases) (Table 5); interobserver agreement was recorded as substantial ($\kappa = 0.69$, 95% CI 0.56–0.82). The sensitivities of the CT findings for TS for Reviewers 1 and 2 were 46% and 38%, and the specificities, 98% and 96%. On average, the sensitivity of the CT findings for TS was 42%, and the specificity 97%. The sensitivities were higher in the acute phase and tended to decrease over time (Table 6). On average, the sensitivity in those who had both orbits entirely scanned (Grade 2, n = 66, 55%) during the 1st month after aSAH was 50%.

Discussion

CT Findings of TS

In this prospective study, we assessed without selection bias the specificity and sensitivity of conventional head CT scan for diagnosing TS in consecutive patients with aSAH; the data suggested that features of TS were present on the CT scans in nearly half the patients with TS. The interobserver agreement between the 2 raters was substantial. Further, we demonstrated the high specificity of reviewing CT scans for TS; since few false-positives emerged, few patients without TS on fundoscopy would be subjected to referral to an ophthalmologist. This issue is important, because while dilated fundoscopy is the method of choice for diagnosing TS, the debilitated state of many patients prevents them from noticing and expressing visual complaints and thus delays referral to an ophthalmologist.11

A limitation of our study (concerning the usefulness of CT imaging in diagnosing TS) involves the balance between achieving adequate visualization and avoiding unnecessary irradiation of the eye. Radioprotection to the eye during a head CT scan includes tilting the CT gantry to exclude the orbits from the primary irradiation area as completely as possible and/or using CT eye shields. We used both methods in our study, although practices varied between institutions. With these radiation protection efforts, some diagnostic ophthalmic information will inevitably be missing. CT scanning is, however, by no means justifiable only for diagnosing TS. Instead, when the patient has already undergone a head CT scan for the diagnosis of aSAH, neuroradiologists should be aware of the possibility of TS and mention suggestive findings in their reports; this may reveal TS without additional costs or radiation exposure.

Akiyama et al. estimated that among 1000 patients with SAH, 1 patient has a subhyaloid hemorrhage detectable by head CT.2 We demonstrated, however, a significantly higher frequency; recent advances in CT technology allowing a thinner slice thickness, adjustable window settings, and reduction in bone artifacts have presented better opportunities for detection of TS. Further, based on the current study, subhyaloid hemorrhages may not be so massive or widespread as Akiyama has speculated.1

Data on concordance between ocular CT abnormali-
ties and the presence of TS are scarce. In their retrospective series comprising 12 patients with intracranial hemorrhage, Swallow et al. described intraocular CT findings in two-thirds of the patients. In their study, clinical diagnosis of intraocular hemorrhage was often delayed for up to several months until discovery of a late visual defect. Consequently, imaging studies and ophthalmic examination may have been performed at quite different times. Assessing only those patients with visual complaints may lead to selection bias, since only patients with the most severe TS seek treatment in the absence of marked cognitive impairment. Further, the case reports that exist represent only those patients with the most difficult intraocular hemorrhages.

Typical CT findings in our study were unchanged from earlier reports. Because CT features were often subtle, the sensitivity remained only fair. As reformatted slice thickness was 2.5–5 mm, CT missed some cases of subhyaloid hemorrhage that occupied widths less than a slice. In addition, as subtle vitreous hemorrhage was not visible in the CT scans, CT missed TS cases that were not accompanied by subhyaloid hemorrhage. Finally, the protocol was not optimized for evaluating orbital findings. Conventional head CT thus misses many mild TS cases but it still detects the most severe subhyaloid hemorrhages—the cases in which the possibility of retinal detachment and other ophthalmic complications is highest, and therefore the need for referral to an ophthalmologist most urgent.

All true-positive findings of TS in our study were visible in the early CT scans, in accordance with results of Swallow et al., and tended to be detectable in several CT scans. Four false-positive findings in the current series resulted, in retrospect, from the position of the globes or

![Fig. 1. A–D: Images from head CT scans showing findings of TS: a crescent-shaped hyperdensity within the posterior pole of the right eye (A), a crescent-shaped hyperdensity within the posterior pole of the left eye (B), a significant crescent-shaped hyperdensity on the retinal surface of the right eye (C), and layering of high-density material on the retinal surface of the right eye (D).](image)

**TABLE 4:** Computed tomography findings suggestive of TS in 121 patients with aSAH treated during 2011

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<th>Reviewer &amp; CT Findings</th>
<th>TS in Fundoscopy</th>
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</tr>
<tr>
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<td>108</td>
<td>121</td>
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<tr>
<td><strong>Reviewer 2</strong></td>
<td></td>
<td></td>
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<tr>
<td>CT positive</td>
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<tr>
<td>total</td>
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CT and Terson’s syndrome

Intraocular Hemorrhages

For some unknown reason, the incidence of aSAH is apparently higher in Finland and in Japan than in the rest of the world, and thus what has been debatable is whether extrapolation of the results of aneurysm studies abroad is valid for the Finnish population. The incidence of TS in the current study was 11%, which is comparable to findings of earlier prospective reports (incidence range 5%—18%). Likewise, 29% of all patients presented with any kind of intraocular hemorrhages; previous incidences have ranged from 17% to 46%.

The most common hypothesis regarding the mechanism of TS suggests that a sudden increase in intracranial pressure and intraocular venous pressure results in venous stasis followed by rupture of the fine optic disc and retinal capillaries. Our logistic regression model identified a higher WFNS grade on admission as a significant, independent predictor of TS. The current results thus confirm previous reports that TS is correlated with more severe aSAH, as assessed using the WFNS or Hunt–Hess grading scales. Similarly, female sex independently predicted TS in our logistic regression analysis. Although a preponderance of female patients has been suggested, the reasons remain speculative. It is possible that hemodynamic responses to aneurysm rupture may differ between men and women, which might lead to an increased incidence of TS in female patients.

Some authors have observed increased mortality among patients with TS, although controversy exists. We could not establish such an association here, but this may not necessarily reflect the true prognosis: excluding patients suffering aSAH who never reached the hospital, or those not surviving until ophthalmic examination with pupil dilation, may lower the true TS incidence. Other factors affecting mortality rates are length of follow-up and whether studies include patients beyond surgical treatment. Moreover, in some articles, the original definition of TS has been widened to include intraretinal hemorrhages.

Complications of intraocular hemorrhages include a macular hole, an epiretinal membrane, retinal detachment, and increased intraocular pressure that may require ophthalmic follow-up and treatment. For retinal detachment, timely recognition and vitrectomy or other surgical intervention is essential for optimizing visual outcome; a delay in treatment limits visual recovery, and if the condition is left entirely untreated, total blindness usually follows. The vitreous hemorrhage itself, without retinal detachment, generally clears spontaneously, but in dense vitreous hemorrhage, vitrectomy hastens visual recovery.

Early vitrectomy may also predict better visual outcome and fewer complications of TS. Two of our patients (2%) underwent vitrectomy—a proportion quite similar to the proportions reported by Frizzell et al. (2%), Ness et al. (4%), and Stiebel-Kalish et al. (4%). TS can contribute to confusion among patients and interfere with stereopsis and rehabilitation; reversal of visual loss by surgical intervention in selected cases can be highly important.

Conclusions

While routine dilated fundoscopic examination by an ophthalmologist can be difficult to achieve for all patients with aSAH, we demonstrate that conventional head CT scan has high specificity for detecting TS: an active search for TS findings can aid in early diagnosis without additional risk, while still minimizing the number of additional unnecessary ophthalmic referrals. The likelihood of a true-positive diagnosis increases if features of TS are visible in early and multiple CT scans. Reviewing CT scans for TS is worthwhile, even though some diagnostic information will be missed due to efforts to protect the eyes from radiation. TS is associated with female sex and poor clinical condition on admission.

Disclosure

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TABLE 5: Observed agreement between the 2 reviewers

<table>
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<tr>
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orbital bone-induced artifacts. One case was explained by marked papilledema. Akiyama has also described false-positive cases due to beam hardening.

TABLE 6: Computed tomography findings, predictive values, specificity, and sensitivity for TS over time in patients with aSAH treated during 2011 and visualization at least to the level of the optic disc (Grade 1 or 2)*

<table>
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<th>Time From aSAH Onset to CT Scan</th>
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<td>false positive (n)</td>
<td>sensitivity (%)</td>
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<td>1–3 Days (81 pts)</td>
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* pts = patients.
References


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