

Prednisone and Tranexamic Acid Oral Treatment in Chronic Subdural Hematoma: Case Series

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Keywords:

Prednisone; Chronic subdural haematoma;
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Abbreviations:

CSDH: Cronical Subdural Hematoma; CT: Computerized Tomography; MRI: Magnetic Resonance Images; TXA: Tranexamic Acid; QOL: Quality of Life; ASDH: Acute Subdural Hematoma; CSF: Cerebrospinal Fluid; VEGF: Vascular Ephetelial Growth Factor

1. Abstract

1.1. Background: During the Covid era, the avoidance of suggest to come to the hospital for patient with symptoms and pathology which can be treated conservatively, have been a diffused habit. Chronic subdural hematoma is a well known neurosurgical pathology, which can be treated by surgical intervention or conservative treatment, and the choice between this two modality of treatment has to be made on the base of many parameters.

1.2. Purpose: Medical treatment of chronic subdural hematoma make the use of corticosteroids and often antifibrinolytic drugs a current practice in selected cases with a proved good efficacy and outcome. We have administered the medical treatment also in cases which could be submitted to surgery as well.

1.3. Study Type: Our case serie include two cases, which would be treated surgically in normal conditions but have been treated conservatively, during the covid era, for a patients' choice in order to avoid hospitalization.

1.4. Population and Results: Both two cases showed a progressive resorbation of the blood collection during administation of ciclyc prednisone and tranexamic acid. Moreover the presenting symptoms improved immediately at the beginning of medical treatment.

1.5. Conclusion: Ciclyc medical treatment could be considered a good option in patients with borderline- chronic subdural hematoma; during covid era the avoidance of hospitalization might be a good habit expecially in fragile patients.

2. Introduction

Chronic subdural hematoma (CSDH) is a long-lasting collection of blood and blood breakdown products in the subdural space. It is a well-defined clinical condition consisting of a slowly progressive accumulation of blood in the subdural space. Such collection may produce hemisphere compression and result in ultimate brain herniation. The general population incidence 2/100.000 per year [1]. The incidence is higher in the elderly for those patients aged 70 years and older (up to 58 per 100.000) and in alcoholics or hepatopaths patients presenting coagulation disorders [1]. The presentation is related to a head injury, mild or serious, occurred few weeks before symptoms presentation. A chronic venous bleeding arising from bridging veins injury and the reactive creation of pseudo-membranes around the subdural clot are recognized pathogenic features in the development of CSH. Recently conservative medical treatment has been proposed with good results in terms of hematoma reabsorption. The Sars cov 2 pandemia have changed our point of view for a long time, and during the lockdown time it was forbidden to go out if not to buy basic necessities or go to the

hospital in case of disease. During the Covid era, hospitalization became more dangerous than the past. In addition to the risk of contracting nosocomial infections such as pneumonia or cystitis, the patients were in contact with medical and paramedical staff and with the other patients, everyone possible carriers of Sars cov 2 infection. The overall habits was to administer conservative medical treatment to patients who can benefit of it in order to avoid overcrowding in the hospital facilities.

3. Material and Methods

We present two cases of patients presenting a chronic subdural hematoma, which would be treated surgically in normal conditions due to the size and presenting symptoms. These two “borderline” subdural hematoma have been treated conservatively, during the covid era, for a patients’ choice in order to avoid hospitalization.

4. Case 1

In September 2020, a 74-year-old woman reported headache, dizziness and gate apraxia. She also suffered from essential hypertension treated with sartans medicines, without antiplatelet or anticoagulant therapy and hypercholesterolemia treated with statins drugs. The patient referred an accidental fall at home occurred about two months before. A Magnetic resonance images (MRI) examination, done on the basis of suggestion of the treating physician, showed a 3 cm- thickness CSDH in left hemisphere (Figure 1). According to the Markwalder Grading Score (MGS) [2], the patient have been classified as grade 2. During the specialist medical consultation, both conservative and surgical treatment have been proposed to the patient, with a complete explanation of noted risks and benefits of both of them. The patient consciously preferred conservative approach, especially in the light of the Sars-Cov 2 pandemia-related risk of hospitalization. Therefore the patient started a cycle of drug treatment administered orally: for the first five days, the patient was treated with 25 mg prednisone two times a day, 0,5 mg tranexamic acid three times a day and omeoprazole and vitamin C integration therapy. The following five days the prednisone administration has been reduced to one a day and after this period to an half a day. At the 30th day of medical treatment, the new MRI examination showed an appreciable reduction of the thickness of CSDH to 2,5 cm (Figure 2). On the same day, the patient started a new therapy cycle, lasting 19 days, of prednisone, tranexamic acid, statins and omeoprazole with the same dosage of the first one. At that time, the patient referred a clinical remission, firstly regarding gate disturbances. The MGS scale examination became grade 1.

On the first days of November the MRI examination revealed a new reduction of CSDH thickness of 1,7 cm (Figure 3). The patient did not take any other drugs since December 11th 2020 to January 10th 2021.

On January 11th, according with the patient, we started the last cycle of therapy of 21 days and the following MRI examination

done on 21th of February revealed a total resorption of the collection (Figure 4). At that time MGS scale became grade 0 with completely symptoms’ remission. The progressive resorption of CSDH have been resumed in the graphic 1.

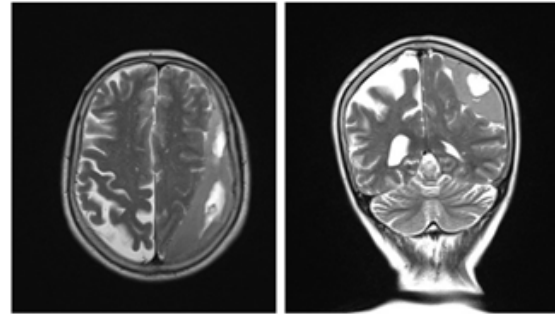


Figure 1: A 74-year-old female complained headache, dizziness and gate apraxia. Initial brain MRI 3 cm- thickness CSDH in left hemisphere with brain compression and mild midline shift.

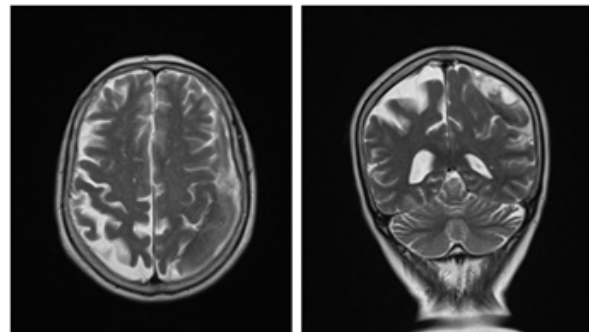


Figure 2: Follow-up brain MRI scan on the 30th day of medical treatment shows reduction subdural hematoma with initial brain re-expansion and midline (subtotal) realignment.

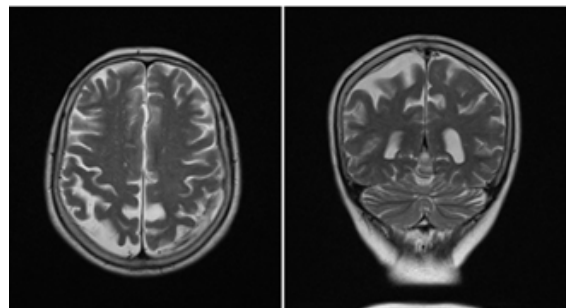


Figure 3: Follow-up brain MRI scan on the first days of November shows a remarkably decreased amount of hematoma with good visualization of cortical sulci and no more shift.

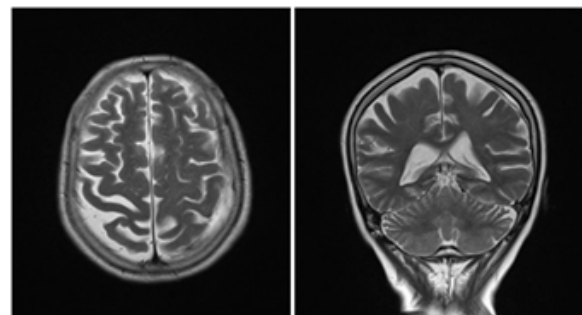


Figure 4: Final brain MRI scan on 21th of February revealed a total resorption of the collection with complete resolution of the hematoma CSDH.

5. Case 2

In March 2020, a 77-year-old man reported a car accident with mild head trauma. He reported an uneventfully clinical history except for insulin resistant diabetes mellitus treated with oral hypoglycaemic agents in good compensation without antiplatelet or anticoagulant therapy. The patient referred that during driving a car buffered his car by not respecting the stop signal. Arrived on-site police and paramedic staff, the patient has been transported to our hospital first-aid where he was submitted to an emergency Computed tomography-scan (CT-scan) total-body examination. No brain injury have been found at that time. The patient, after 24 hours of clinical evaluation, have been discharged and came back home. After one month, the patient did an head CT-scan, as suggested by the treating physician for a referred enlarging headache. The CT-scan revealed a bilateral hemispherical CSDHs, causing brain compression and mass effect in both side (Figure 5). During the specialist medical consultation, both conservative and surgical treatment have been proposed to the patient, with a complete explanation of noted risks and benefits of both of them. The patient consciously preferred conservative approach, especially in the light of the Sars-Cov 2 pandemia-related risk of hospitalization. Therefore the patient started a cycle of drug treatment administered orally: for the first five days, the patient was treated with 25 mg prednisone two times a day, 0,5 mg tranexamic acid three times a day and omeoprazole and vitamin C integration therapy. The following five days the prednisone administration has been reduced to one a day and after this period to an half a day. At the 21th day of medical treatment, the new CT scan showed an initial reduction of the thickness of both CSDH, the left one (9 mm) more than the right one (12 mm) as showed in Figure 6. On the same day, the patient started a new therapy cycle, lasting 19 days, of prednisone, tranexamic acid, statins and omeoprazole with the same dosage of the first one. At that time, the patient referred a headache remission. The MGS scale examination has been graded as 1 from the beginning. On the first days of June 2020 the CT-scan showed a modification in density of both CSDHs with the same thickness of the previous CT-scan. Both CSDHs became hypo-dense for most of their extension and the mass effect provoked by their brain compression was sharply reduced (Figure 7). The patient did not take any other drugs for the following 30 days. On July 1th 2020, according with the patient, we started the last cycle of therapy of 21 days and the following CT-scan done on 20th of July revealed a further resorption of both collection (Figure 8) with right CSDH's 8 mm-thickness and left CSDH's 6 mm-thickness. At that time MGS scale became grade 0 with completely symptoms' remission. After two months, on the 9th of September 2020, the last head CT-scan done showed a complete resorption of both CSDH collections, as showed in Figure 9.

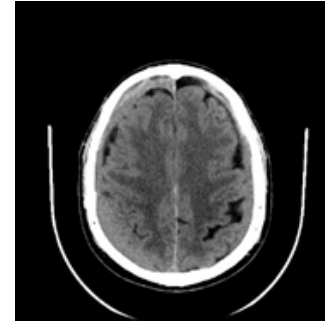


Figure 5: A male 77-year-old patient with car accident- mild head trauma. After one month, the patient did an head CT-scan, as suggested by the treating physician for a referred enlarging headache. The CT-scan revealed a bilateral hemispherical CSDHs, causing brain compression and mass effect in both side.

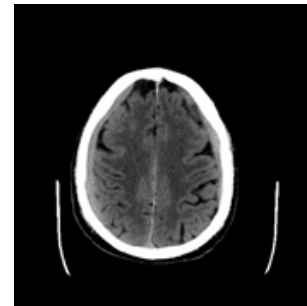


Figure 6: At the 21th day of medical treatment, the new CT scan showed an initial reduction of the thickness of both CSDH, the left one (9 mm) more than the right one (12 mm).

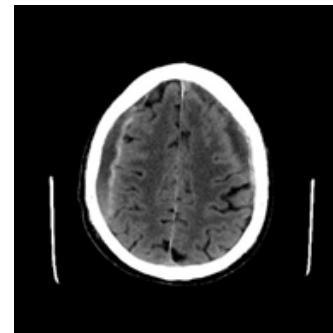


Figure 7: On the first days of June 2020 the CT-scan showed a modification in density of both CSDHs with the same thickness of the previous CT-scan.

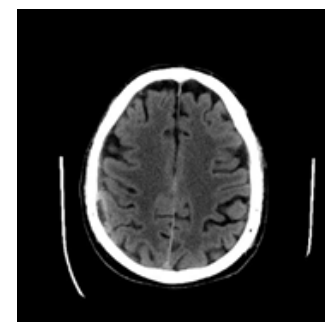


Figure 8: On July 1th 2020, according with the patient, we started the last cycle of therapy of 21 days and the following CT-scan done on 20th of July revealed a further resorption of both collection.



Figure 9: After two months, on the 9th of September 2020, the last head CT-scan done showed a complete resorption of both CSDH collections.

5.1. Radiology

The gold standard for diagnosing CSDH is CT head scan. CSDH is seen as a hypodense (<30 Hounsfield units) crescentic collection along the convexity, but may have isodense (30–60 Hounsfield units) or hyperdense (>60 Hounsfield units) components [3]. Sometimes the CT- isodensity of blood collection can create some doubts in diagnosis, especially in case of bilateral CSDH: to locate the medial displacement of the grey-white matter interface with a widening of the distance between the cortex and the inner table of the skull could be useful. MRI examination doesn't be performed routinely for patients with CSDH, but serves for differential diagnosis with subdural empyema for example.

5.2. Conservative Treatment

The first remark about a non-surgical treatment of CSDH was given by Ambrosetto in 1968 [4]. Thus, the DRESH study will be the first randomized controlled trial (RCT) to evaluate the role of a short postoperative cortisone protocol in the operative treatment of CSDH [5]. Glucocorticoids have a special capacity to block the inflammatory mechanisms in the formation of the CSDH. They specifically inhibit lymphokins and prostaglandins and stimulate inflammatory inhibitors like lipocortin [6].

Moreover the growing of pseudomembranes and neocapillaries is impaired. Otherwise, corticosteroids reduce the expression of vascular epithelial growth factor (VEGF), which inhibits abnormal angiogenesis and induces the secretion of inhibitor of plasminogen, so that the cycle of re-bleeding and lysis is decelerated. Chronic subdural hematoma can also be treated with tranexamic acid without concomitant surgery. Tranexamic acid, antifibrinolytic drug that inhibits plasminogen activation and plasmin activity, might simultaneously inhibit the fibrinolytic and inflammatory (kinin-kallikrein) systems, which might consequently counteract CSDH [7].

Atorvastatin may be a safe and efficacious nonsurgical alternative for treating patients with CSDH. It has been demonstrated that statins could improve CSDH promoting angiogenesis and suppressing inflammation [8, 9]. Atorvastatin seems to be a safe option for the conservative treatment of asymptomatic or mildly symptomatic CSDH, offering a cost-effective alternative to surgery without

drug-related side effects. Mannitol has shown promising results in small retrospective series and may be a valid option. However, the long treatment duration is the main drawback [10, 11].

5.3. Surgery

The standard surgical treatment performed for CSDH consists of a bur-hole craniotomy or mini-craniotomy evacuation of hematoma and following physiological solution 0.9% Na⁺ irrigation of the subdural space.

The surgical effectiveness is often visible during the immediate postoperative time within the patients present a partial or totally remission of symptoms.

The surgical evacuation of hematoma can be obstructed by the presence of internal membranes within the hematoma that prevent the complete evacuation of blood.

Residual hematoma increase the recurrence's risk.

Nakaguchi et al. [12] categorized CSDH into four subtypes (homogeneous, laminar, separated and trabeculated), hypothesizing that these types represented four stages in the natural history of the disease process. The effectiveness of various surgical techniques remains poorly characterized, with sparse level 1 evidence, variable measures, and various surgical techniques [13].

6. Discussion

During Sars-Cov 2 pandemia, the rate of hospitalization has been reduced significantly, decreasing the number of surgical procedures. The lockdown time lessens the incidence of head trauma due to the reduction of car accidents and heavy sport practices.

Moreover during the Covid-era, the hospitalization became more dangerous than the past. In addition to the risk of contracting nosocomial infections such as pneumonia or cystitis, the patients were in contact with medical and paramedical staff and with the other patients, everyone possible carriers of Sars-Cov 2 infection.

These conditions have promoted mostly the use of conservative strategy for CSDH resorption, underlying its efficacy in the management of selected cases. The development of CSDH requires a predisposing factor of a shrinking volume within the cranial vault, as seen in elderly individuals or those abusing alcohol, and a precipitant trauma that can often be minor [14].

The CSDH arises at the dural border cell layer, a thin layer of cells between the dura mater and arachnoid layer with comparatively little extracellular collagen, and intercellular connections that are prone to separation.

The authors found higher recurrence rates in the separated subtype (36%) and lower recurrence rates in the trabecular subtype (0%) than in the homogeneous and laminar subtypes (15% and 19%, respectively), findings that have since been corroborated [15]. However, these investigations regarding the recurrence rate didn't led to a standardized approach to the treatment of CSDH in daily clinical practice.

Two possible etiologies for CSDH have been postulated, although their relative contributions remain open to debate: firstly an acute subdural hematoma (ASDH) may occur due to tearing of the bridging veins trespassing the dural border cell layer or, less commonly, tearing of cortical arteries or veins.

A non-surgical-treated ASDH can resorb itself spontaneously or sometimes it may reach the CT-density typical of chronic subdural hematoma (CSDH) as a consequence of clot lyses.

On the other hand, a collection of cerebrospinal fluid (CSF) may occur in the subdural space due to splitting of the dura mater and arachnoid layer, showing a double thickness border on CT-scan images. In the subdural space, neovascularization occurs and hemorrhage from these new vessels leads to progressive collection of a secondary CSDH.

Regardless of the primary insult, the opening of the dural border cell layer triggers a complex reparatory response that aims to heal the injured tissues. The main features of this response are the proliferation of the dural border cells, formation of granulation tissue with collagen fibers, and macrophage deposition.

This process is often successfully completed, resulting in the resolution of the hematoma or hygroma.

Otherwise, hematoma enlargement is thought to be related to a localized inflammatory reaction, which results in hyperfibrinolysis of the clot and production of angiogenic factors that promote neovascularization and bleeding from fragile capillaries [16].

Formation of pseudomembranes is one of the main features of CSDH—the inner (visceral) membrane is less vascularized and usually thinner than the outer (parietal) membrane.

Risk factors that are thought to contribute to the occurrence of CSDH include advancing age, a history of falls, minor head injury, use of anticoagulants or antiplatelet drugs, bleeding diatheses, alcohol (contributing to globalized brain atrophy, increased risk of falls, and hepatogenic coagulopathy), epilepsy, low intracranial pressure states, and haemodialysis.

Perhaps the most important risk factor that increase the CSDH incidence is the use of anticoagulant and antiplatelet medications. The widespread use of these drugs has made quantification of risk difficult increasing the incidence of both 'atraumatic' CSDH (whereby the trauma is so minor that it is not reported to history) and recurrent CSDH [17].

According to data obtained from large retrospective series [18, 19] we believe that steroids drugs along with statins and fibrinolytics are a feasible and safe option in the management of CSDH. In our experience, cyclic administration of prednisone was able to cure and improve the patient's status. The effectiveness of the therapy as compared to surgical treatment could be ideally tested in a prospective randomized trial.

7. Conclusions

In order to state which is the best treatment option for patients with CSDH, we have investigate conservative options during Covid-era. The treatment modality should be determined according to the patient's symptoms, clinical conditions, and close observation, by well keeping in mind that it should be proposed for CSDH asymptomatic patients or with mild or moderate deficits or disturbances, without progressive neurological deterioration.

This has implications for patient morbidity and mortality as well a potential beneficial effect on the overall health service burden from this condition.

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