Chronic Subdural Hematoma Spontaneous Resolution

Resolução espontânea de hematoma subdural crônico

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Abstract

Introduction Chronic subdural hematoma (CSH) is a hemorrhagic brain injury that persists for more than 21 days after its initial formation. The incidence is predominantly among the elderly population (> 65 years), and varies from 58 to 74/100,000 inhabitants. Spontaneous resolution is considered variable; in the literature series, it is < 1–20% of cases.
Objectives To expose the CSH pathophysiological mechanisms of spontaneous resolution and some treatments that lead to hematoma volume reduction.
Methods Literature review between 1971 to 2016, using the PubMed, Medline, Embase, Scielo, LILACS and Cochrane databases using key-words, with inclusion and exclusion criteria.
Discussion Spontaneous resolution of the CSH pathophysiology is controversial; however, it can be attributed to four basic mechanisms: 1) outer capsule membrane maturation; 2) decreased fibrinolysis; 3) bidirectional flow of blood vessels; and 4) platelet plug. Some drugs, such as mannitol, corticosteroids, tranexamic acid and atorvastatin, contribute to CSH resolution, since they change the capsule membrane permeability, and inhibit the fibrinolytic and inflammatory systems.
Conclusion Spontaneous resolution is unpredictable; in some cases, it has a large temporal evolution (of up to 6 years). It occurs in small or laminar collections, asymptomatic or with transient neurological symptoms, and the pathophysiology is still controversial to this day. Therefore, surgical treatment should remain the first option, even though the conservative management is adopted for some patients. Rigorous outpatient and radiological follow-up are recommended.

Keywords
- chronic subdural hematoma
- spontaneous remission
- brain injury

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Resumo

Introdução O hematoma subdural crônico (HSDC) é uma lesão cerebral hemorrágica que persiste por mais de 21 dias após o começo de sua formação. A sua incidência é predominantemente na população idosa (> 65 anos), e varia de 58–74 /100.000 habitantes, e sua resolução espontânea é considerada rara e variável nas séries da literatura em < 1–20% dos casos.

Objetivos Expor os mecanismos fisiopatológicos que favorecem a resolução espontânea do HSDC e alguns tratamentos que favorecem a redução do volume do hematoma.

Métodos Revisão bibliográfica entre 1971 e 2016, utilizando as bases de dados PubMed, Medline, Embase, Scielo, LILACS e Cochrane, por meio de palavras-chave, com critérios de inclusão e exclusão.

Discussão A fisiopatologia da resolução espontânea dos HSDCs é controversa, porém pode ser atribuída a quatro mecanismos: 1) maturação da membrana externa da cápsula; 2) diminuição da fibrinólise; 3) fluxo bidireccional de vasos sanguíneos; e 4) tampão plaquetário. Alguns medicamentos, tais como manitol, corticoesteroides, ácido tranexâmico e atorvastatina, também podem favorecer a resolução dos HSDCs, uma vez que alteram a permeabilidade da membrana da cápsula e inibem os sistemas fibrinolítico e inflamatório.

Conclusão A resolução espontânea é imprevisível; em alguns casos, tem ampla evolução temporal em até 6 anos. Ocorre em coleções pequenas ou laminares, assintomáticas ou com sintomas neurológicos transitórios, e sua fisiopatologia ainda hoje é controversa. Portanto, o tratamento cirúrgico deve continuar sendo a primeira opção, embora se adote uma conduta conservadora para alguns pacientes. O seguimento ambulatorial e radiológico rigoroso é recomendado.

Palavras chave

- hematoma subdural crônico
- resolução espontânea
- lesão cerebral

Introduction

Chronic subdural hematoma (CSH) is a generally cystic collection composed of liquid blood contents. In several states of coagulation, it is coated by a thin fibrous capsule just below the dura mater, which lasts for more than 21 days after its initial formation.[1–3] The CSH incidence in the general population is estimated at 5–13.5 cases per 100,000 inhabitants per year. It increases with age, and can reach up to 58–74/100,000 inhabitants among the population over 65 years old.[1–4]

Chronic subdural hematoma is diagnosed through a computed tomography (CT) of the skul,l or through magnetic resonance imaging (MRI), mainly in T2 phases (echo gradient) and fluid attenuated inversion recovery (FLAIR). The images can be taken after monitoring the brain injury or suggestive neurological signs and symptoms, such as progressive headache, contralateral motor deficit, and behavioral changes.[5–7] The CSH is constantly changing, and this is reflected in changes in the pattern of the image exams.

Surgical treatment is the gold standard for symptomatic individuals who do not have surgical contraindications.[2] Some cases receive conservative treatment with clinical measures and serial radiological follow-up, which is an individual choice that is considered dangerous in some situations.[1,8,9] However, spontaneous resolution may occur in some cases without surgical intervention, which is rare. There are a few papers reported, and with an extremely variable epidemiology incidence: lower than 1% to ~ 20%. Another important variant found in the literature was the time for CSH spontaneous resolution, which ranged from 3 weeks to 6 years, followed by clinical and radiological follow-up.[8–13]

The objective of the present study is to establish a review exposing the pathophysiological mechanisms, the time of evolution, and the conditions that lead to the spontaneous resolution of the chronic subdural hematoma.

Methods

Literature review using the PubMed, Medline, Embase, Scielo, LILACS and Cochrane databases between 1971 and 2016. The search resulted in total 34 papers on CSH. The included articles associated CSH with spontaneous resolution. Articles with incomplete clinical data or no statistical relevance were not included in this paper.

Discussion

The cases of CSH that present spontaneous resolution are located in small areas, mainly in the frontal region. They can be laminar or thin, with little or no mass effect, and have contact with the cerebrospinal fluid; they can also be old and asymptomatic, or cause mild neurological symptoms.[11,14,15] One study showed that the average volume of the hematoma in the spontaneous resolution group was of 43.1 ml, and the average degree of deviation from the midline was of 6 mm.[13]

Spontaneous resolution of the CSH pathophysiology is controversial; however, it can be attributed to four basic mechanisms: 1) outer capsule membrane maturation; 2) decreased fibrinolysis; 3) bidirectional flow of blood vessels; and 4) platelet plug. Some drugs, such as mannitol, corticosteroids, tranexamic acid and atorvastatin also contribute to CSH resolution.[11,12,15]

Maturation of the External Membrane of the Capsule

The semipermeable external membrane allows the fibroblasts and cytokines chemotaxis pass into collection.[1,8,16] Activated by platelet-derived growth factor (PDGF), and transforming growth factor β (TGF-β). They differentiate tissue into myofibroblasts that are organized as a smooth muscle tissue in the lesion.[17]

These cells reinforce the capsule structure by stabilizing it and favoring its maturation, organization or even calcification over time. Maturation reduces the fibrinolytic system activity and microhemorrhages by leading to the secondary maturation of the blood vessels. Recurrent bleeding is the starting point and the main maintenance factor of the subdural hematoma. Therefore, the main mechanism of resolution is the maturation of the external membrane.[18–20]

Decreased Fibrinolytic Activity

The fibrinolytic system in hematoma formation is increased and leads to recurrent bleeding. In this case, the dynamic equilibrium established between hemostasis and fibrinolysis is interrupted, with blood recirculation greater than the ability to stanch. The larger the external membrane area, the vascularization and the greater the fibrinolytic activity, more blood will increase in the hematoma.[16,20,21]

With the maturation of the membrane, there should be a decrease in fibrinolytic activity and the liquefaction of the hematoma, and hemostasis should increase. Neovascularization stabilized by maturation should also be an adjuvant factor. Therefore, the collection becomes stable and resorbable.[12,20]

Bidirectional Flow of Blood Vessels

With the maturation of the external membrane of the capsule and decreased fibrinolytic activity, the collection becomes more resorbable. The blood vessels of the subdural membrane have communicating walls that allow bidirectional flow, favoring the progressive reabsorption of the hematoma.[10,22]

Platelet Plug

The increased size of the hematoma is made easier by the large number of gap junctions of the capsule vessels that allow sporadic blood leakage and recurrent bleeding.[22,23] A platelet plug, stimulated by myofibroblast collagen and vascular subendothelium molecules, occupies the gap junctions of the vessels, reducing microhemorrhages and the size of the subdural hematoma.[22]

The platelet thrombus is classically desecrated by initiation (platelet adhesion), extension (activation, adhesion and aggregation) and stabilization (thrombus stabilization), and is part of the primary hemostasis.[23,24]

Drugs

Mannitol is capable of changing capsule membrane permeability, thus avoiding the passage of proteins and granulocytes, preventing collection content increase by osmosis or chemotaxis. In a study with 20% intravenous mannitol, some patients presented spontaneous cures over a period ranging from 30 to 100 days.[5,25,26]

Corticosteroids (CE) also change capsule membrane permeability by the same mechanisms as mannitol. Corticosteroids maturate and stabilize the outer membrane. Dexamethasone, for example, reduces the chance of relapses in advanced age, of midline displacement, and of mixed density hematoma, which are independent factors for unilateral recurrence.[27,28]

In one of the reviewed studies, tranexamic acid was used in patients submitted to hematoma drainage and in others who did not receive any type of treatment. In both cases, a reduction of the collection was observed, and there were no cases of recurrence or increase. In another trial, spontaneous resolution was verified after 20 weeks of drug use. It is proposed that the tranexamic acid inhibits the fibrinolytic and inflammatory systems (via kallikrein); their role in the spontaneous resolution was previously explained.[29,30]

Atorvastatin, which has recently been investigated, can induce spontaneous resolution of CSDHs mainly in women, with favorable grades in the Markwalder grading scale (grades 1 and 2) for evaluating the neurologic status of a patient with a CSH.[31] In studies with experimental models, it has been proposed that atorvastatin induces increased expression of angiopoietin-1 and the vascular endothelial growth factor (VEGF), and reduces the expression of matrix metallopeptidase 9 (MMP9) on the capsule outer membrane, leading to the conversion of fragile capillaries into mature vessels. This is an important contribution to hematoma volume stability, since microhemorrhages of fragile capillaries are a predominant factor to increase the hematoma and avoid its resolution.[32,33] It is also known that atorvastatin was able to decrease the amount of neutrophils in the capsule and the cytokines (tumor necrosis factor alpha [TNF-α] and interleukin 6 [IL-6]) in brain tissue.[34]

In short, drug therapy is adjuvant, since spontaneous resolution can occur even without the use of drugs.

The present paper contributes with an algorithm showing the chronic subdural hematoma pathophysiology interrelation (►**Fig. 1**).

Defining Therapy

Drainage with immediate hematoma decompression is considered the first treatment. The surgical management, besides being therapeutic, reduces the chances of unfavorable outcomes.[8,9,13]

Drainage is classically indicated for symptomatic individuals (presenting with headache, motor deficit, altered consciousness, etc.) or those with imaging complications (midline deviation, basal cisterns' compression or compression of other structures of the central nervous system).[8,9,13] Advanced age (> 85 years) is a contraindication for drainage.[34]

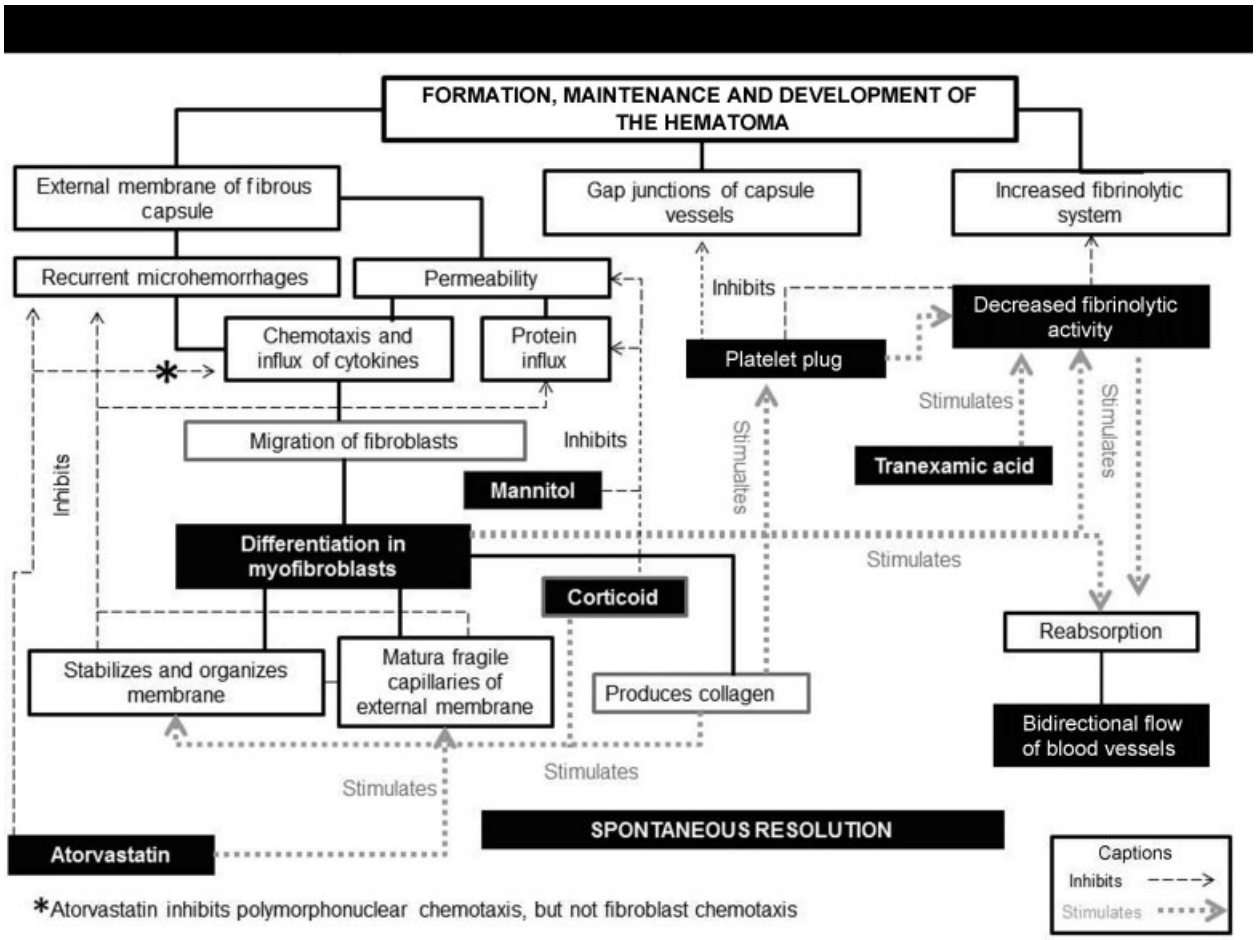

Fig. 1 Physiopathology of the spontaneous resolution of a chronic subdural hematoma.

The conservative treatment, with drugs and/or radiological follow-up, is the choice of follow-up of some professionals for asymptomatic or symptomatic patients without neurological deterioration. Some authors believe that in these cases the risks outweigh the benefits; many patients will need surgery in the future, and the risk of death is higher.[8,9,13]

Therefore, waiting for spontaneous resolution should not be a definitive criterion for this type of conduct, since there is no predictability in its occurrence, or a safe period of time, and even the evidences of drug use need further studies and meta-analyses.[8,9,13]

Conclusion

Generally, spontaneous resolution occurs in collections that: are located in small areas, especially in the frontal region; are laminar; have little or no mass effect; are in contact with the cerebrospinal fluid; are old; and that cause no symptoms or lead to transient neurologic symptoms. Although its pathophysiology is not a consensus, external membrane maturation is considered the initial and main event for its occurrence. Surgical management remains the first treatment option, and should not be replaced by the conservative approach, with the patient waiting for a spontaneous resolution. Therefore, the risks outweigh the benefits, and there is no evidence in the literature to support the effectiveness of this approach.

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