



Nontraumatic Intracranial Epidural Hematoma: Systematic Review of the Literature

Hematoma epidural intracraniano não traumático: revisão sistemática da literatura

Joilson Francisco de Souza Junior¹ Luiz Eduardo Dantas Cerqueira Medeiros¹
Carlos Umberto Pereira²

¹ Departamento de Medicina, Universidade Federal de Sergipe, Aracaju, SE, Brasil

² Serviço de Neurocirurgia, Hospital de Urgência de Sergipe, Aracaju, SE, Brasil

Address for correspondence: Carlos Umberto Pereira, MD, PhD, Av. Augusto Maynard, 245/404, Bairro São José, 49015-380 Aracaju, Sergipe, Brasil (e-mail: umberto@infonet.com.br).

Arq Bras Neurocir 2023;42(1):e52–e65.

Abstract

Introduction Epidural hematoma (EDH) is generally a direct sequela of head injury. Spontaneous EDH is rarely described in the literature. Spontaneous EDH can be caused by infections of adjacent regions, vascular malformations of the dura mater, metastases to the bone skull, and disorders of blood coagulation. The preferred treatment is surgical. The prognosis is directly related to the size, location, and Glasgow Coma Scale score on admission and the underlying disease.

Methods A systematic literature review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. We performed the search in the PubMed/MEDLINE, Embase, and Scopus databases. Abstracts and articles were screened according to our inclusion and exclusion criteria.

Results The literature review yielded 1,156 records from the databases, of which a total of 164 full-text articles were included in the final synthesis, plus 22 additional relevant studies. A total of 89 case report studies were included, providing 95 unique patients. There was a predominance of coagulopathies as the main etiology of spontaneous EDH. A total of 45.3% of the patients presented lesions in > 1 brain lobe. The frontal lobe was the most prevalent location of EDH. The most used neuroimaging exam was computed tomography (CT). Surgical intervention was the most common treatment performed. A total of 24.2% of the patients died.

Conclusion Nontraumatic EDH represents an uncommon manifestation of several pathologies. Clinical investigation should be aware of such a possibility. Healthcare professionals should value the physical examination and clinical history of the patient. Given the scarcity of information on the pathogenesis of spontaneous EDH, further studies are needed to better define intervention strategies and therapies for these patients.

Keywords

- ▶ spontaneous epidural hematoma
- ▶ intracranial
- ▶ nontraumatic
- ▶ extradural hematoma

received
February 7, 2022
accepted
June 22, 2022

DOI <https://doi.org/10.1055/s-0042-1756140>.
ISSN 0103-5355.

© 2022. Sociedade Brasileira de Neurocirurgia. All rights reserved. This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)
Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Resumo

Introdução Geralmente, o hematoma epidural (HED) é decorrente de traumatismo cranioencefálico. O HED espontâneo tem sido ocasionado por infecção de áreas adjacentes, malformação vascular na dura-máter, metástases para osso do crânio e doenças da coagulação sanguínea. Seu prognóstico está diretamente relacionado com o tamanho, a localização, o escore na escala de coma de Glasgow na admissão e a doença de base.

Metodologia Uma revisão sistemática da literatura foi conduzida e seguiu as diretrizes Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA, na sigla em inglês). Realizamos a pesquisa nos bancos de dados PubMed/MEDLINE, Embase e Scopus. Os resumos e artigos foram selecionados de acordo com os nossos critérios de inclusão e exclusão.

Resultados A revisão da literatura resultou em 1,156 registros nas bases de dados, dos quais um total de 164 artigos com texto completo foram incluídos na síntese final; mais 22 estudos relevantes foram adicionados. Um total de 89 estudos de caso foi incluído, fornecendo 95 pacientes únicos. Havia uma predominância de coagulopatias como a principal etiologia do HED espontâneo. Um total de 45,3% dos pacientes apresentava lesões em > 1 lobo cerebral. A intervenção cirúrgica foi o tratamento mais comum realizado. Um total de 24,2% dos pacientes morreu.

Conclusão Hematoma epidural não traumático representa uma manifestação incomum de várias patologias. A investigação clínica deve estar atenta a tal possibilidade e os profissionais de saúde devem valorizar o exame físico e a história clínica do paciente. Dada a escassez de informações sobre a etiopatogenia do HED, mais estudos são necessários para melhor definir estratégias de intervenção e terapias para estes pacientes.

Palavras-chave

- ▶ hematoma epidural espontâneo
- ▶ intracraniano
- ▶ não traumático
- ▶ hematoma epidural

Introduction

The most common cause of epidural hematoma (EDH) is a traumatic brain injury and skull fracture.¹ Spontaneous EDH can arise from various pathological conditions, and its incidence still uncertain in the literature.² The first reported case of spontaneous EDH in the literature was in 1951, published by Schneider et al.³ There have been several reports published since then.

Spontaneous EDH is typically associated with four etiological categories: pericranial infections, dural vascular malformations, cranial metastases, and coagulation disorders.^{4,5} The present study is a systematic review of the literature that aims to identify, compile, and analyze the case reports on EDH of a nontraumatic cause.

Methods

Inclusion Criteria

Abstracts were screened and selected according to the following inclusion criteria: articles published with full text, articles that report at least one case of EDH, and articles published in any language and year.

Exclusion Criteria

We excluded studies following our defined exclusion criteria: articles that did not report at least one original case report of

EDH, case reports of spinal EDH, case reports of traumatic EDH, case reports published in conference proceedings, letters to the editor, book chapters, articles that had not been peer-reviewed, and EDH due to any neurosurgical procedure.

Literature Search

We conducted a systematic review of the literature based on the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.⁶ We performed the search in the PubMed/MEDLINE, Embase, and Scopus databases in December 2020. Ethical approval and patient consent were not required as this is a systematic review based on published studies. Additional studies identified through the selected articles were analyzed and included according to the inclusion and exclusion criteria.

Study Selection

The search yielded 1,039 potentially relevant articles after the removal of duplicates. Two authors (Souza Junior J. F. and Medeiros L. E. D. Q.) independently reviewed and selected the studies using Rayyan QCRI (<https://rayyan.qcri.org>) software.⁷ We performed a selection with the reading of the title and abstract of the articles, followed by full-text reading, and the final inclusion depended on the agreement with all the inclusion and exclusion criteria. The research included a total

of 89 articles, representing 95 reported patients. The included studies in our systematic review were published between 1951 and 2020.

Data Extraction

The demographic data extracted from the reported patients were: age (in years), gender, etiologic cause of the hematoma, location, modality of imaging exams, treatment adopted, and outcome.

Results

The literature review yielded 1,156 records in the databases. After duplicates were removed, 1,039 were screened, 164 full-text articles were assessed for eligibility, and 67 were included in the final synthesis, plus 22 additional relevant studies, providing data on 95 individual patients. The summary of the selected reports is presented in **Table 1**. A total of 89 case report studies were included (**Fig. 1**). The median age of the patients was 24.3 years old, the oldest patient was 70 years old, and the youngest was 28 days old. A total of 65.2% of the patients were male, and 34.7% were female.

Among the etiologies of spontaneous EDH, there was a predominance of coagulopathies (40%), followed by pericranial infections (19%), neoplasms (14.7%), eosinophilic granuloma (7.4%), dural vascular abnormalities (2.1%), kidney disease (5.3%), medication (3.1%), systemic lupus erythematosus (2.1%), cardiac surgery (1%), hysterical crying (1%), intracranial hypotension (1%), and intradiploic epidermoid cyst (1%). The etiology of EDH was unknown in 2 cases (2.1%). A total of 45.3% of the patients presented lesions in > 1 brain lobe. The most prevalent location of spontaneous EDH was the frontal lobe (37.9%), followed by the parietal lobe (29.5%), the temporal lobe (17.9%), and the occipital lobe (8.4%). Other locations, such as cerebellar (1%) and retroclival (1%), were less frequent; the location was not reported in 2 cases (2.1%).

The most used neuroimaging exam was computed tomography (CT) (88.4%), followed by magnetic resonance imaging (MRI) (23.1%), cerebral angiography (12.6%), simple radiography (9.5%), and angio-MRI (2.1%). The treatment performed most frequently was surgical intervention (81%), followed by conservative treatment (14.7%), and not reported (4.3%). Among the cases, 23 patients (24.2%) died and 75.8% progressed satisfactorily with total or partial symptom remission.

Discussion

Epidural Space and Epidural Hematoma Formation

The epidural space is located between the inner layer of the skull bones and the dura mater and is closely adhered to the skullcap and cranial sutures (EDHs are usually limited in their extent by the cranial sutures). The majority of the blood supply of the dura mater arises from the middle meningeal artery. Spontaneous EDH is associated with four etiological categories^{1,4,5}: pericranial infections, dural vascular malformations, skullcap metastasis, and coagulation disorders. In the present study, we observed other infrequent etiologies:

Table 1 Summary of reported cases of nontraumatic epidural hematomas, age/gender

Author, year	Age/gender
Pericranial infections	
Schneider et al., 1951 ³	21/M
Schneider et al., 1951 ³ Novaes et al., 1965 ⁴⁰	21/M 26/M
Kelly et al., 1968 ²⁸	11/M
Clein, 1970 ³⁹	18/M
Sanchis et al., 1975 ¹	13/M
Marks et al., 1982 ²⁹	31/M
Ataya, 1986 ³⁰	31/M
Sakamoto, et al., 1997 ³¹	16/F
Hamamoto et al., 1998 ⁴	15/M
Papadopoulos et al., 2001 ³²	17/M
Griffiths et al., 2002 ³⁴	17/M
Moonis et al., 2002 ³³	21/M
Chaiyasate et al., 2007 ³⁵	14/F
Knopman et al., 2008 ⁷¹	11/M
Takahashi et al., 2010 ³⁶	10/F
Cho et al., 2011 ³⁷	12/F
Spennato et al., 2012 ³⁸	12/F
Neoplasm	
Anegawa et al., 1989 ⁷⁴	32/F
Kuga et al., 1990 ⁷³	65/M
Nakagawa et al., 1992 ⁸⁴	52/M
Simmons et al., 1999 ⁷⁵	67/M
Hayashi et al., 2000 ⁸⁵	70/M
Dufour et al., 2001 ⁷⁶	36/F
Hassan et al., 2009 ²⁶	55/F
Kanai et al., 2009 ⁸¹	56/M
Kim et al., 2010 ⁸⁰	53/M
Woo et al., 2010 ⁸²	46/M
Mahore et al., 2014 ⁷²	12/M
Kim et al., 2016 ⁷⁹	41/M
Ramesh et al., 2017 ⁷⁷	40/F
Zhao et al., 2020 ⁷⁸	45/F
Coagulopathies	
Cooper et al., 1979 ⁵⁵	6 w/F
Kuwayama et al., 1985 ⁵³	21/F
Grabel et al., 1989 ⁵⁹	2/M
Karacostas et al., 1991 ⁴²	19/M
Resar et al., 1996 ⁴³	14/M
Ganesh et al., 2001 ⁴⁴	11/M
Okito et al., 2004 ⁶⁷	12/M
Okito et al., 2004 ⁶⁷	2/M

Table 1 (Continued)

Author, year	Age/gender
Ng et al., 2004 ⁶¹	52/M
Dixit et al., 2004 ⁸⁶	17/M
Dahdaleh et al., 2009 ⁶²	18/M
Iliescu et al., 2009 ⁶⁰	28/F
Pati et al., 2009 ⁵⁷	32/F
Pallotta et al., 2010 ⁶⁹	21/M
Vural et al., 2010 ⁵¹	7/F
Azhar et al., 2010 ⁸⁷	12/M
Arends et al., 2011 ⁴⁵	19/M
Bölke et al., 2012 ⁴⁶	19/M
Babatola, et al., 2012 ²	18/M
Page, et al., 2014 ⁸⁸	7/F
Page et al., 2014 ⁸⁸	20/M
Serarslan et al., 2014 ⁸⁹	19/F
Ilhan et al., 2014 ⁷⁰	15/M
Kilit et al., 2014 ⁵⁶	13/F
Farah et al., 2014 ⁵²	2/M
Hettige et al., 2015 ⁶³	7/F
Oka et al., 2015 ⁶⁴	19/M
Zhang et al., 2015 ⁵⁸	21*/F
Ewane et al., 2016 ⁶⁸	20/M
Saul et al., 2017 ⁶⁶	18/M
Mishra et al., 2017 ⁶⁵	18/M
Komarla, et al., 2018 ⁴⁷	18/F
Komarla et al., 2018 ⁴⁷	17/M
Banerjee et al., 2018 ⁴⁸	-/M
Saha et al., 2019 ⁴⁹	20/F
Prabhu et al., 2019 ⁵⁴	21/F
Tomboravo et al., 2019 ⁵⁰	21/M
Ntantos et al., 2020 ²⁷	44/F
Eosinophilic granuloma:	
Cho et al., 2001 ⁸	2/M
Chen et al., 2002 ⁹	2/M
Mut et al., 2004 ¹⁰	9/M
Bhat et al., 2010 ¹¹	10/M
Sadashiva et al., 2016 ¹²	15/M
Bakhaidar et al., 2016 ¹³	7/M
Al-Mousa et al., 2020 ¹⁴	3/M
Renal disease	
Hamamoto et al., 1998 ⁴	12/F
Shahlaie et al., 2004 ⁵	16/M
Zheng et al., 2009 ¹⁵	54/F
Khan et al., 2017 ¹⁶	40/M
Yadav et al., 2016 ¹⁷	39/M

(Continued)

Table 1 (Continued)

Author, year	Age/gender
Medication	
Ruschel et al., 2016 ¹⁸	39/M
Khan et al., 2017 ¹⁶	30/F
Fukai et al., 2019 ¹⁹	27/F
Systemic lupus erythematosus	
Song et al., 2015 ²⁰	29/F
Yin et al., 2019 ²¹	45/F
Vascular and dural abnormalities	
Sanchis et al., 1975 ¹	59/F
Hasegawa et al., 1983 ⁸³	11/F
Cardiac surgery	
Ahmad et al., 2005 ²²	4/M
Hysterical crying	
Chen et al., 2018 ²³	19/F
Intracranial hypotension	
Cho et al., 2009 ²⁴	36/M
Intradiploic epidermoid cyst	
Wani et al., 2008 ²⁵	60/M
Unknown etiology	
Ng et al., 2004 ⁶¹	23/F
Bolliger et al., 2007 ⁴¹	67/M

Abbreviations: F, female; M, male; w, weeks.

*Age of admission differs from the age of onset of epidural hematoma.

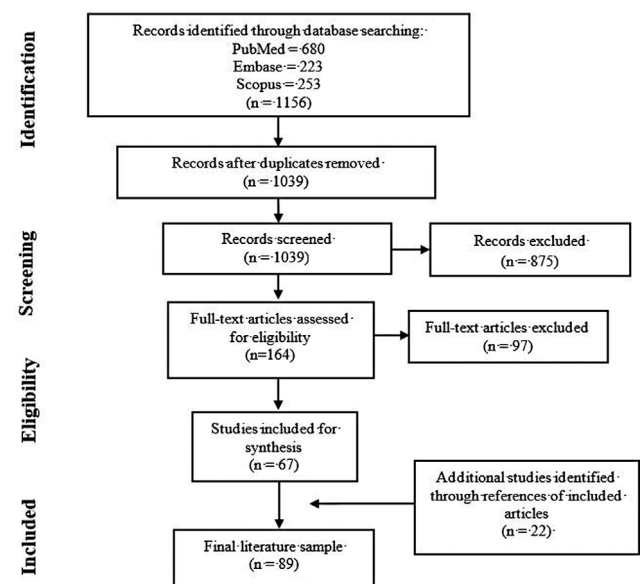


Fig. 1 Flowchart of the present systematic literature review.

eosinophilic granuloma,^{8,9,10,11,12,13,14} kidney disease,^{4,5,15,16,17} associated with drug therapy,^{16,18,19} systemic lupus erythematosus,^{20,21} cardiac surgery,²² hysterical crying,²³ intracranial hypotension,²⁴ and intradiploic

epidermoid cyst.²⁵ Hassan et al.²⁶ suggest that the term nontraumatic is more appropriated than spontaneous to refer to EDH because this kind of EDH is invariably associated with a primary cause. Despite this discussion, we used both expressions as synonyms in the present study.

The CT image of an EDH is an extra-axial collection in the shape of a biconvex lens.²² The mechanisms involved in each etiology are different. There are three propositions about the pathophysiological mechanisms described in the literature:²⁷ cranial injury leading to elevation of the periosteum and rupture of the cortical bone margin and consequent hemorrhage in the epidural space, abnormal anatomy caused by a pathological process of chronic medullary hematopoiesis, and insufficient venous drainage leading to cerebral edema and hemorrhage. The occurrence in the population is rare, with a very uncertain incidence in the literature.

Pericranial Infections

Among the EDH cases associated with pericranial infections, sinusitis^{28,29,30,31,32,33,34,35,36,37,38} was the most common etiology (► **Table 2**). Schneider et al.,³ reported in 1951 the first case in the literature of 2 patients with distinct pericranial infections. These authors also recognized errors in the management of one of the patients, who died, partially in consequence of a failure to consider that the intracranial lesion presented could be of any nature, except an inflammatory condition, as well as a mistake in not having properly

associated the findings of the physical examination and of the topography of the lesion.

There are two possible explanations for epidural bleeding and hematoma formation in patients with pericranial infections: a) extension of the infectious process to the external surface of the dura mater, promoting vasculitis and rupture of epidural vessels, thus causing blood leakage; and b) progressive detachment of the dura mater from the internal bone surface and vascular injury due to excessive accumulation of exudate or air from the infected area.⁴ The first mechanism is justified based on radiological, operative, and histological evidence available, which observed proximity of the bone structures to the infectious process (focal osteitis).^{1,28,32,39} The second possible mechanism is shown by a progressive displacement of the dura mater from the internal bone surface due to excessive accumulation of purulent exudate or air from the infected area, leading to vascular injury and to the development of EDH.¹

It is known that a mechanism involved in EDH formation in patients with pansinusitis involves infection by a retrograde route through the valveless vessels or diploic vascular channels, leading to inflammation weakening the vessel walls, which, in turn, leads them to rupture, as reported by Chaiyasate et al.³⁵ The typical clinical presentation of EDH associated with craniofacial infection occurs with headache, vomiting, and decreased level of consciousness preceded by signs and symptoms of the primary site of infection.³⁴

Table 2 Summary of reported cases of spontaneous epidural hematoma associated with pericranial infection

Author, year	EDH etiology	EDH site	Diagnostic imaging exam					Surgery	Outcome
			CT	MRI	AG	Rx	Others		
Schneider et al., 1951 ³	Otitis media	Right temporal					Autopsy	No	Died
Schneider et al., 1951 ³	Otitis media	Right frontotemporal				x	EEG	Yes	Recovered
Novaes et al., 1965 ⁴⁰	Otitis media	Temporal			x	x		Yes	Recovered
Kelly et al., 1968 ²⁸	Frontal sinusitis	Left frontal				x	T-99 BS	Yes	Recovered
Clein, 1970 ³⁹	Otitis media	Left frontoparietal					Autopsy	No	Died
Sanchis et al., 1975 ¹	Otitis media	Right temporal			x	x		Yes	Recovered
Marks et al., 1982 ²⁹	Sinusitis	Right frontal	x			x		Yes	Recovered
Ataya, et al., 1986 ³⁰	Chronic sinusitis	Left frontal	x			x		Yes	–
Sakamoto et al., 1997 ³¹	Maxillary sinusitis	Left frontal	x					Yes	Recovered
Hamamoto et al., 1998 ⁴	Pansinusitis	Left frontal	x			x		Yes	Died
Papadopoulos et al., 2001 ³²	Frontal sinusitis	Right frontal	x					Yes	Recovered
Moonis et al., 2002 ³³	Sphenoid sinusitis	Left temporal	x	x				Yes	Partially recovered
Griffiths et al., 2002 ³⁴	Frontal sinusitis	Frontal	x					Yes	Recovered
Chaiyasate et al., 2007 ³⁵	Pansinusitis	Right frontal	x					Yes	Recovered
Knopman et al., 2008 ⁷¹	Otitis media	Right temporal	x	x				Yes	Recovered
Takahashi et al., 2010 ³⁶	Sphenoid sinusitis	Right temporal	x	x	x			Yes	Recovered
Cho et al., 2011 ³⁷	Sphenoid sinusitis	Right temporal	x	x				Yes	Recovered
Spennato et al., 2012 ³⁸	Frontal sinusitis	Right frontal	x		x*			Yes	Recovered

Abbreviations: AG, angiography; CT, computed tomography; EEG, electroencephalogram; MRI, magnetic resonance imaging; RX, radiography; T-99 BS, technetium-99m brain scan.

*Angio-CT.

The most frequent symptoms presented by the patients with pericranial infections (► **Table 2**) were: headache, fever, nausea/vomiting, and drowsiness. Among the reports with ocular involvement, the most common sign among the patients was periorbital edema (38.9%),^{3,28,29,30,31,35,38} anisocoria,^{3,40} exophthalmos (11.1%),^{31,38} and papilledema (1%).⁴

Spennato et al.³⁸ reported the following data in a series of cases with pericranial infections: the mean age observed was 20 years old, most common in males (8:2), and frontal location EDH was the most frequent. These data were similar to the findings of Cho et al.³⁷ In Asia, case reports of spontaneous EDH associated with sinus infections were more frequent due to the higher incidence of chronic pericranial infection cases among Asians.³⁷

The most commonly used imaging exam in patients with pericranial infections was CT, followed by x-ray. These imaging exams contribute to evaluate the anatomy of the paranasal sinuses and verify the existence of fractures. The treatment performed in most cases was that of the infection etiology, associated with craniotomy and drainage of the hematoma.

Coagulopathies

It is known that coagulopathies may be responsible for spontaneous bleeding, including epidural bleeding.⁴¹ In the present study, the observed coagulopathies (► **Table 3**) were: sickle cell anemia (SCA),^{2,42,43,44,45,46,47,48,49,50} coagulation factor XIII deficiency,^{51,52} hypofibrinogenemia,^{53,54} vitamin K deficiency,⁵⁵ congenital afibrinogenemia,^{56,57} immune thrombocytopenic purpura,^{27,58} myelodysplastic syndrome,⁵⁹ disseminated intravascular coagulation (DIC),⁶⁰ and liver disease⁶¹. Coagulation disorders and pericranial infections are the two major categories of pathologies with which EDH is associated. In the present literature review, among all the included cases of spontaneous EDH, coagulopathies were predominant. Sickle cell anemia was the most common coagulopathy observed.

The first reported case in the literature was in 1979 by Cooper et al.,⁵⁵ of a 6-week-old patient with vitamin K deficiency who required surgical intervention for hematoma evacuation. The most frequent etiology of spontaneous EDH observed in the present study was SCA, accounting for 27.4% of all 95 patients listed in ► **Table 1**. Sickle cell anemia, characterized by changes in the shape of red blood cells and intermittent intravascular obstruction of blood flow, represents a common genetic disorder, especially among African Americans (1:600).^{62,63}

Epidural hematoma is the most common neurosurgical emergency complication in patients with SCA⁴⁸; however, it still is a rare manifestation. Nevertheless, in patients with SCA, EDH should be suspected if the patient starts presenting with sudden headaches or other signs of intracranial hypertension, leading to a search for bone lesions and hemostatic disorders, such as thrombocytopenia.⁶⁴

The symptoms presented by SCA patients differ from the classical symptoms of EDH caused by trauma, which often have a lucid interval in clinical condition, as suggested by

Babatola et al.² Among homozygous patients, chronic hemolytic anemia may occur, with increased susceptibility to infections, vaso-occlusive crises, and cerebrovascular disorders (especially cerebral ischemia), which can worsen the clinical conditions of the patient.⁶³

A SCA crisis may increase the hematopoietic demand on cranial medullary tissue, predispose to bone margin disruption and subsequent hemorrhage. All patients reported by Mishra et al.⁶⁵ had an SCA crisis that preceded the EDH. The exact mechanism of EDH in patients with SCA is unknown, but it is possibly related to bone infarction.⁶⁴ Bone infarction has been related to hematoma cases, possibly due to periosteal elevation and disruption of the bone margin.² Bone infarction has been reported in long bones, the spine, the sternum, and the ribs and is commonly associated with adjacent edema and hemorrhage.⁶⁶

A literature review conducted in 2015 noted an anatomical correlation between bone infarction and EDH location, but the direct cause has not yet been established.⁶³ In contrast, studies hypothesized that cases of spontaneous EDH are not associated with bone infarction and may occur due to abnormalities in cranial anatomy,² so that chronic expansion of hematopoietic tissue may rupture the inner and outer margins of the bone, causing extravasation of blood and medullary tissue into the subgaleal or epidural spaces. Another proposed mechanism has been less discussed and considers that the insufficient venous drainage in sickle cell pathology is possibly responsible for edema and hemorrhage.⁶⁷

The combination of MRI and angio-MRI is typically performed in patients with SCA to investigate headache, weakness, and vision changes associated with symptoms of a possible stroke, especially in children.⁴⁷ An extradural heterogeneous hypodense lesion presenting on imaging exams can be interpreted as a chronic EDH or an acute EDH with noncoagulated blood due to a low hemoglobin level.⁶⁵ Crisis prevention occurs through adequate hydration, folic acid consumption, and regular rest.⁶⁵ This prevention is essential in the care of SCA patients and prevents neurosurgical events.

There is no cure reported for this condition, and the management of symptomatic events involves the administration of fluids, appropriate analgesia, intravenous antibiotics (in case of isolated focal infection), and low molecular weight heparin as a prophylactic treatment, which can contribute to the prevention of crises due to the reduction of blood flow in the small circulation.⁶³ Studies have shown that general anesthesia and surgical trauma can precipitate red blood cell sickling factors, resulting in post-operative complications previously described in between 25 and 30% of patients.⁶⁸ Therefore, patients with SCA should be evaluated regarding surgical intervention by neurosurgeons, anesthesiologists, and hematologists, to ensure patient safety. In this scenario, early intervention and adequate imaging tests can modify the evolution of the patient.⁶⁹

Another coagulopathy reported as the underlying etiology for EDH formation is factor XIII deficiency.^{51,52} Coagulation factor XIII deficiency is a rare phenomenon of low incidence

Table 3 Summary of reported cases of spontaneous epidural hematoma associated with coagulopathy

Author, year	EDH etiology	EDH site	Diagnostic imaging exam				Surgery	Outcome
			CT	MRI	MRA	Rx		
Cooper et al., 1979 ⁵⁵	Vitamin K deficiency	Temporoparietal (bilateral)	x				Yes	Recovered with sequels
Kuwayama et al., 1985 ⁵³	Hypofibrinogenemia	Temporal (bilateral)	x				Yes	Recovered
Grabel et al., 1989 ⁵⁹	Myelodysplastic syndrome	Left frontal	x				No	Recovered
Karacostas et al., 1991 ⁴²	Sickle cell anemia	Left parietal and frontal (bilateral)	x	x			No	Recovered
Resar et al., 1996 ⁴³	Sickle cell anemia	Right occipitotemporal	x				Yes	Died (renal failure)
Ganesh et al., 2001 ⁴⁴	Sickle cell anemia	Frontal (bilateral)	x			x	No	Recovered
Okito et al., 2004 ⁶⁷	Sickle cell anemia	Right frontotemporal	x				Yes	Died
Okito et al., 2004 ⁶⁷	Sickle cell anemia	Left temporal	x				No	Died (septicemia)
Ng et al., 2004 ⁶¹	Hepatopathy	Left frontoparietal	x				Yes	Recovered
Dixit et al., 2004 ⁸⁶	Sickle cell anemia	Left frontal	x				No	Recovered
Dahdaleh et al., 2009 ⁶²	Sickle cell anemia	Right frontal and parietal (bilateral)	x				Yes	Recovered
Iliescu et al., 2009 ⁶⁰	DIC	Right frontoparietal	x				Yes	Died
Pati et al., 2009 ⁵⁷	Afibrinogenemia	Frontal (bilateral)	x				Yes	Recovered
Pallotta et al., 2010 ⁶⁹	Sickle cell anemia	Right frontal	x	x			Yes	Recovered
Vural et al., 2010 ⁵¹	Factor XIII deficiency	Right parietooccipital	x				Yes	Recovered
Azhar et al., 2010 ⁸⁷	Sickle cell anemia	Left frontal	x				Yes	Partially recovered
Arends et al., 2011 ⁴⁵	Sickle cell anemia	Right parietal	x	x			No	Recovered
Bölke et al., 2012 ⁴⁶	Sickle cell anemia	Left parietal	x				Yes	Recovered
Babatola et al., 2012 ²	Sickle cell anemia	Left frontal	x				Yes	Died (renal failure)
Page et al., 2014 ⁸⁸	Sickle cell anemia	Infratentorial suboccipital (bilateral)	x				Yes	Died
Page et al., 2014 ⁸⁸	Sickle cell anemia	Left frontal	x	x			No	Recovered
Serarslan et al., 2014 ⁸⁹	Sickle cell anemia	Right temporal	x				Yes	Partially recovered
Ilhan et al., 2014 ⁷⁰	Sickle cell anemia	Left parietal	x				Yes	Recovered
Kilit et al., 2014 ⁵⁶	Afibrinogenemia	Right frontal	x	x			No	Recovered
Farah et al., 2014 ⁵²	Factor XIII deficiency	Right frontal and occipital lobe*	x				Yes	Recovered
Hettige et al., 2015 ⁶³	Sickle cell anemia	Parietal (bilateral)	x				Yes	Died (renal failure)
Oka et al., 2015 ⁶⁴	Sickle cell anemia	Occipital lobe	x	x			No	Recovered
Zhang et al., 2015 ⁵⁸	Immune thrombocytopenic purpura	Right frontoparietal	x	x			Yes	Recovered
Ewane et al., 2016 ⁶⁸	Sickle cell anemia	Frontal (bilateral)	x				Yes	Died

Table 3 (Continued)

Author, year	EDH etiology	EDH site	Diagnostic imaging exam					Surgery	Outcome
			CT	MRI	MRA	Rx	Others		
Saul et al., 2017 ⁶⁶	Sickle cell anemia	Parietooccipital (bilateral)	x	x				-	-
Mishra et al., 2017 ⁶⁵	Sickle cell anemia	Right parietal	x			x	Yes	Recovered	Recovered
Komarila et al., 2018 ⁴⁷	Sickle cell anemia	Right cerebral hemisphere	x	x	x		Yes	Recovered	Recovered
Komarila et al., 2018 ⁴⁷	Sickle cell anemia	Frontal (bilateral)	x				Yes	Died	Died
Banerjee et al., 2018 ⁴⁸	Sickle cell anemia	Frontal (bilateral)	x	x	x		No	Recovered	Recovered
Saha et al., 2019 ⁴⁹	Sickle cell anemia	Right frontal	x				Yes	Recovered	Recovered
Prabhhu et al., 2019 ⁵⁴	Hypofibrinogenemia	Right frontoparietal	x				Yes	Died	Died
Tombravo et al., 2019 ⁵⁰	Sickle cell anemia	Right frontal	x				Yes	Recovered	Recovered
Ntontos et al., 2020 ²⁷	Immune thrombocytopenic purpura	Parietal (bilateral)	x				Yes	Died	Died

Abbreviations: CT, computed tomography; DIC, disseminated intravascular coagulation; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; RX, radiography. *At different times

worldwide, defined as an autosomal recessive disorder.⁴⁶ Farah et al.⁴⁶ reported the first case of EDH in a child with coagulation factor XIII deficiency. The diagnosis of coagulation factor XIII deficiency can be performed by quantitative analysis of the plasma levels of factor XIII in both the patient and family members.

Hypofibrinogenemia is a rare disorder defined by a deficiency in bloodstream fibrinogen levels (< 2 g/L), but not by its complete absence.⁵⁴ The frequency of intracranial bleeding in patients with hypofibrinogenemia is known to be between 7.3 and 13%.^{36,37} Medical professionals must pay attention to the immediate correction of the coagulation profile. This correction is possible through transfusion of fresh frozen plasma and cryoprecipitate, preoperatively or intraoperatively. Tranexamic acid can also be added to the therapy.⁵⁴

A coagulopathy that is similar to hypofibrinogenemia is afibrinogenemia.^{56,57} Afibrinogenemia is considered a rare coagulation disorder with an estimated prevalence of 1/1,000,000 worldwide. Half of the congenital afibrinogenemia cases reported in the literature result from a consanguineous marriage in the family history. Pati et al.⁷⁰ suggested that the ideal level of fibrinogen in the bloodstream should be > 1 g/L, while Kilit et al.⁶³ suggested that these levels should be ~ 1.5 g/L.

Disseminated intravascular coagulation (DIC) has been reported as a cause of EDH, either alone or associated with SCA. Iliescu et al.⁶⁰ reported one case of a pregnant woman who underwent curettage after spontaneous termination of pregnancy and evolved with spontaneous EDH and subsequent death due to DIC. Intrauterine fetal demise is often responsible for the onset of severe DIC, and according to the medicolegal literature, several forms of intracerebral hemorrhage may be complications of this hematologic entity.⁶⁰ Other studies reported the same condition secondarily to metastatic processes^{66,68} or SCA.^{11,12,48} Saha et al.⁴⁹ observed 100% mortality in patients with spontaneous EDH who suffered from DIC, which is similar to that observed in the present study.

Immune thrombocytopenic purpura (ITP) is another coagulopathy correlated with the occurrence of spontaneous EDH. However, its pathophysiological role has been explained by different mechanisms. Zheng et al.¹⁵ reported a patient with spontaneous EDH with chronic evolution who, although presenting only with headache, had large volume and advanced calcification. Thus, thrombocytopenia may be directly associated with chronic bleeding. Ntontos et al.²⁷ reported a case of acute development with multiple neurological deficits in a patient with ITP refractory to pharmacological treatment. It is relevant to consider that the escalating therapy in these cases uses thrombopoietin receptor agonist drugs, assuming the risk of cerebral thrombotic events. Given this, hypercoagulability and venous stasis may be the connective link between ITP and spontaneous subdural and epidural hemorrhages, by venous rupture and dissection of the periosteal layer of the meningeal, respectively.^{27,71}

There is a case report in the literature of spontaneous EDH associated with myelodysplastic syndrome (MDS) described

by Grabel et al.⁵⁹ in a child on daily warfarin use. The cause of bleeding remains obscure due to the previous coagulopathy of the patient. Grabel et al.⁵⁹ recommended the regular use of CT to evaluate pediatric patients with coagulopathy who presented altered mental status.

Neoplasms

Spontaneous EDH caused by neoplasms is a rare condition, with the most common lesions being hepatocellular carcinomas.⁷² In the present literature review, among the patients who presented neoplastic lesions (–Table 4),^{26,72,73,74,75,76,77,78} reports involving metastasis from hepatocellular carcinoma prevailed (50%), followed by metastasis from lung carcinoma. The reason why cranial metastases derived from hepatocellular carcinoma cause EDH more often than other tumors still uncertain, but it is known that they may frequently contribute to intracranial bleeding⁷⁹; what is already known is that carcinomas should be considered as a differential diagnosis in the evaluation of patients with EDH.⁸⁰

The first report of spontaneous EDH involving a primary tumor was described by Mahore et al.,⁷² and the lesion located in the patient was an angiosarcoma. The most common location of hematomas in patients with neoplastic lesions is intratumoral or intraparenchymal, and rarely epidural.⁸⁰ Among EDHs caused by neoplastic disease in the present study (–Table 3), the most common location observed was in the parietal region (78.6%); the hematoma was present overlapping > 1 brain lobe in 50% of the cases. Based on the report by Hassan et al.,²⁶ the possible mechanism involved in the formation of HE in patients with dural metastasis is the rupture of cerebral blood vessels from micrometastases.

In a pediatric case reported in India,⁷² the authors concluded that the possible triggering factor for intracranial bleeding and EDH formation would be the fragility and dysplasia of the thin vessels in the tumor tissue, associated with tissue necrosis. Similar observations were made by Anegawa et al.,⁷⁴ who suggested that hemorrhages initiated in a small intratumoral artery accelerate the displacement of the dura mater.

Cranial metastases due to hepatocellular carcinoma are rare among patients with this neoplasm, ranging from 0.4 to 1.6%.⁸¹ In most EDH cases due to hepatocellular carcinoma, the bleeding derives from the middle meningeal artery, the emissary veins, and the venous sinus.⁸⁰ Woo et al.⁸² reported the case of a patient with hepatocellular carcinoma located at the base of the skull, and the authors demonstrated that the bleeding arose from the diploic space and that the liver dysfunction was an intensifying factor of the bleeding.

Lung carcinomas, especially small cell carcinomas, commonly metastasize to the central nervous system (CNS) and account for between 60 and 70% of CNS metastases, being rarer in the epidural space, with a frequency of < 3.6%.⁷⁵

Simmons et al.⁷⁵ suggested that the treatment of neurological involvement in patients with metastasis should have an aggressiveness proportional to the oncologic treatment, justified in the high potential for deterioration of the clinical picture. In the present review, 57.1% of the patients with a neoplastic lesion died due to failure in the primary tumor organ or went into a permanent vegetative state. Among the other case reports, the prognosis ranged from the partial improvement of the clinical status to complete improvement and return to chemotherapy.

Table 4 Summary of reported cases of spontaneous epidural hematoma associated with neoplastic disease

Author(s), year	EDH etiology	EDH site	Diagnostic imaging exam				Surgery	Outcome
			CT	MRI	AG	Rx		
Anegawa et al., 1989 ⁷⁴	Metastasis of ovarian carcinoma	Right parieto-occipital	x				Yes	Recovered
Kuga et al., 1990 ⁷³	Metastasis of hepatocellular carcinoma	Right parietal	x		x		Yes	Died
Nakagawa et al., 1992 ⁸⁴	Metastasis of hepatocellular carcinoma	Occipital	x				Yes	Died
Simmons et al., 1999 ⁷⁵	Lung carcinoma metastasis	Right parietal	x				Yes	Partially recovered
Hayashi et al., 2000 ⁸⁵	Metastasis of hepatocellular carcinoma	Right parietal	x	x	x		Yes	Died
Dufour et al., 2001 ⁷⁶	Meningioma	Parietal	x	x	x		No	Recovered
Hassan et al., 2009 ²⁶	Lung carcinoma metastasis	Right parieto-temporal	x				Yes	Partially recovered
Kanai et al., 2009 ⁸¹	Metastasis of hepatocellular carcinoma	Left parieto-occipital	x				Yes	Died
Kim, et al., 2010 ⁸⁰	Metastasis of hepatocellular carcinoma	Right temporal	x				Yes	Died
Woo et al., 2010 ⁸²	Metastasis of hepatocellular carcinoma	Right parieto-temporal	x				Yes	Vegetative state
Mahore et al., 2014 ⁷²	Angiosarcoma	Left cerebellar hemisphere	x	x			Yes	Recovered
Kim et al., 2016 ⁷⁹	Metastasis of hepatocellular carcinoma	Left parieto-occipital	x				Yes	Died
Ramesh et al., 2017 ⁷⁷	Peripheral nerve sheath metastasis	Right parietal	x			x	Yes	Recovered
Zhao et al., 2020 ⁷⁸	Gastric carcinoma metastasis	Parietotemporal	x				Yes	Died

Abbreviations: AG, angiography; CT, computed tomography; MRI, magnetic resonance imaging; RX, radiography.

Eosinophilic Granuloma

The case reports of spontaneous EDH due to eosinophilic granuloma (EG) represented 7.3% of all patients in the present study (► **Table 5**). Eosinophilic granuloma is related to Langerhans cell histiocytosis, a rare immunological disorder characterized by histiocytic proliferation in multiple organs. In this context, EG represents the local form of histiocytosis and occurs predominantly in children and adolescents.¹² In our literature review, we observed, among the EG group, that the mean age of the patients was 6.8 years old, ranging from 2 to 15 years old, which reinforces the occurrence among young patients.

Al-Mousa et al.¹⁴ reported a case of a 3-year-old child who presented an EDH associated with EG, verified through CT in an osteolytic lesion closely associated with the hematoma and histopathological analysis confirming the type of lesion. The association between EG and HE is rare, and the patho-

genesis is explained in several ways: stretching of the dura mater during granuloma growth, bleeding of dural neovascularization, erosion of dural surface vessels, and intradiploic erosion.¹² We observed in the present study that the highest occurrence of EG was in the parietal region, followed by the occipital region. In all cases, CT was performed for diagnosis. Surgical intervention was also performed in all patients. All patients listed in ► **Table 5** were male.

Chronic Renal Disease

Chronic renal disease is currently a worldwide public health problem, with an increasing incidence, and it is known that intracranial hemorrhages are a rare but possible presentation, usually spontaneous.¹⁷ In some case reports,^{4,5} renal disease was considered the etiology of spontaneous EDH. The exact mechanism by which chronic renal disease causes bleeding is not understood, but it is comprised that platelet

Table 5 Summary of reported cases of spontaneous epidural hematoma associated with other causes

Author, year	EDH etiology	EDH site	Diagnostic imaging exam				Surgery	Outcome
			CT	MRI	AG	Rx		
Hamamoto et al., 1998 ⁴	Kidney disease	Right occipitotemporal	x			x	Yes	Died
Cho et al., 2001 ⁸	Eosinophilic granuloma	Left occipital	x				Yes	—
Chen et al., 2002 ⁹	Eosinophilic granuloma	Left occipital	x				Yes	—
Mut et al., 2004 ¹⁰	Eosinophilic granuloma	Occipital (bilateral)	x	x			Yes	Recovered
Shahlaie et al., 2004 ⁵	Chronic kidney disease	Left temporoparietal	x				Yes	Died
Ahmad et al., 2005 ²²	Cardiac surgery	Posterior fossa	x				Yes	Recovered
Wani et al., 2008 ²⁵	Intradiploic epidermoid cyst	Left parietooccipital	x				Yes	Recovered
Cho et al., 2009 ²⁴	Intracranial hypotension	Retroclival region		x	x		No	Recovered
Zheng et al., 2009 ¹⁵	Chronic kidney disease	Left temporoparietal	x		x		No	Recovered
Bhat et al., 2010 ¹¹	Eosinophilic granuloma	Right parietal	x				Yes	
Song et al., 2015 ²⁰	Systemic lupus erythematosus	Right frontal and right temporoparietal	x				Yes	Recovered
Yadav et al., 2016 ¹⁷	Chronic kidney disease	Frontal (bilateral)	x				Yes	Recovered
Ruschel et al., 2016 ¹⁸	Drug therapy	Left parietal	x				Yes	Partially recovered
Sadashiva et al., 2016 ¹²	Eosinophilic granuloma	Right temporoparietal	x	x			Yes	Recovered
Bakhaidar et al., 2016 ¹³	Eosinophilic granuloma	Right parietal	x				Yes	Recovered
Khan et al., 2017 ¹⁶	Chronic kidney disease	Frontal (bilateral)	x				No	Recovered
Khan et al., 2017 ¹⁶	Drug therapy	Frontoparietal	x				Yes	Recovered
Chen et al., 2018 ²³	Hysterical crying	Left frontal and right frontal*	x				Yes	Recovered
Fukai et al., 2019 ¹⁹	Drug therapy	Right frontal	x	x	x		Yes	Recovered
Yin et al., 2019 ²¹	Systemic lupus erythematosus	Left temporoparietal. Frontal and left occipital*	x				Yes	Died
Al-Mousa et al., 2020 ¹⁴	Eosinophilic granuloma	Left parietal	x				Yes	Recovered

Abbreviations: AG, angiography; CT, computed tomography; MRI, magnetic resonance imaging; RX, radiography.

*At different times.

dysfunctions have been documented in patients with uremia, a condition that predisposes to the appearance of spontaneous bleeding.¹⁵ Shahlai et al.⁵ reported a case of a patient in end-stage renal disease in the absence of hemodialysis, associating the pathogenesis to the uremia or hypertension of the patient. In an attempt to elucidate the pathogenesis of EDH in the light of chronic renal disease, Khan et al.¹⁶ reported the following causes: fluctuations in ICP during hemodialysis, associated arterial hypertension, uremic platelet dysfunction, use of heparin during hemodialysis, and direct activation of tissue plasminogen activator as a result of hemodialysis.

It is not understood in the literature whether hematoma drainage and brain decompression contribute significantly to the bleeding process in patients with an evident propensity for epidural bleeding,⁵ but it is known that early diagnosis and treatment of coagulopathies should be done if available.¹⁷ Thus, signs such as sudden and severe headache associated with nausea and vomiting, despite the absence of trauma, should be investigated, and spontaneous EDH must be taken into consideration.¹⁷

Medication

Among the reports of spontaneous EDH, some case reports^{16,18,19} have been related to drug therapy. Ruschel et al.¹⁸ reported a case of EDH in a 39-year-old patient using rivaroxaban. The use of rivaroxaban poses a risk of developing hematomas that is 40% lower than the risks posed by the use of Warfarin.¹⁸ Khan et al.¹⁶ reported a patient in treatment for tuberculosis, which led to decreased renal function and consequent EDH formation. As in reports of EDH resulting from renal disease, the exact mechanism for hematoma formation is still not widely understood.

Fukai et al.¹⁹ reported a patient using fingolimod who developed EDH, which may cause arterial vasospasm and reversible posterior encephalopathy syndrome. In this report, the patient had multiple sclerosis, and it is known that this group of patients is more vulnerable to vascular damage, especially those who use fingolimod, which may induce hemorrhage or ischemia, either by vasospasm or vascular rupture, but this fact is still controversial.

Systemic Lupus Erythematosus

Systemic lupus erythematosus (SLE) constitutes an autoimmune disease characterized by clinical heterogeneity. In patients with SLE, EDH can result from thrombocytopenia, hypertension, hemorrhagic infarction, hyperlipidemia, coagulation disorder, and cerebrovascular disease, presenting as a severe comorbidity among these patients.²¹ Song et al.²⁰ also suggested that EDH secondary to SLE may regress more rapidly than EDH of traumatic origin and that increasing the dosage corticotherapy drugs is a relevant condition in the treatment of these patients. The thrombocytopenia presented can derive from several situations, such as platelet destruction by antibodies, therapy with immunosuppressive agents, antiphospholipid antibody, thrombotic microangi-

opathy, medullary depression, and disorder in the maturation of megakaryocytes.²¹

Vascular and Dural Abnormalities

Dural vascular malformations are considered rare lesions with an infrequent occurrence of EDH. In 1983, Hasegawa et al. reported a case of spontaneous EDH associated with a pseudoaneurysm of the middle meningeal artery, and the patient also had frequent reports of otitis media.⁸³ Sanchis et al.¹ reported a case of a patient with a saccular aneurysm of the right middle meningeal artery and parietal dural angioma associated with an EDH. Both patients in the reported cases reported no history of trauma. Dural vascular malformations rarely lead to hematoma formation, but when they occur, they can be seen in the epidural space.⁴

Other Etiologies

Besides the already mentioned reports, Chen et al.²³ reported an uncommon case of spontaneous EDH due to a hysterical crisis; the authors associate the formation of the hematoma to hyperventilation during the crisis. The patient described by Chen et al.²³ presented to the emergency room twice, at 2-year intervals, both times with EDH due to hysterical crying. In the first admission, the EDH was located in the left frontal lobe, and 2 years later, during the second admission, the EDH was located in the right frontal lobe. In the report, the patient did not have any comorbidities or clinical, laboratory, and imaging findings that would explain the bleeding. The authors further reported that crying induces hypertension and microbleeding of the dural vessels, which may cease spontaneously under normal conditions. Hysterical crying may be followed by acute hyperventilation, hypocapnia, and arterial constriction, which leads to a reduction in cerebral blood flow. The decrease in cerebral flow leads to decreased ICP, promoting dural detachment from the bone tissue, thereby triggering the formation of EDHs.

Ahmad et al. reported a case of a patient with EDH following cardiac surgery. Deterioration of the neurological status after cardiac surgery usually occurs due to cerebral edema or embolization. Patients with deteriorating neurological conditions after cardiac surgery should also be investigated for the presence of a hematoma. The cause may be heparinization during the procedure or even hypotension during cardiac arrest.²³ In the present review, one report²⁴ considered that the formation of EDH was due to intracranial hypotension and possibly resulted from a systemic condition. This latter event may cause the rupture of vessels in the dura mater with the variation in brain volume.²²

Wani et al.²⁵ reported the case of an EDH secondary to an intradiploic epidermoid cyst. Intradiploic epidermoid cysts can elevate ICP or eventually evolve into malignancy. Imaging examination can define well the radiolucent lesion with sclerotic borders centered in diploe. The mechanism suggested by the authors²⁵ consists of continuous dural detachment and consequent bleeding from dural vessels or of

bleeding from diploid vessels and extravasation from unnoticed trauma.

Evaluation and Diagnosis

The signs and symptoms of acute EDH involve neurological impairment, sometimes indicating the need for surgical intervention. Sudden headache and consciousness disturbances are the main manifestations of EDH.⁵⁰ In the present study, the clinical picture of the patients varied according to their underlying etiology, location, and EDH volume.

Regarding the evaluation of the patients with spontaneous EDH, clinical examination is the main form of exploring the complaints of the patients. We should pay special attention to the physical examination of the sinuses, the ears, and the chest. Other methods of investigation are sinus radiography (sinus infection), lung radiography (lung mass), abdominal CT (liver neoplasms or other vascular changes), coagulogram (coagulopathies), and histological analysis of hematomas and abnormal tissues.²⁶ Among the imaging examinations, CT remains the most widely used because of the lower cost and the ease and quickness of image acquisition. The diagnosis of EDH is confirmed with CT, and if specific findings associated or not with clinical deterioration are found, emergency surgery should be performed.¹⁷

Epidural hematomas present at CT as an extra-axial collection in the shape of a biconvex lens.²² In the evaluation of the CT, the size and the mass effect of the hematoma and the deviation of midline structures should be observed. The CT has also been useful to evaluate osteolytic lesions in the skull cap.⁹ Magnetic resonance imaging (MRI) has been indicated in case of doubt in the diagnosis and in the differential diagnosis.³⁵ Magnetic resonance imaging examination can reveal cranial convexity infarcts where the EDH is located, a common condition among EDH secondary to SCA.⁶³

Treatment

The choice between conservative treatment and a surgical intervention depends not only on the size of the hematoma but also on the severity of symptoms and disease progression.⁷⁶ Deterioration of neurological conditions is a relevant factor influencing surgical indication.

In our study, the most common treatment was surgery, representing 81% of the cases. Among the surgical interventions, osteoplastic craniotomy followed by hematoma drainage was the most common procedure. Conservative treatment represented 14.7% of the cases and is related to the management of the underlying disease that triggered the formation of the hematoma. Deaths were more frequent among patients who presented neoplastic lesions as the etiology for the formation of the hematoma. The time course of the patients in each study was different, ranging from observation during hospital discharge to a 4-year prospective follow-up.

Conclusion

Nontraumatic EDH represents an uncommon manifestation of several pathologies. A clinical investigation should be attentive to such a possibility since this condition is amenable to medical intervention and presents a good prognosis when diagnosed early. Health professionals must pay attention to the physical examination and to the clinical history of the patient to better understand and approach the patient with EDH. In this sense, it is also important to study the pathogenesis of spontaneous EDH in each etiology, due to the scarcity of precise information about the nature of these events. These strategies may improve the therapies for the treatment of this condition, especially in prevention.

Conflict of Interests

The authors have no conflict of interests to declare.

References

- Sanchis JFF, Orozco M, Cabanes J. Spontaneous extradural hematomas. *J Neurol Neurosurg Psychiatry* 1975;38(06):577-580
- Babatola BOBO, Salman YAYA, Abiola AMAM, Okezie KOKO, Oladele ASAS. Spontaneous epidural haematoma in sickle cell anaemia: case report and literature review. *J Surg Tech Case Rep* 2012;4(02):135-137
- Schneider RC, Hegarty WM, Arbor ANN. Extradural hemorrhage as a complication of otological and rhinological infections. *Ann Otol Rhinol Laryngol* 1951;60(01):197-206
- Hamamoto O, Nakano H, Guerreiro NE, et al. [Spontaneous epidural hematoma. Report of two cases]. *Arq Neuropsiquiatr* 1998;56(3A):453-456
- Shahlaie K, Fox A, Butani L, Boggan JE. Spontaneous epidural hemorrhage in chronic renal failure. A case report and review. *Pediatr Nephrol* 2004;19(10):1168-1172
- Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009;6(07):e1000100
- Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. *Syst Rev* 2016;5(01):210. Doi: 10.1186/s13643-016-0384-4
- Cho DY, Liao WR, Chiang IP. Eosinophilic granuloma with acute epidural hematoma: a case report. *Pediatr Neurosurg* 2001;35(05):266-269
- Chen H-C, Shen W-C, Chou D-Y, Chiang IP. Langerhans cell histiocytosis of the skull complicated with an epidural hematoma. *AJNR Am J Neuroradiol* 2002;23(03):493-495
- Mut M, Çataltepe O, Bakar B, Cila A, Akalan N. Eosinophilic granuloma of the skull associated with epidural haematoma: a case report and review of the literature. *Childs Nerv Syst* 2004;20(10):765-769
- Bhat ARAR, Jain AKAK, Kirmani ARR, Nizami F. Pathological intracranial extradural hematoma in a 10-year-old child. *J Pediatr Neurosci* 2010;5(02):164-166
- Sadashiva N, Baruah S, Rao S, et al. Eosinophilic Granuloma of Skull with Fluid Level and Epidural Hematoma: A Case Report and Review of the Literature. *Pediatr Neurosurg* 2017;52(01):41-45 <https://pubmed.ncbi.nlm.nih.gov/27595542/>
- Bakhaidar MGGM, Alghamdi FAFA, Baeesa SSSSS. Spontaneous extradural hemorrhage due to Langerhans cell histiocytosis of the skull in a child: A rare presentation. *J Pediatr Neurosci* 2016;11(01):52-55
- Al-Mousa A, Altarawneh M, Alqatawneh O, Bashir Z, Al-Dwairy S, Shtaya A. Eosinophilic granuloma of the skull presenting as non-

- traumatic extradural haematoma in children. *Int J Gen Med* 2020; 13:1229–1234 <https://www.embase.com/search/results?subaction=viewrecord&id=L2005497645&from=export> cited 2020Dec8 [Internet]
- 15 Zheng FX, Chao Y, Zheng FX, Chao Y. Spontaneous intracranial extradural hematoma: case report and literature review. *Neurol India* 2009;57(03):324–326
 - 16 Khan KAKA, Chhabra S, Sharma S, Purohit D. Spontaneous extradural hematoma: a rare entity. *Br J Neurosurg* 2020;34(01):86–88
 - 17 Yadav P, Verma A, Chatterjee A, Srivastava D, Riaz MR, Kannaujia A. Spontaneous Extradural Hemorrhage in a Patient with Chronic Kidney Disease: A Case Report and Review of Literature. *World Neurosurg* 2016;90:707.e13–707.e16 <https://pubmed.ncbi.nlm.nih.gov/27004756/> [Internet]
 - 18 Ruschel LGLG, Rego FM, Milano JBJB, Jung GS, Silva LF Jr, Ramina R. Spontaneous intracranial epidural hematoma during rivaroxaban treatment. *Rev Assoc Med Bras* (1992) 2016;62(08):721–724 <https://pubmed.ncbi.nlm.nih.gov/27992010/> [Internet]
 - 19 Fukai R, Takahashi K, Abe H, et al. Non-traumatic acute epidural hematoma in multiple sclerosis treated with fingolimod. *Front Neurol* 2019 ;10(JUL):763 <https://pubmed.ncbi.nlm.nih.gov/31379717/> cited 2020Dec8 [Internet]
 - 20 Song W, Li M, Zhu B, Chen W, Bao J, Wang D, Xu F. Spontaneous epidural hematoma complicated by systemic lupus erythematosus: one case report. *Int J Clin Exp Med* 2015;8(09):16813–16816
 - 21 Yin R, Qiu CC-X, Yin L, Zhang Y. Case report multiple spontaneous intracranial hemorrhages in a patient with systemic lupus erythematosus: A case report. *Int J Clin Exp Med* 2019;12(08):10900–10904 Available from [Internet] <https://www.embase.com/search/results?subaction=viewrecord&id=L2002644987&from=export>
 - 22 Ahmad FU, Pandey P, Mahapatra AK. Spontaneous posterior fossa extradural hematoma—a rare complication following cardiac surgery. *Pediatr Neurosurg* 2005;41(01):49–51 <https://pubmed.ncbi.nlm.nih.gov/15886514/>
 - 23 Chen C-TC-T, Lai H-YH-Y, Chang T-WT-W, Lee CY. Repeated Spontaneous Intracranial Epidural Hemorrhage After Hysterical Crying. *World Neurosurg* 2018;114:34–36
 - 24 Cho CB, Park HK, Chough CK, Lee KJ. Spontaneous bilateral supratentorial subdural and retroclival extradural hematomas in association with cervical epidural venous engorgement. *J Korean Neurosurg Soc* 2009;46(02):172–175 <https://pubmed.ncbi.nlm.nih.gov/19763223/> cited 2020Dec8 [Internet]
 - 25 Wani AAA, Ramzan AUUU, Kirmani ARAR, Bhatt AR, Hamdani N, Zargar J. Intradiploic epidermoid causing spontaneous extradural hematoma: case report. *Neurosurgery* 2008;62(04):E971–, discussion E971 <https://pubmed.ncbi.nlm.nih.gov/18496165/> [Internet]
 - 26 Hassan MFMF, Dhamija B, Palmer JDJD, Hilton D, Adams W. Spontaneous cranial extradural hematoma: case report and review of literature. *Neuropathology* 2009;29(04):480–484
 - 27 Ntantos D, Karantali E, Prevezianou A, Angelopoulos P, Bostantjopoulou S. Spontaneous Epidural Hematomas due to Cerebral Venous Thrombosis in a Patient with Immune Thrombocytopenic Purpura. *J Stroke Cerebrovasc Dis* 2020;29(11):105244
 - 28 Kelly DL Jr, Smith JM. Epidural hematoma secondary to frontal sinusitis. Case report. *J Neurosurg* 1968;28(01):67–69
 - 29 Marks SM, Shaw MD, Marks SMM. Spontaneous intracranial extradural hematoma. Case report. *J Neurosurg* 1982;57(05):708–709 <https://pubmed.ncbi.nlm.nih.gov/7131075/>
 - 30 Ataya NL. Extradural haematoma secondary to chronic sinusitis: a case report. *J Laryngol Otol* 1986;100(08):951–953
 - 31 Sakamoto T, Harimoto K, Inoue S, Konishi A. Extradural hematoma following maxillary sinusitis. Case illustration. *J Neurosurg* 1997; 87(01):132
 - 32 Papadopoulos MCC, Dyer A, Hardwidge C. Spontaneous extradural haematoma with sinusitis. *J R Soc Med* 2001;94(11):588–589
 - 33 Moonis G, Granados A, Simon SL. Epidural hematoma as a complication of sphenoid sinusitis and epidural abscess: a case report and literature review. *Clin Imaging* 2002;26(06):382–385
 - 34 Griffiths SJ, Jatavallabhula NS, Mitchell RD. Spontaneous extradural haematoma associated with craniofacial infections: case report and review of the literature. *Br J Neurosurg* 2002;16(02):188–191
 - 35 Chaiyasate S, Halewyck S, Van Rompaey K, Clement P. Spontaneous extradural hematoma as a presentation of sinusitis: case report and literature review. *Int J Pediatr Otorhinolaryngol* 2007; 71(05):827–830
 - 36 Takahashi Y, Hashimoto N, Hino A. Spontaneous epidural hematoma secondary to sphenoid sinusitis -case report-. *Neurol Med Chir (Tokyo)* 2010;50(05):399–401
 - 37 Cho K-SK-S, Cho W-HW-H, Kim H-JH-J, Roh HJ. Epidural hematoma accompanied by oculomotor nerve palsy due to sphenoid sinusitis. *Am J Otolaryngol* 2011;32(04):355–357
 - 38 Spennato P, De Paulis D, Bocchetti A, Michele Pipola A, Sica G, Galzio RJ. Spontaneous intracranial extradural haematoma associated with frontal sinusitis and orbital involvement. *Neurol Sci* 2012;33(02):435–439
 - 39 Clein LJ. Extradural hematoma associated with middle-ear infection. *Can Med Assoc J* 1970;102(11):1183–1184
 - 40 Novaes V, Gorbitz C. Extradural hematoma complicating middle-ear infection. Report of a case. *J Neurosurg* 1965;23(03):352–353
 - 41 Bolliger SASA, Thali MJMJ, Zollinger U. Nontraumatic intracranial epidural hematoma: a case report. *Am J Forensic Med Pathol* 2007;28(03):227–229
 - 42 Karacostas D, Artemis N, Papadopoulou M, Christakis J. Case report: epidural and bilateral retroorbital hematomas complicating sickle cell anemia. *Am J Med Sci* 1991;302(02):107–109
 - 43 Resar LMS, Oliva MM, Casella JF. Skull infarction and epidural hematomas in a patient with sickle cell anemia. *J Pediatr Hematol Oncol* 1996;18(04):413–415
 - 44 Ganesh A, William RR, Mitra S, et al. Orbital involvement in sickle cell disease: a report of five cases and review literature. *Eye (Lond)* 2001;15(Pt 6):774–780
 - 45 Arends S, Coebergh JAJA, Kerkhoffs JJJL, van Gils A, Koppen H. Severe unilateral headache caused by skull bone infarction with epidural haematoma in a patient with sickle cell disease. *Cephalalgia* 2011;31(12):1325–1328
 - 46 Bölke E, Scherer A. Sickle cell disease. *CMAJ* 2012;184(03):E201
 - 47 Komarla R, Soares BPPB, Chern JJJJ, Milla SS. Spontaneous epidural hematoma secondary to bone infarction in sickle cell anemia: case report. *J Neurosurg Pediatr* 2018;22(01):18–21
 - 48 Banerjee C, Yowtak J, Fridlyand D, Alleyne C Jr. Acute spontaneous intracranial epidural haematoma and disseminated intravascular coagulation in a paediatric sickle cell patient. *BMJ Case Rep* 2018; 2018:bcr-2018-224504
 - 49 Saha B, Saha A. Spontaneous Epidural Hemorrhage in Sickle Cell Disease, Are They All the Same? A Case Report and Comprehensive Review of the Literature. *Case Rep Hematol* 2019;2019:8974580
 - 50 Tomboravo C, Rajaonarison Ny Ony LHN, Andrianarimanitra HU, Rakoto Alison OA, Ahmad A. Epidural hematoma: a rare complication of sickle cell disease. *Sang Thromb Vaiss* 2019;31(01):29–31
 - 51 Vural M, Yazar C, Durmaz R, Atasoy MA. Spontaneous acute subdural hematoma and chronic epidural hematoma in a child with F XIII deficiency. *J Emerg Med* 2010;38(01):25–29
 - 52 Farah RARA, Al Danaf JZJZ, Chahinian RARA, et al. Spontaneous epidural hematoma in a child with inherited factor XIII deficiency. *J Pediatr Hematol Oncol* 2014;36(01):62–65 <https://pubmed.ncbi.nlm.nih.gov/23619114/> [Internet]
 - 53 Kuwayama N, Takahashi S, Sonobe M, Sugita K. Spontaneous bilateral extradural hematomas. Case report. *J Neurosurg* 1985; 62(01):139–141
 - 54 Prabhu S, Agarwal S, Prabhu S. Spontaneous Intracranial Extradural Hematoma Secondary to Hypofibrinogenemia: A Rare Case

- Report. *Asian J Neurosurg* 2019;14(04):1288–1290 <https://pubmed.ncbi.nlm.nih.gov/31903380/> cited 2020Dec8 [Internet]
- 55 Cooper NA, Lynch MA. Delayed haemorrhagic disease of the newborn with extradural haematoma. *BMJ* 1979;1(6157):164–165
- 56 y AK, Yaman Y, Isguder R, et al. Spontaneous epidural and subdural hematoma in a child with afibrinogenemia and postoperative management. *Blood Coagul Fibrinolysis* 2014;25(04):398–400
- 57 Pati S, Kombogiorgas D, Anwar A, Price RF. Spontaneous extra-axial intracranial hemorrhage followed by thrombosis in congenital afibrinogenemia: perioperative management of this rare combination. *Surg Neurol* 2009;71(06):689–692, discussion 692
- 58 Zhang W, Zhang W, Gao Z, Wang J. Gigantic ossified chronic epidural haematoma and contralateral postoperative subdural haematoma: A case report and literature review. *Br J Neurosurg* 2015;29(01):85–86
- 59 Grabel JC, Sacher M, Rothman AS. Bilateral extradural hematomas in a thrombocytopenic infant receiving anticoagulants: case report. *Neurosurgery* 1989;25(05):828–830
- 60 Iliescu DBDB, Ioan BGBG, Zetu I, Astărăstoae V. Non-traumatic spontaneous acute epidural hematoma - Case report. *Rev Med Leg* 2009;17(02):111–114
- 61 Ng WHH, Yeo TTT, Seow WTT. Non-traumatic spontaneous acute epidural haematoma - report of two cases and review of the literature. *J Clin Neurosci* 2004;11(07):791–793
- 62 Dahdaleh NS, Lindley TE, Kirby PA, Oya H, Howard MAA III. A “neurosurgical crisis” of sickle cell disease. *J Neurosurg Pediatr* 2009;4(06):532–535
- 63 Hettige S, Sofela A, Bassi S, Chandler C. A review of spontaneous intracranial extradural hematoma in sickle-cell disease. *Acta Neurochir (Wien)* 2015;157(11):2025–2029, discussion 2029
- 64 N'dri Oka D, Tokpa A, Bah A, Derou L. Spontaneous Intracranial Extradural Hematoma in Sickle Cell Disease. *J Neurol Surg Rep* 2015;76(01):e97–e99
- 65 Mishra SS, Senapati SB, Gouda AK, Behera SK, Patnaik A. Spontaneous extradural and subgaleal hematoma: A rare neurosurgical crisis of sickle cell disease. *Asian J Neurosurg* 2017;12(01):47–50 <http://www.ncbi.nlm.nih.gov/pubmed/28413532> cited 2020Dec8 [Internet]
- 66 Saul D, Pollock AN, Saul D. Skull Bone/Calvarial Infarction and Spontaneous Epidural Hematoma as Cause of Severe Headache in the Emergency Department. *Pediatr Emerg Care* 2017;33(12):809–810
- 67 Kalala Okito JPJ-P, Van Damme O, Calliauw L, Al Moutaery K, Servadei F. Are spontaneous epidural haematomas a rare complication in sickle cell disease? A report of two new cases. *Acta Neurochir (Wien)* 2004;146(04):407–410
- 68 Ewane HBMBMBM, Himmiche M, Segbedi F. Interdisciplinary Neurosurgery: Advanced Techniques and Case Management Management of Spontaneous frontal epidural and subarachnoid hemorrhage in a sickle cell patient: A tragic end. *INAT [Internet]* 2016;3:17–18. Doi: 10.1016/j.inat.2015.12.001
- 69 Pallotta R, De Souza Andrade A, Almeida D, Lima DF, Gomes IML. Bilateral epidural and retro-orbital hematoma as a complication of sickle cell anemia - Case report. *Rev Bras Neurol Psiquiatr* 2010;14(01):27–29
- 70 Ilhan N, Acipayam C, Aydogan F, et al. Orbital compression syndrome complicated by epidural hematoma and wide cephalohematoma in a patient with sickle cell disease. *J AAPOS* 2014;18(02):189–191. Doi: 10.1016/j.jaapos.2013.11.011
- 71 Knopman J, Tsiouris AJ, Souweidane MM. Atraumatic epidural hematoma secondary to a venous sinus thrombosis: a novel finding. *J Neurosurg Pediatr* 2008;2(06):416–419
- 72 Mahore A, Ramdasi RVRV, Pauranik A, Epari S. Tumour bleed manifesting as spontaneous extradural haematoma in posterior fossa. *BMJ Case Rep* 2014;2014:bcr2014205175
- 73 Kuga Y, Waga S, Itoh H. Intracranial hemorrhage due to brain metastasis from hepatocellular carcinoma—case report. *Neurol Med Chir (Tokyo)* 1990;30(10):768–771
- 74 Anegawa S, Hirohata S, Tokutomi T, Kuramoto S. Spontaneous epidural hematoma secondary to dural metastasis from an ovarian carcinoma—case report. *Neurol Med Chir (Tokyo)* 1989;29(09):854–856
- 75 Simmons NEE, Elias WJJ, Henson SLL, Laws ER. Small cell lung carcinoma causing epidural hematoma: case report. *Surg Neurol* 1999;51(01):56–59
- 76 Dufour H, Métellus P, Manera L, Fuentes S, Do L, Grisoli F. Spontaneous vertex extradural hematoma: considerations about causes. Case report and review of the literature. *J Neurosurg* 2001;94(04):633–636
- 77 Ramesh ASS, Singh P, Jacob SESE, Madhugiri VS. Metastatic malignant peripheral nerve sheath tumour presenting as a spontaneous extradural haematoma - A case report. *Br J Neurosurg* 2017;31(03):382–384
- 78 Zhao C, Wei Y, Liu J, Xu S, Jiang X, Di G. Spontaneous acute epidural hematoma associated with chronic subdural hematoma due to dural metastasis of gastric carcinoma: a case report and literature review. *Int J Neurosci* 2020
- 79 Kim YSY-S, Moon KSK-S, Lee KHK-H, et al. Spontaneous acute epidural hematoma developed due to skull metastasis of hepatocellular carcinoma: A case report and review of the literature. *Oncol Lett* 2016;11(01):741–744
- 80 Kim BG, Yoon SM, Bae HG, Yun IG. Spontaneous intracranial epidural hematoma originating from dural metastasis of hepatocellular carcinoma. *J Korean Neurosurg Soc* 2010;48(02):166–169
- 81 Kanai R, Kubota H, Terada T, Hata T, Tawarayama E, Fujii K. Spontaneous epidural hematoma due to skull metastasis of hepatocellular carcinoma. *J Clin Neurosci* 2009;16(01):137–140
- 82 Woo KMKM, Kim BCB-CB-CC, Cho K-TTK-T, Kim EJ. Spontaneous epidural hematoma from skull base metastasis of hepatocellular carcinoma. *J Korean Neurosurg Soc* 2010;47(06):461–463
- 83 Hasegawa H, Bitoh S, Fujiwara M, Ohtsuki H. [Spontaneous intracranial extradural hematoma]. *Neurol Med Chir (Tokyo)* 1983;23(12):968–971
- 84 Nakagawa Y, Yoshino E, Suzuki K, Tatebe A, Andachi H. Spontaneous epidural hematoma from a hepatocellular carcinoma metastasis to the skull—case report. *Neurol Med Chir (Tokyo)* 1992;32(05):300–302
- 85 Hayashi K, Matsuo T, Kurihara M, Daikoku M, Kitange G, Shibata S. Skull metastasis of hepatocellular carcinoma associated with acute epidural hematoma: a case report. *Surg Neurol* 2000;53(04):379–382
- 86 Dixit A, Chatterjee TC, Papneja M, et al. Sickle beta-thalassemia presenting as orbital compression syndrome. *Ann Hematol* 2004;83(08):536–540
- 87 Azhar MJ. Extradural hemorrhage: A rare complication and manifestation of stroke in sickle cell disease. *Oman Med J* 2010;25(04):e017
- 88 Page C, Gardner K, Height S, Rees DC, Hampton T, Thein SL. Nontraumatic extradural hematoma in sickle cell anemia: a rare neurological complication not to be missed. *Am J Hematol* 2014;89(02):225–227
- 89 Serarslan Y, Aras M, Altaş M, Kaya H, Urfalı B. Non-traumatic spontaneous acute epidural hematoma in a patient with sickle cell disease. *Neurocirugia (Astur)* 2014;25(03):128–131