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Review Article

Coexistence of intracranial dysraphic cyst and aneurysm: A qualitative systematic review and multiple management portraits

Francesco Calvanese [a,1], Anna Maria Auricchio [a,b,1,*], Anni Pohjola [a], Rahul Raj [a], Mika Niemelä [a]

[a] Department of Neurosurgery, Helsinki University Hospital and University of Helsinki, Helsinki, Finland
[b] Department of Neurosurgery, Fondazione Policlinico Universitario A. Gemelli IRCCS Università Cattolica del Sacro Cuore, Rome, Italy

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ABSTRACT

Background: The coexistence of intracranial aneurysms and dysraphic cysts is a rare manifestation. The response triggered by the cyst and its proinflammatory content could play a role in the rupture or growth of a neighboring aneurysm.

Methods: We performed a systematic review according to the PRISMA guidelines searching PubMed, Medline, Google Scholar and Embase. Additionally, we report a case of one patient with both a dermoid cyst and an ipsilateral anterior cerebral artery aneurysm, illustrating a progressive formation of the vascular lesion during the follow-up of the cyst.

Results: Out of 103 papers fulfilling the inclusion criteria for the systematic review, 79 articles were selected for eligibility. Finally, a total of 9 cases, including our own case, were considered for the review. We found that all aneurysms were in the anterior circulation and all cysts were supratentorial. The aneurysms or parent vessels were in proximity or in contact with the dysraphic lesion, presenting a strong adherence to its capsule. The 3 dermoids presented with cysts rupture and showed simultaneous or delayed subarachnoid aneurysmal hemorrhage. Two epidermoid cysts were diagnosed after aneurysm rupture, while the others due to focal mass effect, as in the case of the neurenteric cyst.

Conclusions: Coexistence of intracranial aneurysm and disraphic cyst is a rare finding with multiple possible presentations. In managing patients harboring disraphic cyst, the presence of the aneurysm should be ruled out during the standard workup. A coexistence of these pathologies could affect their natural histories, and this could justify a more active management protocol.

1. Introduction

The association between intracranial aneurysms (IA) and neoplasms (both intra- and extraparenchymal) has been reported as 1 %, even though it might be higher in the more recent series due to the improvement of neuroimaging techniques [1,2]. Intracranial epidermoids, dermoids and neuroenteric cysts represent rare dysraphic malformations accounting for less than 2 % of all intracranial masses. Their aetiology is related to a combination of a failed neural tube closure and an ectopic tissue inclusion during the gastrulation phase of human development [3,4]. The prevalence of IAs is up to 6.6 % in the adult population [5,6] and a possible role of vessel wall inflammation has been postulated regarding their aetiopathogenesis [7,8]. In the cases of association between dysembriogenetic cysts and aneurysms, it has been hypothesized that the response triggered by the cyst and its proinflammatory content may play a role in the rupture or in growing of a neighboring IAs [2,9]. However, the coexistence of these entities is rare, and therefore the natural history has remained unclear. To the best of our knowledge, no systematic review addressing this topic has been performed yet. The aim of this study was to perform a systematic review

Abbreviations: ACoA, anterior communication artery; An, aneurysm; Cy, cyst; CN, cranial nerve; CSF, cerebrospinal fluid; F, female; ICA T, internal carotid artery terminus tract; M, male; M1, first middle cerebral artery tract; M2, second middle cerebral artery tract; MCA bif, middle cerebral artery bifurcation; Rup, ruptured; Unrup, unruptured.

* Corresponding author at: Department of Neurosurgery, Helsinki University and University Hospital, Topeliuksenkatu 5, 00260 Helsinki, Finland.
E-mail address: anna.maria90a@gmail.com (A.M. Auricchio).

[1] These authors equally contributed.

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about the association between intracranial dysraphic cysts (IDC) and IAs, describing possible pathogenesis, changes in the natural history and in the management. Additionally, we report a case of association between a dermoid cyst and a homolateral anterior cerebral artery IA.

2. Material and Methods

This study was conducted according to the ethico-legal policies of our Research Institute. We retrospectively identified all cases of IAs with a coexistent diagnosis of epidermoid/dermoid/neuroenteric cyst referred to the department of Neurosurgery of the Helsinki University Hospital between January 2003 and December 2022. All patients included in the study expressed their consent to the anonymous publication of data.

The systematic review was conducted in accordance with the PRISMA-P (Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols) guidelines. An online literature search was launched on PubMed, Medline, Google Scholar and Embase using the following research string: "aneurysm" AND "intracranial" AND "epidermoid cyst" OR "dermoid cyst" OR "neuroenteric cyst"; "vascular malformation" AND "intracranial" AND "epidermoid cyst" OR "dermoid cyst" OR "neuroenteric cyst; "aneurysm" AND "intracranial" AND "dysraphic malformation". The last search was conducted on 22nd May 2023. Using the bibliographies of articles identified in our primary search, we then performed a secondary search. Articles were reviewed by the title and abstract for potential relevance. If the title and abstract did not indicate the degree of relevance, the full-text article was analysed. All papers were independently reviewed by two authors (A.M.A. and F.C.). Any discordance was solved by the consensus of the senior author (M.N.). Studies reporting the coexistence of aneurysm and epidermoid, dermoid, neuroenteric cysts in the same patient were selected. Inclusion criteria were the availability of clinical and radiological reports for the single patients; human subjects; papers written in English, Italian and French and full-text available articles. We excluded guidelines, reviews, commentaries, and letters to the editor. According to the rarity of this coexistence, also case reports were included for the final analysis.

The result of systematic literature review was critically interpretated and synthetized in line with the most important clinical and preclinical studies exploring the relation between aneurysm development and rupture with vessel wall inflammation [10–12] according to ENTREQ statement (Enhancing transparency in reporting the synthesis of qualitative research) [13].

3. Results

3.1. Systematic review of the literature

Our primary literature search identified 103 papers fulfilling the inclusion criteria. After exclusion of duplicates, 79 articles were selected for eligibility. Seventy-one papers were excluded because they did not focus on the topic of our study, or no clinical and radiological data were available. Finally, 8 articles were selected for the systematic review [2,9,14–19]. Fig. 1 summarizes the PRISMA flow chart for the selection of 8 full-text articles included in the review. Illustrating the extremely rare concurrence between IAs and dysraphic malformations, only eight case reports were found.

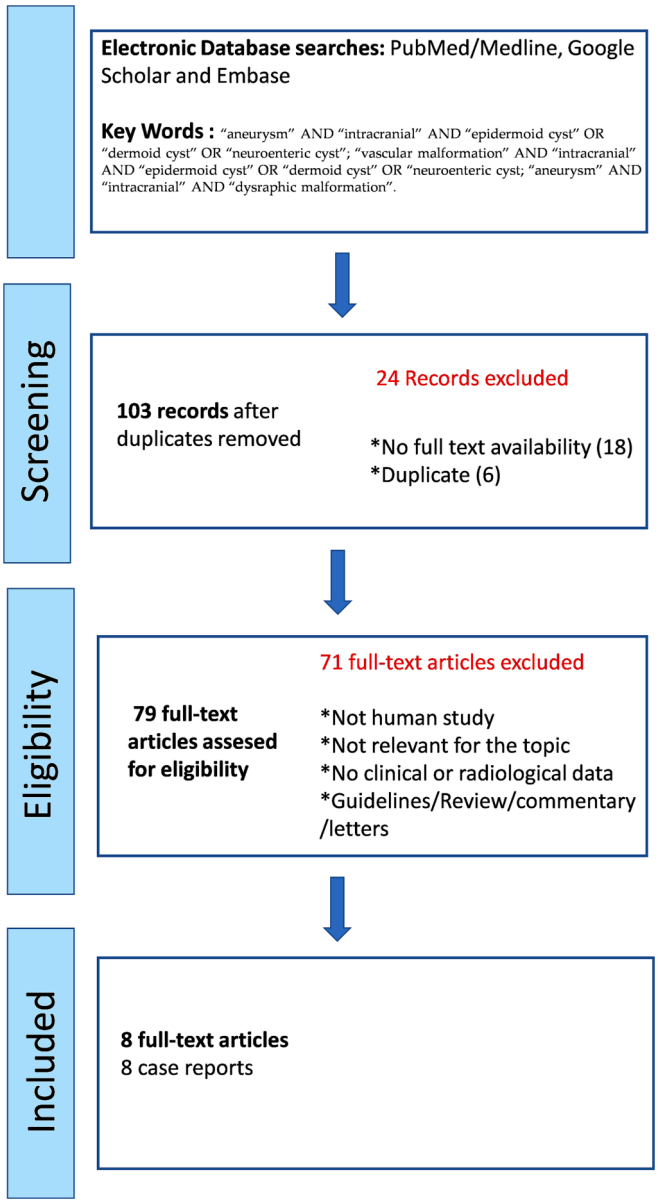

Fig. 1. PRISMA flow chart.

3.2. Case series

We identified one patient with a concurrent IA and dermoid cyst from our prospective aneurysm database. This, in addition to the 8 cases reported previously in the literature, are illustrated in Table 1. Owing to the limited number of cases, only a descriptive analysis was performed. Median age was 46.8 years and male:female ratio was 5:4. Five cases [2,15,17,19] with an epidermoid and 3 with dermoid cysts [9,16] (including our case) were associated with an IA. Only one case of multiple association between a neuroenteric cyst, epidermoid cyst and multiple aneurysms was reported [18]. The previous medical history was available for 8 patients. No risk factors (smoking or hypertension) for IA development or rupture in any of the patients were reported. All aneurysms were in the anterior circulation and all cysts were supratentorial, with a predominance of the sellar/parasellar region (5 cases, 56 %).

Two cases with an epidermoid cyst and IA were diagnosed after an IA rupture, while the rest (n = 3) due to the focal mass effect of the lesion. Among them, only one case of intracystic aneurysm rupture was identified.

All 3 dermoid cysts associated with IAs, presented with a cyst rupture, with severe symptoms related either to aseptic meningitis or seizures. Among them, two cases (67 %) demonstrated a simultaneous or delayed (our case) IA rupture.

In all cases the IA or the parent vessel was in the proximity or in contact with the IDC. Moreover, all operative reports described a strong adherence between the IDC capsule and the aneurysm wall or parent vessel. This finding was much more evident in the case with ruptured IA or previous cystic rupture.

Table 1
Cases of association between aneurysm and dysraphic cysts in literature.

Author, year	Age/Sex	Aneursym Rupture Risk Factors	Symptoms and Signs	Type of cyst	Size (mm)/Location		Ruptured/unruptured presentation	Complications	Treatment	Outcome
					Cyst	Aneurysm				
Sakaki, 1981 [17]	51/M	None	Rigor nucalis, right III CN palsy	Epidermoid	NA, Right parasellar	7 mm, Right ICA	Unrup Cy, Rup An	Vasospasm	Cy exeresis and An clipping	Improved
Goodman and Nelson, 1988 [15]	48/F	None	Right visual loss, left quadrantopsia,	Epidermoid	NA, Midline suprasellar	NA, ACoA	Unrup Cy; Unrup An	CSF leakage	Cy exeresis and An clipping	Improved
Ahmad, 1992 [9]	21/F	None	Seizure	Dermoid	NA, Right parasellar and temporal fossa	NA, Right M1	Rup Cy; Unrup An	None	Cy exeresis and An wrapping	Stable
Schonauer, 1999 [19]	42/F	None	Bilateral papillaedema, partial III NC palsy, left hemiparesis, ataxia	Epidermoid	NA, Right supra-parasellar and interpeduncular cistern	14 mm, Left ICA T	Unrup Cy; Unrup An	None	Cy exeresis and An Clipping	Improved
Kurt, 2010 [2]	45/M	NA	Headache, vomiting, loss of consciousness, left hemiparesis	Epidermoid	NA, Right frontotemporobasal	NA, Right MCA bif and ACoA	Unrup Cy; Rup An	None	Cy exeresis and An MCA Clipping	Improved
Kim, 2011 [16]	50/M	None	Headache, Coma	Dermoid	43 × 21 mm, Right frontotemporobasal	NA, Right ICA T	Rup Cy, Rup An	Aseptic Meningitis	Cy exeresis and An Clipping	Improved
Yao, 2017 [2]	42/M	None	Headache, Dizziness	Epidermoid	NA, Right parasellar and petroux apex	NA, Right M2 distal and ICA clinoid	Unrup Cy; Unrup An	None	Cy exeresis and An M2 Clipping	Improved
Salem, 2022 [18]	67/M	None	None (Incidental finding)	Epidermoid and Neuroenteric	EC: NA, Right frontal; NC: 64 × 40 mm, Right frontotemporal	4 mm, MCA bif (with right frontal cavernoma)	Unrup Cy; Unrup An	None	EC fenestration (previously); NC exeresis and An Clipping	Stable
Present case	56/F	None	Aseptic meningitis, visual loss, loss consciousness	Dermoid	27 × 25 × 20 mm, Right parasellar	8 mm, Right A1	Rup Cy; Rup An	Bilateral visual loss	An Coiling	Dead

Concerning treatment, all the cases, except the case from our own institute, were treated with a surgical excision of the cyst and clipping of the aneurysm. Although no quantitative scale was used in previous case reports, six patients were reported to have improved (66.6 %) after treatment, and the other two remained clinically stable. The remaining case was treated conservatively after cyst rupture and after subsequent subarachnoid hemorrhage, with coil embolization. Unfortunately, this was the only one case where the patient died.

3.3. *Case report*

A 56-year-old woman with no medical history of cigarette smoking or hypertension was referred to the emergency department of Helsinki University Hospital in March 2021, complaining headache with a subsequent loss of consciousness. An unenhanced head computed tomography (CT) scan documenting fatty hypointense “droplets” disseminated in the basal cisterns raised a suspicion of a ruptured dermoid cyst (Fig. 2**A, B**). In fact, the patient presented with a right supra- and parasellar dermoid cyst which had already been treated 45 years before. The treatment had taken place in another institute and consisted of a partial resection and drainage of the cyst, due to the progressive bilateral visual impairing. At that time, no evidence of any vascular malformations was reported.

The gadolinium enhanced magnetic resonance imaging (MRI) confirmed the presence of fat in the basal cisterns and in the contralateral Sylvian fissure and documented a leptomeningeal enhancement associated with a vasospasm on TOF sequence. The cyst was heterogeneously hyperintense on FLAIR and T1-WI and was now diagnosed in coexistence of a new IA - an ipsilateral right-sided unruptured A1 saccular 8 mm aneurysm (Fig. 2 **C–H**). The rupture of the dermoid cyst had resulted in an aseptic meningitis, with a consequent vasoconstriction, which was treated with oral nimodipine. After the acute phase, the patient started a rehabilitation programme, with no improvement in the cognitive or memory impairments.

Patient reported new visual deficits in the right eye in summer 2021 and underwent MRI which showed a slight increase in the size of the unruptured right-sided A1 aneurysm. Patient refused endovascular diagnosis or treatment with DSA and only agreed for non-invasive radiological follow-up (FU). After 1 year of FU the patient underwent a new MRI showing no change in the aneurysm size. The patient was clinically stable until February 2023, when she came to the emergency department complaining headache, visual disturbance, neck pain and progressive consciousness deterioration. A new head CT scan showed an aneurysmal subarachnoid haemorrhage (SAH) with intraventricular blood collection and hydrocephalus related to a likely A1 aneurysm rupture (Fig. 3 **A**). Despite the patient being in a poor neurological condition, a successful coil embolization of the IA was performed (Fig. 3 **C-E**) and an external ventricular drainage was positioned. Unfortunately, after few days the patient died due to a sudden cardiac arrest.

4. Discussion

The coexistence of IAs with any kind of an intracranial neoplasm is reported to be approximately 1 % [2]. The concurrence of IA and IDC is rare, and therefore the management of these entities is challenging [2.] In the systematic review we found only 8 previous cases which were reported after 1965 [2,9,15–17,17–19]. Furthermore, 67 % of the cases with dermoid cystic rupture were associated with a simultaneous or delayed IA rupture. This could indicate a relationship between inflammatory processes of the IDC and IA. Strengthening this hypothesis, we reported a case showing a possible progressive formation of A1 aneurysm after a rupture of a dermoid cyst (Fig. 2). Unfortunately, our patient refused the treatment for the IA and later deceased because of SAH. This event suggests a strict FU and/or management of both lesions in the same or subsequential treatment sessions. The coexistence could cause an alteration in the natural histories of these lesions, which could

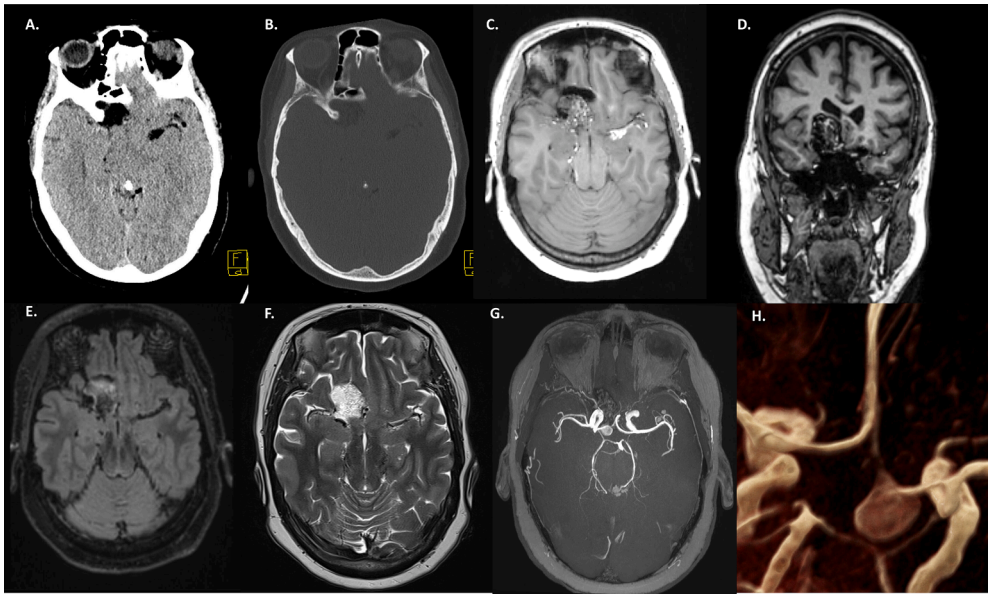

Fig. 2. A., B. Axial CT scan showing fatty hypointense "droplets" disseminated in the basal cisterns and Sylvian fissure after the rupture of the dermoid cyst. **C.** Axial post gadolinium MRI confirming the disseminated fat "droplets" of the cyst in the Sylvian fissure and slightly pachimeningeal enhancement. **D., E., F.** Coronal T1WI, axial FLAIR and T2WI MRI showing the disomogenous intensity of the cyst. **G., H.** TOF MRI imaging and 3D MRI reconstruction showing the 8-mm A1-Acom complex aneurysm angioarchitecture.

indicate a more active management protocol.

Due to the rarity of this coexistence, it has been postulated that these lesions develop separately with different pathophysiological mechanisms [15]. However, the incidence of this coexistence could be underestimated and underreported, because the interest of medical literature and journals (i.e., difficulties in publishing case reports) has been shifting towards different topics. Reasons for this include that, first, when considering all intracranial masses, the IDCs are relatively rare, considered as benign lesions, and treated or followed-up only if symptomatic [3]. Second, many of the existing scientific reports of the coexistence are old, thus, the topic has not had much scientific attention.

4.1. *Pathophysiological findings*

Based on current knowledge, IA development and rupture are associated with vessel wall inflammation [11,12,20]. Moreover, some recent studies have suggested the presence of concurrent periodontitis or the alterations in the bowel microbiota as a possible inflammatory trigger for IA development [21,22]. Hence, the presence of IDC and especially their content after surgery and/or rupture, could be an important stimulus for vessel wall inflammation. Many studies are focusing on the role of flow-driven intramural vessel inflammation in IA development, trying to find biological or radiological markers for clinical use [21,23–25]. Conveniently, the cases of coexistence between IA and IDC can be considered as excellent "in-vivo" models.

Epidermoid and dermoid cysts are slow-growing lesions with a linear growth curve [3]. They develop by wedging between the cisternal neurovascular structures, compressing and stretching the vessel wall as well as creating adhesions with it [2,15]. This can create changes in the intravascular blood flow by creating turbulences and increasing the vascular wall shear stress [2,15,21]. This could be lead to IA formation, even on to the opposite side of the IDC-IA contact (i.e., case reported by Shonauer et al. [19]). Furthermore, the adhesions to the vessel wall can change the elasticity of the vessel and lead to increase the transmural pressure and intramural stress [21]. Flow-driven stress can induce endothelial dysfunction and stimulate the inflammatory response caused by type 1 macrophages [26]. This produces a consequent degradation of the extracellular matrix mediated by metalloproteinases, an increasing of NFkb (Nuclear factor kappa-light-chain-enhancer of activated B cells) expression in leucocytes and vessel cells, leading to phenotypic vessel muscle cells change [12,21,24,27]. At the same time, the adhesions of cyst's ectopic cells in contact with the vessel wall could increase the chronic inflammatory response sustained by the COX2-PGE_2-EP2-NFkB (Cyclooxygenae2-Prostaglandin E2) pathway [21,24], and the macrophagic and lymphocytic secretion of MCP1 (Monocyte Chemoattractant Protein-1), TNF-alpha (Tumor Necrosis Factor- alpha), IL1B (Interleukin 1beta), SDF1alfa (Stromal cell-derived factor-1alfa) [20,24,25,28]. This could increase the chemotactic stimulus for inflammatory cells to adventitia with a consequent vessel wall damage and remodeling [21].

This inflammatory response could be intensified in the case of ruptured dermoid or neuroenteric cysts, with a release of their content into the subarachnoid space [29,30]. This produces an inflammatory trigger and potentially the development and/or increased rupture risk of the aneurysm. For instance, two cases of ruptured IA associated with epidermoid cysts, the intraoperative reports described pseudofibrotic attachments between the aneurysm wall and cyst capsule [2,17]. This could be the result of previous subclinical episode of Mollaret meningitis [31,32]. In our review, two of the three cases of ruptured dermoid cysts presented with a concurrent SAH. Additionally, in the case presented by Ahmad et al. [9] the M1 aneurysm was an intraoperative finding and clipped at same time of cyst removal preventing the future rupture.

4.2. *Clinical findings and management*

The clinical presentation of epidermoid, dermoid and neuroenteric cysts depends on their anatomical location, size, and possible rupture status. IDCs usually present with a benign natural history. The only possible critical event is the rupture of dermoid or neuroenteric cyst; and Mollaret's meningitis in epidermoid [29,31]. However, these events are rare, as cystic rupture accounts for less than 0.5 % of the reported cases [29,30,33]. Furthermore, in even more rare occasions patients present with recurrent meningitis [29–31,33].

However, the coexistence with an IA could modify the natural history of the cyst, and vice versa. Naturally this should affect also the pattern of diagnosis and FU, as the similar symptoms shared by SAH and IDC-related critical events (i.e., rupture or aseptic meningitis) can be misinterpreted [2,9,16,17]. Imaging studies should be analysed

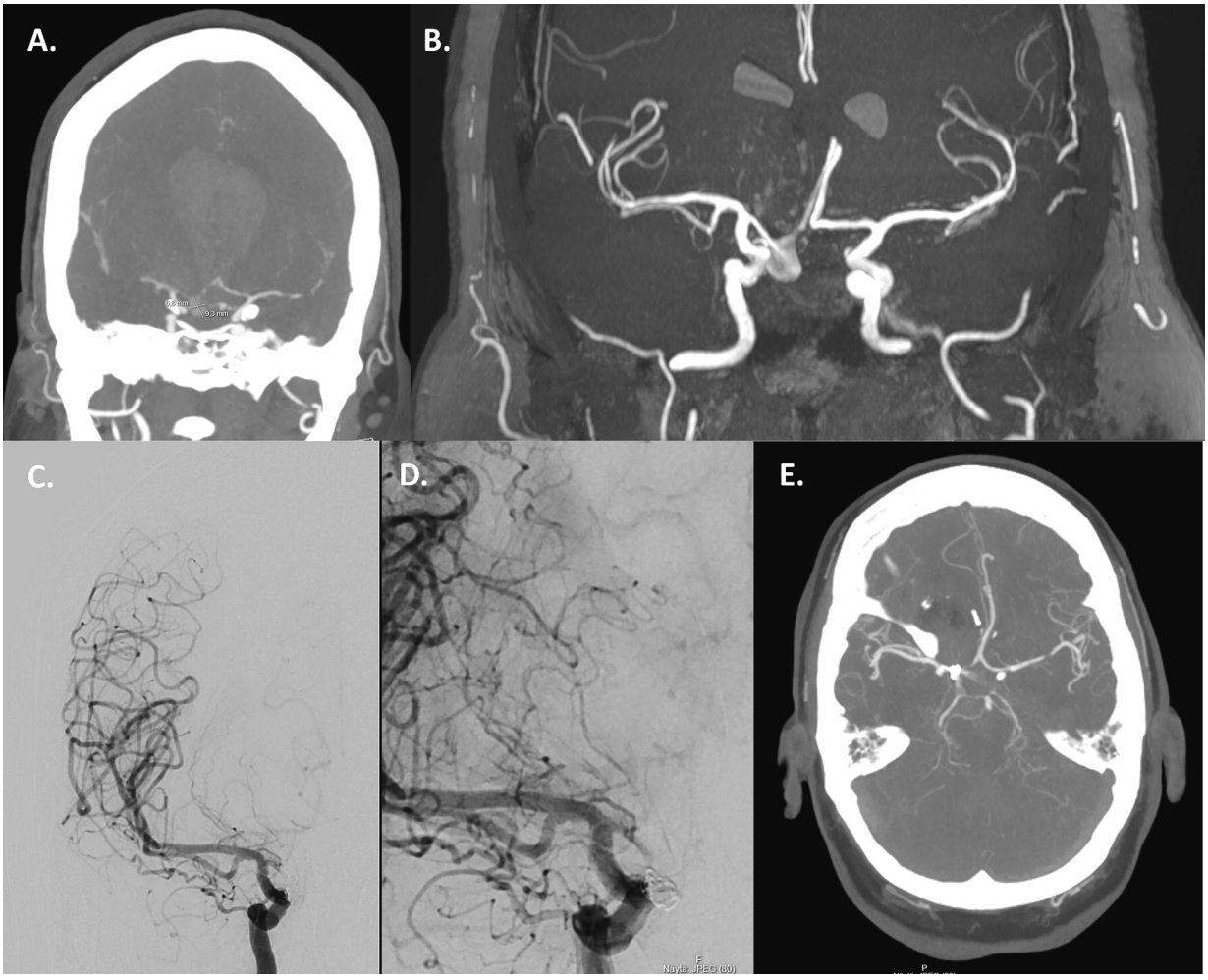

Fig. 3. A., B. Coronal CTA and TOF MRI showing an aneurysmal subarachnoid haemorrhage (SAH) with intraventricular blood collection and hydrocephalus related to a A1 aneurysm rupture B. **C., D.:** DSA in sagittal angiogram with intracarotid contrast showing the aneurysmal coiling. **D:** CTA in axial view showing the coiled aneurysm.

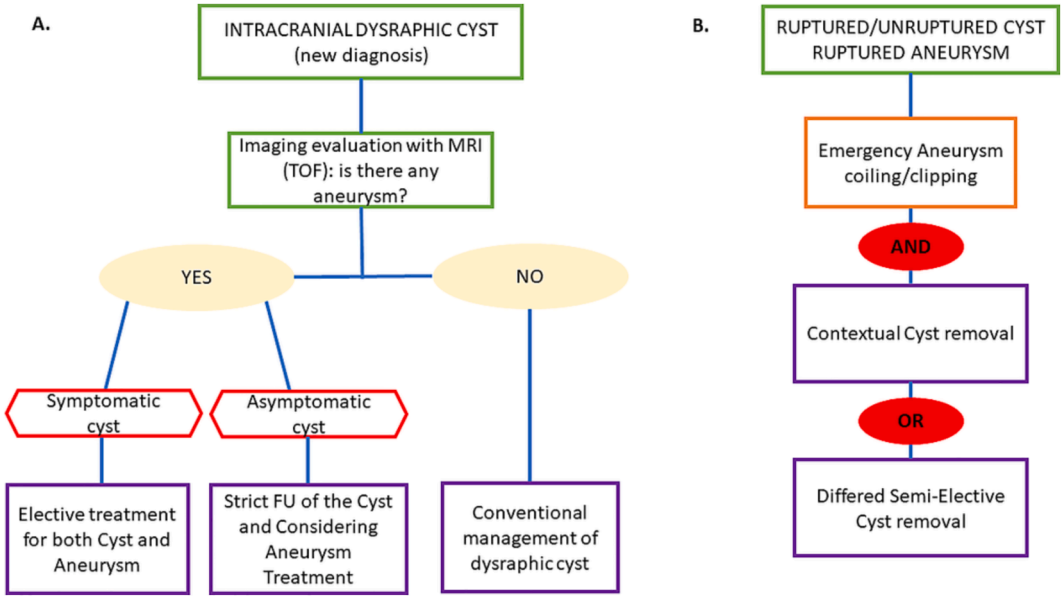

Fig. 4. Proposed decision-making process in case of intracranial dysraphic cyst and coexistent ruptured (**A**) and unruptured aneurysm (**B**).

thoroughly to rule out the presence of coexistent aneurysm. However, considering the rarity of this coexistence, in our opinion, the routinary use of DSA or CTA is not justified; rather aneurysms could be detected by a specific MRI sequence (i.e. TOF) during ordinary diagnostic work-up [34]. Fig. 4 summarizes the possible strategies in all clinical scenarios. Considering the close spatial relationship between IA and IDC, and the related clinical issues, in the newly diagnosed unruptured cases a semi-elective treatment should be considered. According to the literature, the resection of the symptomatic cyst and conjoint aneurysm clipping represents the safest and most efficient option (Table 1). There is insufficient data to suggest the correct timing for management [24,35], however, the inflammation related to cyst rupture or other inflammatory events could encourage a more active approach.

At the same time, metachronous diagnosis of IA after complete or partial resection of an IDC requires rigorous FU and interventional attitude as soon as possible, especially in case of recurrent meningitis or after cyst rupture.

In the case of a IA rupture, a possible management approach might be to perform an emergency aneurysm coiling or clipping with the conjoint cyst removal as reported in some of the published cases [14,30,33]. Alternatively, a differed cyst removal might be considered [35,36]. In both cases, however, the treatment of the ruptured IA should be prioritized.

In the case of both IA and cyst rupture, an open surgical treatment was used in the one previously reported case, to urgently secure both IA and IDC (Table 1). Considering the advancements in neurointervention, an endovascular treatment might be considered as a valid alternative to clipping, in such cases where an urgent surgical resection of cyst is unnecessary [35–37].

5. Conclusion

The coexistence of IA and IDC is a rare finding with multiple possible presentations. This coexistence could represent an “in vivo” model for hemodynamic alteration and inflammation leading into IA formation. In the management of patients harbouring IDC, the presence of the aneurysm should be ruled out during the standard MRI workup. The coexistence of these pathologies might influence the natural histories these lesions, which could justify a more “aggressive” management strategy.

Authorship statement

Conceptualization: M.N., F.C, A.M.A; Data curation: A.M.A, F.C, A.P; Formal analysis: A.M.A., F.C, R.R; Methodology: F.C., A.M.A; Supervision: M.N., R.R.; Validation: All the authors; Visualization, Roles/Writing – original draft: F.C., A.M.A; Writing – review & editing: All the authors.

Ethics approval

Ethical approval was waived by the local Ethics Committee in view of the retrospective nature of the study and all the procedures being performed were part of the routine care. The authors state that the patient gave his informed consent for surgical procedure and utilization of clinical data for the present study. The corresponding authors confirm on his responsibility that the patient and other authors have given consent for publication of data and results related to the present article.

Informed consent

The authors state that the patient gave his informed consent for surgical procedure and utilization of clinical data for the present study. The corresponding authors confirm on his responsibility that the patient and other authors have given consent for publication of data and results related to the present article.

Authors’ contributions

Concept and design: M.N; Acquisition of data: F.C. and A.M.A., Analysis and interpretation of data: All authors; Drafting the article: F.C and A.M.A., Critically revising the article: All Authors.

Availability of data and material

The authors confirm that the data supporting the findings of this study are available within the article and from corresponding authors (A.M.A.) upon reasonable request.

CRediT authorship contribution statement

Francesco Calvanese: Conceptualization, Data curation, Methodology, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. **Anna Maria Auricchio:** Data curation, Formal analysis, Software, Visualization, Writing – review & editing. **Anni Pohjola:** . **Rahul Raj:** . **Mika Niemelä:** Conceptualization, Investigation, Resources, Software, Supervision, Validation, Visualization, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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