Research Article

Characteristics of Patients with Carotid-Cavernous Fistula who Underwent Endovascular Intervention

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Abstract

Carotid cavernous fistula (CCF) is an abnormal connection between the arterial and venous systems within the cavernous sinus. Direct CCF is usually created from a tear in the intracavernous carotid artery wall. Indirect CCF often develops spontaneously and causes subtle manifestations. Direct CCF, commonly characterized by high blood flow, usually exhibits oculo-orbital venous congestion and cephalic bruit. The low-flow indirect CCF commonly presents with similar manifestations but is more subtle in nature. Generally, direct CCF requires endovascular treatment. This is done to seal the fistula while preserving the patency of the internal carotid artery (ICA). A retrospective descriptive study was conducted on 44 patients with CCF who underwent endovascular intervention at Cipto Mangunkusumo Hospital, Indonesia, between 2014 and 2021. Data from medical records were analyzed to assess patient characteristics, clinical presentations, radiological findings, and treatment modalities. Most patients presented with ocular bruit (74.4%) and proptosis (68.1%), with high-flow (59.1%) and type A (90.9%) CCF being predominant. Endovascular interventions included balloon insertion (80.9%), coil insertion (9.1%), and combined balloon and coil procedures (9.1%). When performed by an experienced interventionist, the success rates of fistula closure could be as high as 85-99% and 70-78% for direct and indirect fistula, respectively. CCF is a non-life-threatening condition but can lead to severe clinical consequences. Recognition of characteristics is significant in helping to guide appropriate and timely treatment for patients. Serious complications are rare.
Keywords: *Carotid Cavernous Fistula, endovascular procedure, angiography.*

Karakteristik Pasien dengan Fistula Karotis-Kavernosus yang Menjalani Intervensi Endovaskuler

Abstrak

Fistula Karotis-Kavernosus (CCF) adalah hubungan abnormal antara sistem arteri dan vena di dalam sinus kavernosus. CCF langsung biasanya terjadi akibat robekan pada dinding arteri karotis intrakavernosa. CCF tidak langsung sering berkembang secara spontan dan menyebabkan manifestasi yang tidak kentara. CCF langsung, umumnya ditandai dengan aliran darah yang tinggi, biasanya menunjukkan kongesti vena okulo-orbital dan bruit sefalik. CCF tidak langsung dengan aliran rendah biasanya muncul dengan manifestasi serupa tetapi lebih halus. Umumnya, CCF langsung memerlukan tata laksana endovaskuler. Hal ini dilakukan untuk menutup fistula sekaligus menjaga patensi arteri karotis interna (ICA).Sebuah studi deskriptif retrospektif dilakukan pada 44 pasien CCF yang menjalani intervensi endovaskuler di Rumah Sakit Cipto Mangunkusumo, Indonesia, sejak tahun 2014 hingga 2021. Data dari rekam medis dianalisis untuk menilai karakteristik pasien, presentasi klinis, temuan radiologis, dan modalitas pengobatan.Sebagian besar pasien datang dengan bruit okuler (74,4%) dan proptosis (68,1%), dengan aliran tinggi (59,1%) dan CCF tipe A (90,9%) yang paling banyak ditemukan. Intervensi endovaskuler meliputi pemasangan balon (80,9%), pemasangan koil (9,1%), dan kombinasi prosedur balon dan koil (9,1%). Ketika dilakukan oleh ahli bedah yang berpengalaman, tingkat keberhasilan penutupan fistula dapat mencapai 85-99% dan 70-78% untuk fistula langsung dan tidak langsung.CCF adalah kondisi yang tidak mengancam jiwa, tetapi dapat menyebabkan konsekuensi klinis yang parah. Pengenalan karakteristik sangat penting dalam membantu memandu pengobatan yang sesuai dan tepat waktu bagi pasien. Komplikasi serius jarang terjadi.
Kata kunci: *Fistula Karotis Kavernosus, prosedur endovaskuler, angiografi.*

Introduction

Carotid cavernous fistula (CCF) is an abnormal connection between the arterial and venous systems within the cavernous sinus. Based on the underlying pathomechanism, it is classified into direct and indirect (dural) CCF. Direct CCF is a high-flow fistula directly connecting the internal carotid artery (ICA) and the cavernous sinus. On the other hand, dural CCF is defined as a low-flow fistula created by connecting the cavernous artery and sinus.[1,2]

The cavernous sinus supplies blood flow to the jugular bulb via the superior and inferior petrosal sinuses. Meanwhile, superior and inferior ophthalmic veins supply blood flow from the orbit to the cavernous sinus. Fistula formation induces a low-resistance trajectory between the high-pressure carotid artery and the low-pressure venous system. Suppose basilar veins and the petrosal system cannot optimally accommodate the increase in blood flow. In that case, the subsequent increase in cavernous sinus pressure shall be compensated by the superior and inferior ophthalmic veins, causing congestion of the ipsilateral orbital vein.[1,3]

The first case of dural arteriovenous fistula was described in the 1930s. The clinical manifestations can be well recognized; however, its pathophysiology remains poorly explained. From the 1970s to the 1980s, research was performed to study the cavernous sinus's anatomy rigorously. Burrow and colleagues developed a classification of carotid-cavernous fistula in 1985 that is still used. The cavernous sinus is a venous system network traversed by the ICA's intracranial part.

ICA forms several intracavernous branches called mining-hypophyseal and inferolateral branches. This vessel branches off to supply arterial blood to cavernous sinus dura, innervation, and hypophysis. External carotid artery (ECA) provides several branches to the dura and eventually forms an anastomosis with intracavernous branches of ICA.[4-6] This descriptive study was aimed at explaining the detail of characteristics of patients with CCF which were treated via endovascular intervention. The data we produced from this study can be used to further improve the management of CCF globally.

Methods

This study was conducted as a retrospective descriptive study with data collected from the medical records of past eligible patients. The study subjects were patients with CCF who underwent endovascular intervention at Cipto Mangunkusumo Hospital, Indonesia between 2014 and 2021. All patients who had CCF and were treated with endovascular balloon or/and coil insertion within the timeframe were included in the study. The exclusion criteria were patients without detailed endovascular intervention and with incomplete data.

Results

From January 2014 to December 2021, 44 patients were diagnosed with CCF and underwent surgery. Most patients were male (79.5%) with a median age of 28 (15-51) years. Trauma was the most common cause of CCF (n=42, 95.5%). In this study, most of the patients were presented with ocular bruit (74.4%) and proptosis (68.1%) (Table 1).

From the radiological examination, it was shown that the majority of patients had a proptosis index of >0.3 (68.2%). Elongation of the ophthalmic vein was visible on CT scan images in most patients (58.1%). The imaging study did not indicate any signs of skull base fracture in most patients (81.8%). Angiographic images showed that a large proportion of this cohort had type A (n=40, 90.9%) and high-flow (n = 26, 59.1%) CCF. The most frequent inflow was from posterior drainage (derived from the petrosal and Sylvian arteries) (n=22, 51.2%), and most had large orifices (n=24, 54.5%). In this study, 23 patients (52.3%) underwent a single balloon insertion and 17 patients (38.6%) required >1 balloon. In addition, seven patients (15.9%) underwent gradual balloon insertion. Out of 44 patients, only four patients (9.1%) underwent coiling, while the combination of balloon and coiling was performed simultaneously in 4 (9.1%) patients (Table 1).

In this study, there was a significant association between clinical presentation among patients, including bruit and chemosis (p=0.002), bruit and proptosis (p=0.008), and chemosis and proptosis (p<0.001). In addition, we also assessed the association between blood drainage and clinical presentations, where the association was found to be significant with proptosis (p=0.002) and chemosis (p=0.01) but not with bruit (p=0.242). Statistical analysis for the association between CCF flow and bruit showed no significant association (p=0.276). In one-stage balloon insertion, there was no significant association between CCF flow and the number of balloons inserted (p=0.896) and between orifice size and the number of balloons inserted (p=0.289).

Discussion

In seven years, 44 CCF cases were diagnosed at dr. Cipto Mangunkusumo Hospital. Compared to

Table 1. Characteristics of the Study Subjects

Characteristics	n = 44	%
Gender		
Male	35	79.5
Female	9	20.5
Etiology		
Traumatic	42	95.5
Spontaneous	2	4.5
Bruit		
Yes	32	74.4
No	11	25.6
Chemosis		
Yes	25	56.8
No	19	43.2
Proptosis		
Yes	30	68.2
No	14	31.8
Proptosis index >0.3		
Yes	30	68.2
No	14	31.8
Ophthalmic vein elongation		
Yes	25	58.1
No	18	41.9
Cranial base fracture		
Yes	8	18.2
No	36	81.8
Type of CCF		
A	40	90.9
B	2	4.5
C	1	2.3
D	1	2.3
Flow		
High	18	40.9
Low	26	59.1
Drainage		
Anterior	21	48.8
Posterior	22	51.2
Orifice size		
Small	20	45.5
Large	24	54.5
Balloon insertion		
One balloon	23	42.3
>1 balloon	17	38.6
Gradual balloon insertion (>1 stage)		
Yes	7	15.9
No	37	84.1
Coil insertion		
Yes	4	9.1
No	40	90.9
Balloon and coil insertion		
Yes	4	91
No	40	90.9

other hospitals, it is one of the most common cases in vascular neurosurgery. The leading cause of CCF in our cohort was trauma, which is in line with the literature, where 70-90% of CCF cases are associated with laceration of the ICA wall or its attachment to the duramater following injury. Head injury can lead to the formation of small tears in the intracavernous arteries' wall that can subsequently trigger the development of a fistula. The most common symptoms of CCF include proptosis, chemosis, and bruits caused by high pressure in the cavernous sinus, which generally has low pressure and leads to disruption of drainage pattern and blood flow in the cavernous sinus and orbit. In our study, we found significant association between the three most common symptoms of CCF. Although conducted in the center with one of the most CCF cases in our country, considering the descriptive nature in our study, this finding has the potential to be researched further with analytical studies.

Injury has been the leading cause of about 70-90% of direct CCF cases, primarily in the setting of ICA laceration around its dural attachment or cranial base fracture-induced penetrating injury. Other causes include iatrogenic injuries, such as those that occur during carotid angioplasty or endarterectomy, trans-sphenoidal hypophysectomy, trigeminal rhizotomy, and nasopharyngeal biopsy. CCF can also occur spontaneously due to rupture of intracranial vessel aneurysm.[1]

Indirect CCF is created by rupture of a dural branch of the carotid artery in attribution to genetic predisposition or underlying comorbidities, including hypertension. Blunt force head trauma can lead to a small tear in the intracavernous artery wall, causing the development of a fistula. Penetrating head trauma can also lead to fistula formation by directly lacerating intracavernous vessels. Spontaneous fistula formation has been associated with rupture of intracavernous aneurysm, fibromuscular dysplasia, Ehlers-Danlos syndrome, and pregnancy.[7,8]

CCF can be classified by its hemodynamic profile, etiology, or shunt anatomy. Regarding hemodynamic profile, CCF can be classified into high-flow and low-flow CCF. Based on the underlying pathomechanism, CCF is categorized into traumatic and spontaneous CCF.[1,5,6] A triad of pulsatile proptosis, chemosis, and intracranial whistling usually characterizes direct CCF. Another symptom that may arise is ophthalmoplegia, caused by a deficit in cranial nerve VI function. In the case of an indirect CCF, moderate ocular congestion, mild proptosis, and ocular pulsation on aplanotonometry may develop. Bruits and headaches may also be present as part of the clinical manifestations. A CCF causes high-pressure arterial blood to enter the low-pressure cavernous sinus. This disrupts the normal venous drainage pattern and impairs blood flow within the cavernous sinus and the orbit.[1,5,6]

Ophthalmic vein obstruction leads to chemosis, pulsative exophthalmos, eyelid swelling, proptosis, restriction of eye movement, secondary glaucoma (9%), and impaired retinal perfusion (30%).

The mass can affect the orbital organ, leading to ophthalmoplegia, pupillary dilatation (paresis of cranial nerves III, IV, VI), and ipsilateral facial hypesthesia. The shunt leads to the development of vascular bruit that can be perceived by the patient/ heard by the examiner on orbital auscultation. Long-term orbital manifestations associated with CCF vary from keratitis, corneal ulcers, visual disturbances (85%) to blindness (25%). Mortality rates related to CCF are considerably low. The risk of non-ophthalmologic neurologic complications is not significant; however, persistently untreated lesions can lead to neurological complications. If left untreated, CCF can lead to vision loss, cranial nerve palsies and cosmetic problems such as proptosis. Therefore, CCF should be appropriately managed.[1,9,10]

Complete ophthalmological examinations must be performed, including visual acuity, pupillary function, intraocular pressure, funduscopy (both direct and indirect), and gonioscopy. Digital subtraction angiography (DSA) is required to specify the characteristics of vascular abnormalities and guide endovascular intervention. The initial angiographic evaluation helps to assess the size and location of the fistula, detect the presence of a carotid aneurysm, classify whether the CCF is direct or indirect, identify the outflow of the cavernous sinus, detect those with high-risk hemodynamic instability (such as those with cortical venous drainage, pseudo-aneurysm, or cavernous sinus varices), and to establish diagnosis of vascular injury in the setting of trauma.[7] Angiographic criteria for differentiating high-flow from low-flow fistula are subjective. In high-flow fistula, contrast fills the cavernous sinus and efferent vein in a very short fraction, and intracranial ICA branches may be partially visualized or not. In low-flow fistula, contrast drainage into the venous system is much slower and contrast filling of the intracranial ICA branches can be seen clearly. In high-flow fistula, it is challenging to determine anatomical abnormalities using standard angiography, therefore a particular technique should be employed.

Laboratory examinations may include routine pre-angiographic tests. These include evaluation of coagulation and renal function before contrast administration (complete blood count, platelet count, prothrombin time [PT], and partial thromboplastin time [PTT]), serum electrolytes, blood urea nitrogen (BUN), and creatinine. In a study of 6 CCF patients undergoing MRA, typical morphological characteristics (superior ophthalmic vein enlargement, exophthalmos) were found in all patients. A study of 98 suspected CCF cases evaluated by MR imaging reported an overall accuracy, sensitivity, and specificity of 88.8%, 97.4%, and 83.3%, respectively. Abnormal contours of the cavernous sinus, internal signal voids of the cavernous sinus, prominent venous drainage inflow, and orbital/periorbital soft tissue swelling are proposed as possible predictive findings.[1,11-15]

Several treatment options for managing CCF are available, and the selection depends on the flow rate. The goal is to achieve complete fistula occlusion while maintaining normal ICA flow. In the case of an indirect low-flow fistula, spontaneous closure may be possible. Therefore, compression treatment can be the least invasive option for low-flow fistula, consisting of compressions several times a day for 4-6 weeks to achieve fistula thrombosis.[16-18] Direct or type A fistulas rarely undergo spontaneous closure. Treatment is recommended in patients with intolerable bruits, progressive vision loss, and cosmetic effects of proptosis. Indirect fistulas, the types B, C and D, have a higher incidence of spontaneous resolution. In type A fistulas, intervention is usually performed using the ICA approach. A detachable balloon or endovascular coil is positioned to seal the fistula while maintaining the patency of the internal carotid artery. Alternatively, the venous approach via the internal jugular vein and petrous sinus allows access to the fistula from the venous side. Type B, C, and D fistulas have smaller fistula connections and are usually not amenable to the therapeutic approaches described above.[19-21]

Patients with CCF generally have a favorable prognosis. Persistent lesions respond well to intervention. Treatment complications may include complications of cerebral angiography. Arterial and venous compromise may also occur, resulting in cerebral or retinal ischemia and even infarction. Although recurrence of a direct carotid-cavernous fistula following balloon-assisted closure is generally rare, it is not uncommon for a dural carotid-cavernous sinus fistula to recanalize or form new abnormal blood vessels after embolization. The ocular pulse amplitude should be monitored postoperatively in all patients, preferably using a pneumotonometer. After the fistula is sealed, symptoms and signs usually improve within a few hours to days. The degree and extent of improvement are associated with the severity and the length of time the fistula appears. Pre-existing ocular bruits, ocular pulsations and

sensations usually disappear soon after surgery. Eyelid swelling, conjunctival chemosis, conjunctival vascular dilatation, stasis retinopathy, disc swelling, and increased intraocular pressure generally return to normal within weeks to months.[1]

Our study had limitations as it was only conducted in a single center and the data was collected in retrospective manner. Further studies can increase the range of endovascular facilities to obtain larger samples and prospective methods can acquire more detailed data. Our study could be a baseline for further research regarding the management of CCF to improve the holistic approach and care of the disease.

Conclusion

CCF is a non-life-threatening condition but can lead to severe clinical consequences, including visual impairment and eventual blindness. Recognition of symptoms and radiological and angiographic findings is significant in helping to guide appropriate and timely treatment for patients.

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