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ORIGINAL ARTICLE **ÖZGÜN ARAŞTIRMA**

ENDOVASCULAR TREATMENT OF CAROTICO-CAVERNOUS FISTULAS: EXPERIENCES OF TWO CENTERS

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ABSTRACT

INTRODUCTION: Carotico-cavernous fistula (CCF) are abnormal connections between arteries and veins within the cavernous sinus. The aim of the treatment is to close the connection between the cavernous sinus while maintaining the arteriovenous flow. There are treatment options with endovascular approach such as detachable balloons, coils, embolic agents and in recent years, flow-diverter stent.
METHODS: A total of 7 patients diagnosed with CCF between 2020-2022 in two centers were retrospectively analyzed. Patients were classified according to their anatomy (direct and dural) and Barrow classification (Type A, Type B, Type C, Type D).
RESULTS: In 6 of 7 patients, endovascular access could be achieved and embolizations were performed with coils. Flow diverter stent was applied in the same session with coiling in a patient with type A.In one patient with a failed endovascular access, spontaneous occlusion of the fistula was observed in follow-up control examinations.
DISCUSSION AND CONCLUSION: Coiling of direct type CCF by transarterial approach and of dural type CCF by transvenous approach is safe and effective. In cases of incomplete occlusion of the fistula with these treatments, the flow-diverter stent applied to the internal carotid artery contributes to the occlusion of the fistula in the long term by reducing the passage through the dural branches.
Keywords: Carotico-cavernous fistula, endovascular treatment, coiling, flow-diverter stent

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KAROTİKO-KAVERNÖZ FİSTÜLLERİN ENDOVASKÜLER TEDAVİSİ: İKİ MERKEZ DENEYİMİ

ÖZ

GİRİŞ ve AMAÇ: Karotiko-kavernöz fistül (KKF), kavernöz sinüs içindeki arterler ve venler arasındaki anormal bağlantılardır. Tedavide amaç arteriyovenöz akımını koruyarak kavernöz sinüs arasındaki bağlantıyı kapatmaktır. Endovasküler olarak ayrılabilir balonlar, koiller, embolizan ajanlar ve son yıllarda akım yönlendirici stent ile tedavi seçenekleri bulunmaktadır.

YÖNTEM ve GEREÇLER: İki merkezde 2020-2022 yıllarında KKF tanısı konulan toplam 7 hasta retrospektif olarak incelendi. Hastalar anatomilerine (direkt ve dural) ve Barrow sınıflamasına (Tip A, Tip B, Tip C, Tip D) göre sınıflandırıldı.

BULGULAR: Endovasküler olarak ulaşım sağlanan tüm hastalara koil ile embolizasyon sağlandı. Tip A olan bir hastada koilleme ile aynı seansta akım yönlendirici stent uygulandı. Endovasküler erişim sağlanamayan 1 hastanın takiplerinde fistülün spontan kapandığı izlendi.

TARTIŞMA ve SONUÇ: Karotiko-kavernöz fistüllerin direkt tipinde transarteryel yolla, dural tiplerinde de transvenöz yolla koil tedavisi güvenli ve etkindir. Bu tedavilerle fistülün tam kapanmadığı durumlarda internal karotis artere uygulanan akım yönlendirici stent, dural dallardan geçişi azaltarak uzun dönemde fistülün kapanmasına katkı sağlar.

Anahtar Sözcükler: Karotiko-kavernöz fistül, endovasküler tedavi, koilleme, akım yönlendirici stent.

INTRODUCTION

Carotico-cavernous fistula (CCF) are abnormal connections formed between arteries and veins within the cavernous sinus. CCFs can be classified based on the hemodynamic properties (high flow or low flow), the anatomy of the fistula (direct or indirect), or the etiology (traumatic or spontaneous) (1,2). Classification according to the feeding artery in CCFs is shown in Table 1 (1).

Table 1. Barrow classification.

Barrow type A	Direct fistula
Barrow type B	Indirect fistula, filling only from ICA
Barrow type C	Indirect fistula, filling only from ECA
Barrow type D	Indirect fistula, filling from both ICA and ECA

Since the artery and sinus are directly connected in direct CCFs, they are almost always high-flow fistulas. They most commonly occur due to trauma, iatrogenic injuries, or the rupture of an aneurysm.

Dural, that is, indirect fistulas, consist of the connection between the cavernous sinus and the internal carotid artery (ICA), the external carotid artery (ECA), or the dural branches of both and the sinus; therefore, they are low-flow fistulas (1,2).

Symptoms vary depending on the location of the fistula and the venous drainage pattern. The aim of treatment is to close the connection between the cavernous sinus while maintaining normal ICA-ECA flow. Indirect fistulas can resolve spontaneously or with conservative treatment owing to their lower flow rate (3). However, high-flow direct fistulas rarely respond to conservative treatment and require more aggressive treatment approaches. The main treatment method for CCF is endovascular intervention due to high cure and low mortality and morbidity rates. In some necessary cases, endovascular treatment can be combined with surgery or radiosurgery (1-3).

In our study, we aimed to share the results of our 7 patients in the light of the literature, in which we used the endovascular primary coiling and applied flow diverting stent as an additional treatment in one case.

METHODS

The files of 7 patients who were diagnosed with CCF and treated endovascularly at Kartal Dr. Lutfi Kirdar City Hospital Stroke Center and Eskisehir Osmangazi University Hospital Stroke Center between 2020 and 2022 were examined retrospectively. The study was conducted in accordance with the ethical standards of the Declaration of Helsinki. It was approved by Kartal Dr. Lutfi Kirdar City Hospital Clinical Research Ethics Committee (Date: 27.04.2022, No: 2023/514/248/8). Informed consent was not obtained from the patients due to its retrospective design.

Two male and 5 female patients, between the ages of 18 and 80, with a median age of 55 years (interquartile range (IQR), 43-58) at the time of the procedure, were included in the study. Complaints and demographic characteristics of the patients were recorded, and in addition to the neurological examination, neuro-ophthalmological examinations were performed. The first radiological evaluation was performed as cranial and orbital magnetic resonance (MR) imaging and computed tomography (CT) angiography. Then,

with the standard transfemoral approach before treatment, diagnostic angiographic imaging, including bilateral selective ICA, ECA, and Vertebral Artery (VA) injections in anteroposterior (AP) and lateral views, as well as 3D rotational angiography, was performed.

Statistical analysis: Continuous variables were reported as median and interquartile range (IQR). Categorical variables were reported as n (%). IBM SPSS Statistics Software 21 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

RESULTS

Demographic data and admission complaints: 5 of the 7 patients were female (71%) and 2 were male (29%). The median age at admission was 55 years (IQR, 43-58). The period between the complaints and admission to the clinic varied between 3 days and 4 months. 4 patients had a history of hypertension (57%), 1 patient had a history of diabetes mellitus (DM) (14%), and 1 patient (14%) had a history of venous sinus thrombosis. There was no known or concurrent disease in 3 (43%) patients. Chemosis was present in 5 of 7 patients (71%) at the time of admission. Cranial nerve paralysis was present in 3 patients (43%), proptosis in 4 patients (57%), decreased visual acuity in 1 patient (14%), orbital pain and/or headache in all patients, and diplopia in 3 patients (43%) (Table 2).

Imaging results: In DSA imaging, 5 (71%) patients had indirect fistula, and according to Barrow classification, 3 (43%) patients were typed D (2 of them bilateral), 2 patients were (29%) type B, and 2 patients (29%) had direct fistula, Type A (Table 2).

Table 2. Demographic and clinical findings of the patients.

Gender	Age	Clinical symptoms	Comorbidity	Localization	Fistula type	Treatment
F	69	Proptosis Decreased visual acuity Headache	Hypertension, Diabetes mellitus	Bilateral	Indirect, TYPE D	Transvenous
F	60	Cranial nerve paralysis Headache Diplopia	Hypertension, cerebral venous thrombosis	Left	Indirect, TYPE D	No access could be achieved
F	55	Conjunctival chemosis Headache	Hypertension	Left	Direct, TYPE A	Transarterial
F	56	Cranial nerve paralysis Conjunctival chemosis Headache Diplopia	No	Bilateral	Indirect, TYPE D	Transvenous
M	40	Proptosis Conjunctival chemosis Headache Diplopia	Hypertension, trauma	Left	Direct, TYPE A	Transarterial
F	46	Proptosis Conjunctival chemosis Headache	No	Right	Indirect, TYPE B	Transvenous
M	26	Cranial nerve paralysis Proptosis Conjunctival chemosis Headache Tinnitus	No	Right	2, TYPE B	Transarterial+transvenous

Treatment: All our patients were treated with an endovascular transfemoral approach. Only coiling was applied to 6 of the patients, and flow-diverting stent was applied in addition to coiling to 1 patient with indirect type B. Coiling was performed with the transvenous approach in two patients with indirect Type D. Access to the cavernous sinus could not be achieved in 1 patient. During the follow-up of this patient, it was observed that the fistula was closed with a conservative approach. Coiling was performed with the transarterial approach in all patients with direct Type A. Of the 2 patients with indirect Type B, one was treated transvenously and the other was treated both transarterially and transvenously. In one of these patients, a flow-diverting stent was applied in the same session in addition to coiling. Of the 3 patients treated with transarterial embolization, 2 had direct and 1 patient had indirect CCF. All patients treated with the transvenous approach

had indirect type CCF and the most common fistula was Type D (60%). Before and after treatment images of a patient treated with a transarterial approach are shown in Figure 1, and before and after treatment images of a patient treated with the transvenous approach are shown in Figure 2.

Complications: No complications were observed during the procedures. Existing symptoms of two patients were worsened in the early period due to the mass effect of the coil and cavernous sinus thrombosis. All patients underwent control CTA at 3 months and control DSA at 6 months. No recurrence was observed in any patient. Spontaneous closure of the fistula was observed in the 6th-month control DSA imaging of the patient, who was followed up with conservative treatment.

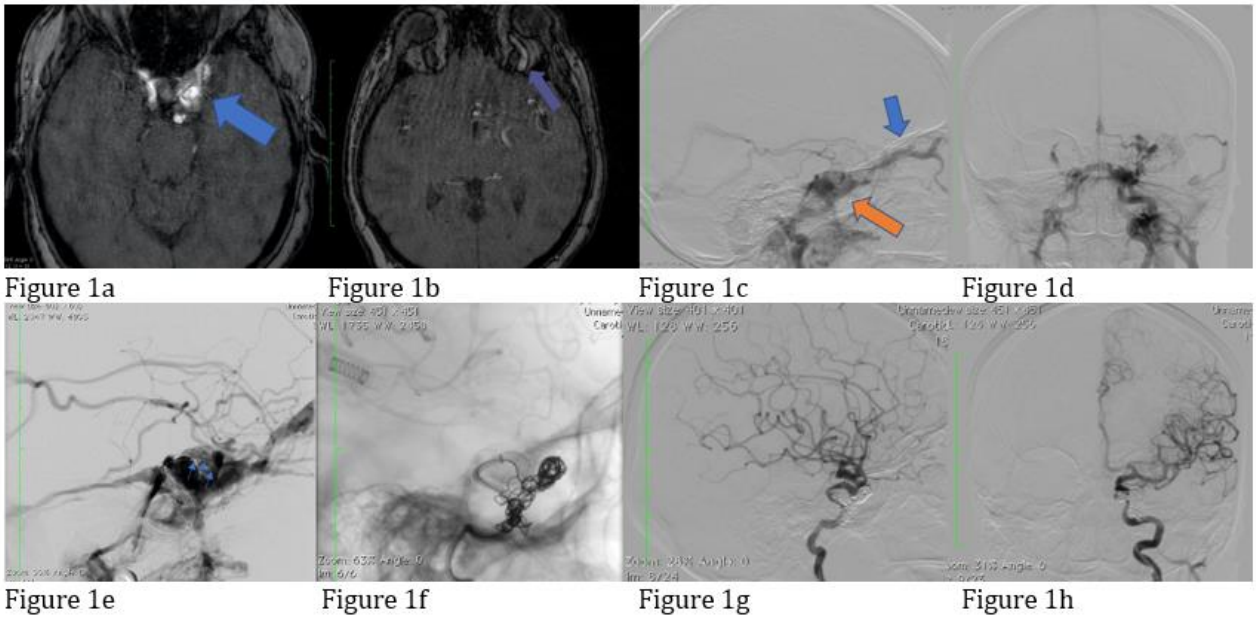

Figure 1. Imaging findings of a Type A caroticocavernous fistula patient before and after treatment. **a**. In axial MRA arterial phase raw images, increased vascularity was observed around the ICA on the left (blue arrow). **b.** Dilated ophthalmic vein image in axial MRA raw images (blue arrow). **c.** Dilated ophthalmic vein (blue arrow) and high-flow transition to the cavernous sinus (orange arrow) on the lateral DSA image before the procedure. **d.** In the antero-posterior DSA image before the procedure, a transition from the left ICA to the right and left cavernous sinuses and the jugular veins via the petrosal sinuses is observed, and no contrast transition to the distal ICA is observed. **e.** Image of microwire and microcatheter placed from the left ICA to the left cavernous sinus on the lateral DSA image during the procedure (blue arrow). **f.** Image of a coil placed in the cavernous sinus on the lateral DSA image. **g-h.** Post-operative lateral and antero-posterior DSA images show that contrast passage to the cavernous sinus has disappeared and distal ICA filling has been restored.

DISCUSSION AND CONCLUSION

CCF are abnormal connections formed between arteries and veins within the cavernous sinus. If there is a direct connection between the ICA and the cavernous sinus, they are called direct, and if there is an indirect connection involving the cavernous artery branches and the cavernous sinus, they are called indirect CCF. In the Barrow classification, which is based on arterial nutrition, Type A fistulas are direct connections between the ICA and the cavernous sinus, Type B fistula results from dural branches of ICA indirectly, Type C results from dural branches from ECA indirectly, and Type D results from dural branches from ICA and ECA indirectly (1). 5 patients included in the study had indirect fistula and 2 patients had direct fistula; 2 of them were type A, 2 were type B and 3 were type D.

Dural, or indirect, CCFs are usually seen in middle-aged or elderly women; however, symptoms can occur in both genders at any age, even in childhood or infancy (2). 4 of our 5 indirect fistula patients were female; the median age was 56 years (IQR, 46-60), and one of our patients was a 26-year-old male.

Direct CCFs are often high-flow fistulas. The most common causes are trauma, aneurysm rupture in the cavernous sinus, and iatrogenic injuries. Causes of indirect CCFs include

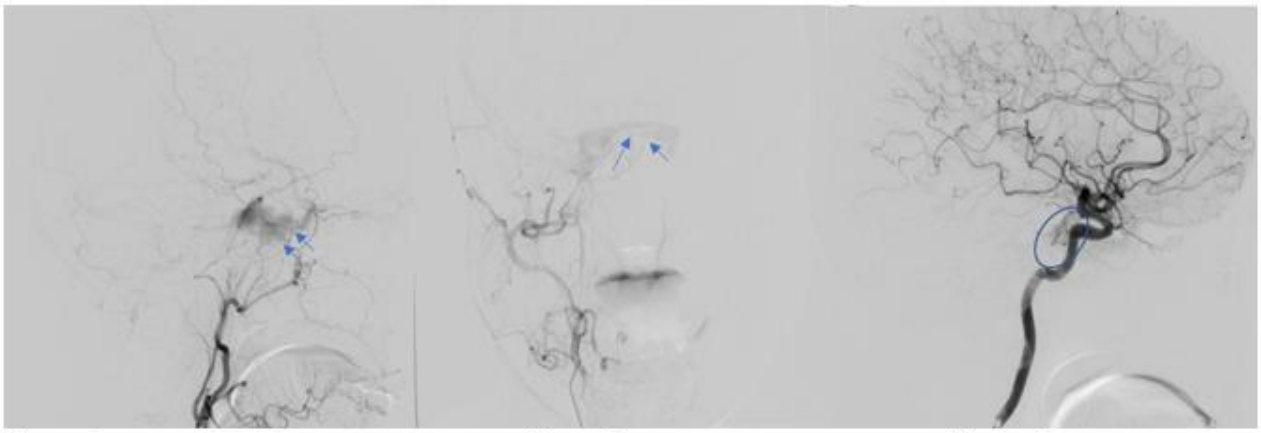

Figure 2a Figure 2b Figure 2c

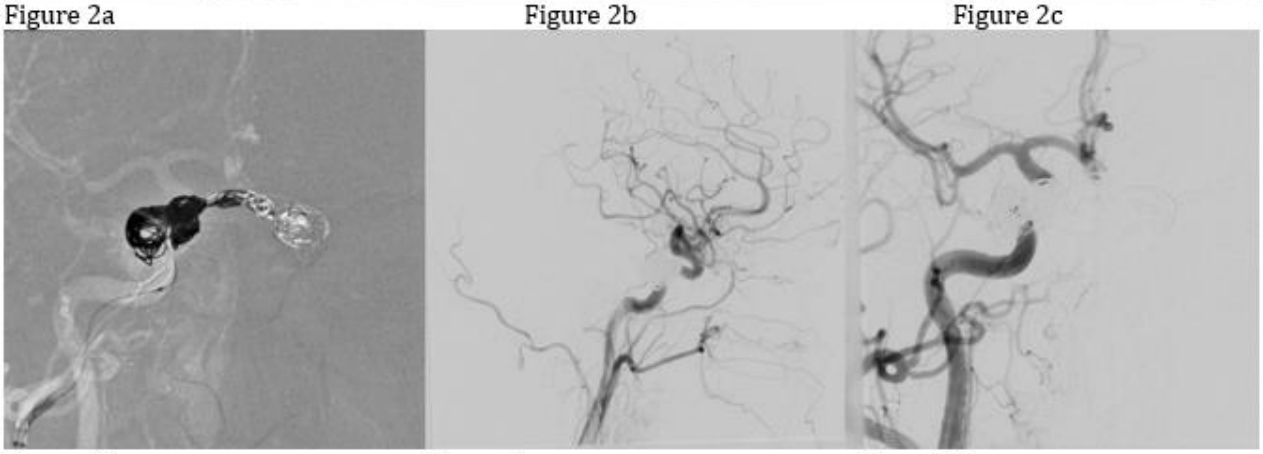

Figure 2d Figure 2e Figure 2f

Figure 2. Imaging findings before and after treatment of a Type D caroticocavernous fistula patient. **2a-b.** Before the procedure, lateral and antero-posterior DSA imaging shows the transition from the ECA to the cavernous sinus (blue arrows). **c.** Before the procedure, lateral DSA imaging shows the transition from the ICA dural branches to the cavernous sinus (blue circle). Figure 2d. Coil placement into the cavernous sinus via the inferior petrosal sinus via transvenous route. **e-f.** Post-operative lateral and antero-posterior DSA images show loss of contrast passage to the cavernous sinus.

pregnancy, systemic hypertension, atherosclerotic vascular disease, connective tissue disease (such as Ehlers-Danlos syndrome), and minor traumas (2) . 2 patients with direct CCF had HT, 1 of these patients had a trauma history, 2 of 5 indirect CCF patients had HT, 1 had DM, and 1 had a transverse sinus thrombosis history.

Symptoms vary depending on the location of the fistula and the venous drainage pattern. CCFs with anterior drainage may present with ophthalmological symptoms such as orbital pain, pulsatile proptosis, and conjunctival chemosis.

Fistulas with posterior drainage are often asymptomatic when they drain into the superior and inferior petrosal sinuses. When they show symptoms, cranial neuropathies, mostly the oculomotor nerve, appear as the first symptoms of fistula. Eye findings are usually unilateral, but bilateral cases usually have cortical venous drainage and carry the risk of intracerebral hematoma (3). The most common admission reason for our patients was orbital pain and/or headache, which was seen in all of them (100%). Of 7 patients, 5 of them had chemosis (71%), 4 had proptosis (57%), 3 had cranial nerve paralysis (43%), 3 had diplopia (43%), and 1 had decreased visual acuity (14%).

Due to low flow rates, indirect fistulas can resolve spontaneously or with conservative treatment. Spontaneous closure is reported to be 20-60% in the literature. Treatment with compression is an alternative method, especially

in slow-flow fistulas. The aim of endovascular treatment of direct fistulas is to close the connection with the cavernous sinus while maintaining normal ICA flow(4). However, high-flow direct fistulas rarely respond to conservative treatment and require more aggressive treatment approaches (5). In our 1 case in our study with indirect type D, which could not be accessed, it was observed that the condition improved with compression therapy during follow-up.

The aim of endovascular treatment of direct fistulas is to close the connection with the cavernous sinus while maintaining normal ICA flow. As they have high flow, the transarterial approach is generally preferred. Once accessed, embolization is achieved with coils or liquid embolizing agents. Less frequently, covered stents may be placed in the artery. In direct fistulas that cannot be reached via the transarterial route, embolization can be performed via the transvenous route (5,6). Two of our patients had direct fistula and were treated with transarterial coiling.

Dural type CCFs are fed by many small dural branches from the ICA and ECA, and because these thin branches are tortuous, the transvenous approach is generally used. The aim of the transvenous approach is to superselectively catheterize the abnormal cavernous sinus and occlude the fistula without diverting venous drainage to cortical structures. In a meta-analysis by Texalidis et al., transvenous embolization showed an 86% complete obliteration rate for indirect fistulas, which is consistent with the 70-90% success rate in the literature. Our 5 patients had dural type fistula and endovascular treatment could be applied to 4 of them. Three of these patients were treated transvenously, and 1 was treated both transvenously and transarterially (5). In our 4 patients who were treated endovascularly, it was observed that the fistulas were completely closed in the 1st year control angiography.

Due to anatomical ease of access, the cavernous sinus is most accessed through the inferior petrosal sinus. Alternative routes can be used, including the superior ophthalmic vein through the facial vein or other venous routes (5). In all our patients to whom we applied the transvenous approach, the cavernous sinus was reached from the inferior petrosal sinus.

Coil is the most preferred material in indirect type fistulas and can be used alone or with liquid embolic agents such as Onyx (Medtronic, Irvine, California, USA), n-butyl cyanoacrylate (NBCA) or covered stent support (1,5). In the meta-analysis conducted by Texalidis et al., 16 studies included patients with indirect fistula, and it was reported that complete obliteration occurred in the majority of cases (86.03%, N=425/494). More importantly, transvenous coil embolization achieved occlusion in 87.54% (N=232/265), compared to 83.33% (N=10/10) with the use of different types of liquid embolic agents (Onyx, glue, N-BCA, PVA) along with the coil (5). We achieved complete obliteration with only coil support in 5 of the 7 patients we included in the study, and with flow-diverting stent support in 1 patient.

Information about the use of flow-diverting stents in the treatment of CCF is limited. In a literature review examining a total of 16 studies, 38 cases in which single or multiple flow-diverting stents were used together with embolizing agents were examined, and it was determined that there was clinical improvement in 35 patients (92.1%) and the long-term occlusion rate was 100% with variable follow-up periods. It was concluded that the best response was achieved in type A and type B CCFs (3,6). We also treated one of our cases with indirect Type B using flow-diverting stents simultaneously with coiling.

Complications of treatment include cranial nerve damage, central retinal vein occlusion, ophthalmic artery occlusion, intracranial or ocular hemorrhage, and ischemic stroke. After the procedure, cranial nerve paralysis may develop, or existing findings may worsen due to the mass effect of the coil and cavernous sinus thrombosis (1,7,8). Hence, in our 2 cases, due to the worsening of eye pain and chemosis due to impaired ophthalmic drainage, anticoagulant treatment with subcutaneous low molecular weight heparin was given in the early period and controlled thrombosis was targeted. During the follow-up of both patients, it was observed that the ocular symptoms resolved at the end of the first month.

The results of treatment with coiling in our cases showed that endovascular approaches are effective and safe for direct and dural CCFs. Transarterial and transvenous coil embolization is associated with high closure rates and a low risk of complications for both direct and indirect

fistulas. In cases where the fistula is incompletely closed with these treatments, a flow-diverting stent applied to the internal carotid artery contributes to the closure of the fistula in the long term by reducing the passage through the dural branches.

REFERENCES

1. Henderson AD, Miller NR. Carotid-cavernous fistula: Current concepts in aetiology, investigation, and management. Eye (Lond) 2018; 32(2): 164-172.
2. Miller NR. Diagnosis and management of dural carotid-cavernous sinus fistulas. Neurosurg Focus 2007; 23(5): E13.
3. Kısabay Ak A, Çınar C, Doğan GN, et al. Clinical improvement in indirect carotid cavernous fistulas treated endovascularly: A patient based review. Clin Neurol Neurosurg 2021; 207: 106750.
4. Kohli GS, Patel BC. Carotid Cavernous Fistula. 2018 Dec 16. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2019 Jan-. https://www.ncbi.nlm.nih.gov/books/NBK535409/. Accessed 20 Nov 2019.
5. Texakalidis P, Tzoumas A, Xenos D, et al. Carotid cavernous fistula (CCF) treatment approaches: A systematic literature review and meta-analysis of transarterial and transvenous embolization for direct and indirect CCFs. Clin Neurol Neurosurg 2021; 204: 106601.
6. Stamatopoulos T, Anagnostou E, Plakas S, et al. Treatment of carotid cavernous sinus fistulas with flow diverters. A case report and systematic review. Interv Neuroradiol 2022; 28(1): 70-83.
7. Ohlsson M, Consoli A, Rodesch G. Endovascular treatment of carotico-cavernous fistulas with acrylic glue: A series of nine cases. Neuroradiology 2016; 58(12): 1181-1188.
8. Hou K, Li G, Luan T, et al. Endovascular treatment of the cavernous sinus dural arteriovenous fistula: Current status and considerations. Int J Med Sci 2020; 17(8): 1121-1130.

Ethics

Ethics Committee Approval: The study was approved by Clinical Research Ethics Committee of Kartal Dr. Lütfi Kırdar City Hospital (Date: 27.04.2022, No: 2023/514/248/8).

Informed Consent: The author declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

Authorship Contributions: Surgical and Medical Practices: AÖ, EG, ÖA, ZUK, AÖÖ. Concept: AÖ, EG, ÖA, ZUK, AÖÖ. Design: AÖ, EG, ÖA, ZUK, AÖÖ. Data Collection or Processing: AÖ, EG, ÖA, ZUK, AÖÖ. Analysis or Interpretation: AÖ, EG, ÖA, ZUK, AÖÖ. Literature Search: AÖ, EG, ÖA, ZUK, AÖÖ. Writing: AÖ, EG, ÖA, ZUK, AÖÖ.

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