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Evaluation of sporadic intracranial cavernous malformations for detecting associated developmental venous anomalies: added diagnostic value of C-arm contrast-enhanced cone-beam CT to routine contrast-enhanced MRI

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Abstract

Objective Our purpose was to investigate the added diagnostic value of C-arm contrast-enhanced cone-beam CT (CE-CBCT) to routine contrast-enhanced MRI (CE-MRI) in detecting associated developmental venous anomalies (DVAs) in patients with sporadic intracranial cavernous malformations (ICMs).

Methods Fifty-six patients (53 with single and three with double ICMs) met the inclusion criteria. All patients had routine CE-MRI scans performed at 1.5 Tesla. The imaging studies (CE-MRI and CE-CBCT) were retrospectively and independently reviewed by two observers, with consensus by a third. Group difference, intra- and interobserver agreement, and diagnostic performance of the modalities in detecting associated DVAs were calculated. Reference standard was CE-MRI.

Results On CE-MRI and CE-CBCT, 37 (66%; of 56) and 47 patients (84%; of 56) had associated DVAs, respectively. In 10 patients (52.6%; of CE-MRI negatives [n=19]), CE-CBCT improved the diagnosis. Nine patients (16%; of 56) had no DVA on both imaging techniques. Difference in proportions of associated DVAs on CE-MRI and CE-CBCT was statistically significant, $p < 0.05$. Sensitivity, specificity, positive likelihood ratio, and area under the curve of CE-CBCT were 100% (95% confidence interval [CI]: 90.5-100%), 47.3% (95% CI: 24.4-71.1%), 1.9 (95%CI: 1.240-2.911), 0.737 (95%CI: 0.602-0.845), respectively. Intraobserver agreement was excellent for CE-MRI, kappa (κ) coefficient = 0.960, and CE-CBCT, κ=0.931. Interobserver agreement was substantial for CE-MRI, κ=0.803, and excellent for CE-CBCT, κ=0.810.

Conclusions CE-CBCT is a useful imaging technique especially in patients with negative routine CE-MRI in terms of detecting associated DVAs. In nearly half of these particular patients, it reveals an associated DVA as a new diagnosis.

Key Points

• *Although it is known to be the gold standard, some of the DVAs associated with ICMs are underdiagnosed with CE-MRI.*
• *In nearly half of the patients with negative routine CE-MRI, CE-CBCT reveals an associated DVA as a new diagnosis.*
• *Intra- and interobserver agreement on CE-CBCT is excellent in terms of detecting associated DVAs.*

Keywords Cavernous haemangioma · Cone-beam computed tomography · Magnetic resonance imaging · Central nervous system venous angioma

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Abbreviations

CBCT	C-arm cone-beam computed tomography
CE-CBCT	C-arm contrast-enhanced cone-beam computed tomography
CE-MRI	Contrast-enhanced magnetic resonance imaging
DSA	Digital subtraction angiography
DVA	Developmental venous anomaly
FOV	Field of view
GRE	Gradient -echo
ICM	Intracranial cavernous malformation
MRI	Magnetic resonance imaging
NLR	Negative likelihood ratio
SWI	Susceptibility-weighted imaging

Introduction

In the literature on sporadic intracranial cavernous malformations (ICMs), the relative importance of their association with developmental venous anomalies (DVAs) has been subject to considerable debate. Many authors have suggested that sporadic ICMs along with DVAs have a more aggressive clinical course [1–6]. Therefore, several attempts have been made to document whether the coexistence is systematic and causative [7–10]. Despite the fact that there are a number of case series and studies demonstrating *de novo* formation of sporadic ICMs in the setting of developmental venous anomalies (DVAs), recent developments in the field of high-resolution imaging have led to a renewed interest and debate in association of ICMs and DVAs [1, 7, 8, 11–15]. However, the association rates obtained by different imaging modalities remained inconsistent [7, 8, 10].

Even though susceptibility-weighted imaging (SWI) and gradient-echo imaging (GRE or T2*-weighted imaging) are widely used as non-enhanced MRI sequences in clinical practice, contrast-enhanced magnetic resonance imaging (contrast-enhanced T1-weighted; CE-MRI) is generally considered as gold standard for evaluation of DVAs [16]. Current research also suggests that CE-MRI has a higher sensitivity than non-enhanced MRI sequences in terms of detection of DVAs in 1.5-Tesla MRI scanners [16].

C-arm cone-beam computed tomography (CBCT) lets us produce computed tomography-like reconstructions from datasets obtained by conventional rotational angiography techniques using certain advanced algorithms [17, 18]. Using a contrast medium, this advanced imaging method lets us visualise smaller parts of the vascular structures in ultra-high resolution images [8, 19, 20]. In the literature, use of C-arm contrast-enhanced cone-beam computed tomography (CE-CBCT) for evaluation of associated DVAs in patients with ICMs is limited with only small case series [8, 21]. In a previous study, which was a comparison between their results and the related literature, it was reported that CE-CBCT was able to reveal about threefold higher association rate for DVA coexistence in patients with sporadic ICMs [8]. On the other hand, studies making comparisons with other imaging modalities are needed to confirm these findings and the added diagnostic value of CE-CBCT.

In this study, we retrospectively investigated the added diagnostic value of CE-CBCT to routinely used CE-MRI in detecting associated DVAs in patients with sporadic ICMs.

Materials and methods

Study design

The institutional review board approved this retrospective, observational cohort study. Although the IRB waived the informed consent requirement, it was a routine procedure in our department.

In this study, we retrospectively evaluated imaging data (magnetic resonance imaging [MRI], digital subtraction angiography [DSA], and CE-CBCT) of the patients who had been referred to our department for cranial DSA and following CE-CBCT procedures between July 2011 and September 2017. The retrospective review revealed 56 patients who met the inclusion criteria of the study. CE-CBCT raw (not reconstructed) datasets of 24 patients were included in this study from the authors' previous publication, but reconstructed and re-analysed with a different objective and study design [8]. Major differences between current and previous studies are that the current one covers a broader time range, has different inclusion/exclusion criteria, and makes comparison with a gold standard imaging modality to assess the added value of CE-CBCT to CE-MRI using a different methodology.

Inclusion/exclusion criteria

Inclusion criteria were as follows: *(i)* patients with single ICMs, *(ii)* patients with two ICMs along with clustered distribution pattern, *(iii)* patients that have all of the following procedures: CE-MRI along with non-enhanced sequences (T1-weighted, T2-weighted, T2*-weighted imaging or SWI), DSA, and CE-CBCT.

Exclusion criteria were as follows: *(i)*, post-operative patients, *(ii)* patients with more than two ICMs or "familial" pattern, *(iii)* patients with two ICMs along with a scattered distribution pattern, i.e., "indefinite" pattern, *(iv)* patients with radiotherapy history, *(v)* patients with arteriovenous malformations or fistulas on DSA, and *(vi)* patients with imaging studies of poor quality or missing sequences.

Patient population

Fifty-six patients with 59 ICMs met the inclusion criteria. Mean age was 34.7 years (range, 3-66). Thirty-four patients (60.7%; of 56) were female; 22 patients (39.3%; of 56) were male. Fifty-three patients (94.6%; of 56) had single ICM. On the other hand, three patients (5.4%; of 56) had double ICMs. Forty-three ICMs were in the cerebrum, nine in the cerebellum, six were in the brainstem, and one was in the brainstem with cerebral extension. In eight patients (14.2%; of 56), more than one consecutive CE-CBCT scan was performed because of motion artefacts (n=1) and localisation of ICMs around arterial border-zones (n=7), which necessitates bilateral anterior or unilateral anterior-posterior circulation injections.

MRI protocol

Reference imaging modality for evaluation of associated DVAs was the CE-MRI [16]. All patients included in the study were scanned in 1.5-Tesla MRI scanners (Magnetom Avanto and Symphony, Siemens Healthcare). Our representative standard CE-MRI protocol was as follows: repetition time, 670 ms; echo time, 17 ms; section thickness, 5 mm; field of view, 190x240 mm; and acquisition matrix size, 320 × 192. Dose of intravenous gadolinium-based MRI contrast agent was 0.1 mmol/kg. Besides uniform CE-MRI sequences with at least two orthogonal planes (axial, sagittal or coronal), all patients also had T1-weighted, T2-weighted, T2*-weighted imaging or SWI sequences. The studies having poor image qualities (significant motion artefacts, poor enhancement, etc.) were excluded by consensus of experienced neuroradiologists.

CE-CBCT protocol

The CE-CBCT studies were performed in a flat-panel biplane angiography system (Allura Xper 20/20; Philips Healthcare) following a digital subtraction angiography (DSA) study. Image acquisition parameters were: c-arm rotational speed, 10 °/s; C-arm rotation angle, 200°; scan duration, 20 s; number of frames, 620; field of view, 10.4 × 10.4 cm^2; tube current, 80 kV; and x-ray dose, 50 mGy.

An automatic power injector (Angiomat, Liebel Flarsheim) was used for contrast injections. Contrast medium was injected from the proximal internal carotid artery or vertebral artery being ipsilateral to the location of the ICM of interest. Contrast injection parameters were: X-ray delay for maximum opacification, 4 s; injection time, 24 s; injection rate, 4 mL/s; and contrast medium to saline ratio, 3:17 (15 mL of contrast medium diluted with 85 mL of saline). In patients with multiple scans, the contrast injection parameters were same to obtain the optimal vascular opacification.

A dedicated workstation (XtraVision, Philips Healthcare) was used for reconstruction of the rotational fluoroscopic frames to obtain isotropic three-dimensional images. Depending on the need for the level of anatomic details, reconstruction parameters used were as following: matrix size, 256×256 or 384×384 or 512×512; cubic sampling volume, 67% or 50% or 33% or 17%; and reconstruction time, approximately 35 to 50 s.

Image analysis

The MRI and reconstructed CE-CBCT datasets were retrospectively and independently reviewed in different time settings by *(i),* a radiology specialist with a particular interest in neuroradiology and a significant experience in evaluation of CE-CBCT datasets and *(ii),* a third-year radiology resident, who had completed her 6-month neuroradiology rotation and 2 weeks of special training in CE-CBCT evaluation. In case of a disagreement, the final diagnosis was made by consensus with a senior neuroradiologist. The consensus data were used for the final analysis. In order to assess the interobserver reproducibility of the results, a radiology resident was deliberately included in the image analysis to represent trained, but relatively inexperienced observers. The first observer reviewed the datasets twice for the assessment of intraobserver reproducibility. The second evaluation was done 1 month after the first one.

The ICMs were grouped according to their number and distribution on non-enhanced MRI sequences (T1-weighted, T2-weighted, T2*-weighted imaging, or SWI) with consensus of both observers. Single ICMs were grouped as “sporadic”. Double ICMs were grouped as: *(i)*, “sporadic” if the both ICMs were located in proximity or in clustered pattern, and *(ii),* “indefinite” if located far from each other or in scattered pattern. Multiple ICMs (>2) and that had a scattered distribution were grouped as “familial”.

The sequence of evaluation of CE-MRI datasets was as follows. First, number and distribution of ICM or ICMs were evaluated on available non-enhanced MRI sequences (T1-weighted, T2-weighted, T2*-weighted imaging or SWI). Second, presence or absence of a venous abnormality or abnormalities in proximity of ICM of interest was assessed in CE-MRI.

The sequence of CE-CBCT evaluation was as follows. First, with using available non-enhanced MRI sequences (T1-weighted, T2-weighted, T2*-weighted imaging or SWI), the region of ICM was determined in CE-CBCT reconstructions as accurately as possible. For this purpose, calcified components or certain anatomic landmarks (e.g., ventricles, bony landmarks) were used. Second, presence or absence of a DVA in proximity of an ICM of interest was evaluated in reconstructed CE-CBCT images. While evaluating the CE-CBCT images, readers were blind to the diagnosis on CE-MRI. There was a time interval of 1 week between CE-MRI and CE-CBCT evaluations.

Terminology used

On CE-MRI, DVA term was used for the abnormal venous structures that have *(i)* a solitary appearance or *(ii)* a branching pattern that has at least two veins that converge and drain towards a vein or veins [16]. On CE-CBCT, it was used for the abnormal venous structures that have a branching pattern having at least two veins that converge and drain towards a vein or veins [8]. It is important to note that venous structures that have a solitary appearance or non-branching pattern were not considered as DVA on CE-CBCT in this study because possible importance of their presence has not been well understood yet [8]. Figure 1 illustrates these DVA definitions on CE-MRI and CE-CBCT in a simplistic way for a better understanding.

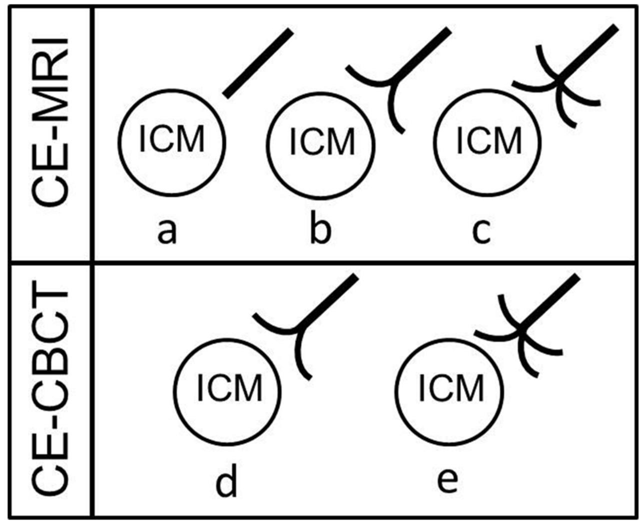

Fig. 1 Simplified drawings illustrate the definitions of DVA spectrum on CE-MRI and CE-CBCT. On CE-MRI, the DVA term was used for the abnormal venous structures that have **(a)** a solitary appearance or **(b, c)** a branching pattern that has at least two branches converging and draining towards a vein or veins. On CE-CBCT, the DVA term was used for the abnormal venous structures that have **(d, e)** at least two branches that converge and drain towards a vein or veins. The illustration was drawn by the first author

Statistical analysis

Statistical analysis of the data was performed using IBM SPSS version 20 (SPSS Inc.) and MedCalc statistical software version 18 (MedCalc Software bvba). The number of patients rather than ICMs was used in calculations. Consensus data were used in the statistical analysis of group differences and diagnostic performance parameters. *McNemar's test* was used for group difference. Sensitivity, specificity, positive likelihood ratio, negative likelihood ratio (NLR), and area under the curve for CE-CBCT in detecting associated DVAs were calculated. CE-MRI was considered as reference in calculations [16]. In addition, the same diagnostic metrics were calculated for CE-MRI because CE-CBCT performed better than CE-MRI in our study. Since the true prevalence of the DVA and ICM coexistence in sporadic ICM patients is currently unknown in the literature, we did not calculate positive and negative predictive values, which are influenced by the prevalence.

Cohen's kappa (κ) was run to determine intra- and interobserver agreement on whether ICMs were associated with DVAs. Strength of agreement was assessed according to the following scale of *kappa (κ) coefficient*: 0.00–0.20 = slight; 0.21–0.40 = fair; 0.41–0.60 = moderate; 0.61–0.80 = substantial; and 0.81–1.00 = excellent.

The statistical significance threshold (*p*-value) was set at 0.05.

Results

ICM and DVA association

On CE-MRI, 37 patients (66.1%; of 56) had associated DVAs in either branching (Fig. 2 and Video 1) or solitary (Fig. 3 and Video 2) form. Meanwhile, 19 patients (33.9%; of 56) had no DVA. All of the associated DVAs visualised on CE-MRI were also detected on CE-CBCT. Of 19 patients with no DVA on CE-MRI, 10 patients (52.6%; of 19) had a DVA on CE-CBCT as a new diagnosis (Fig. 4 and Video 3). The remaining nine patients (47.4%; of 19) had no associated DVA on CE-CBCT as well. On CE-CBCT, 47 patients (83.9%; of 56) had associated DVAs. Meanwhile, nine patients (16.1%; of 56) had no DVA. The differences in the proportions of associated DVAs on CE-MRI and CE-CBCT was statistically significant, $p<0.05$.

Diagnostic value of CE-CBCT

Considering the CE-MRI as the reference standard, the sensitivity, specificity, positive likelihood ratio, negative likelihood ratio (NLR), and area under the curve for CE-CBCT were 100% (95% confidence interval [CI]: 90.5-100%), 47.3% (95%CI: 24.4-71.1%), 1.9 (95%CI: 1.240-2.911), 0 (NLR), and 0.737 (95%CI: 0.602-0.845), respectively.

Diagnostic value of CE-MRI

Owing to the fact that CE-CBCT performed better than the gold standard CE-MRI in our study, the diagnostic value of CE-MRI was also calculated considering the CE-CBCT as the reference. The sensitivity, specificity, negative likelihood ratio (NLR), and area under the curve for CE-CBCT were 78.7% (95% confidence interval [CI]: 64.3-89.3%), 100% (95%CI: 66.4-100%), 0.21 (95%CI: 0.12-0.37), and 0.894 (95%CI: 0.782-0.960), respectively.

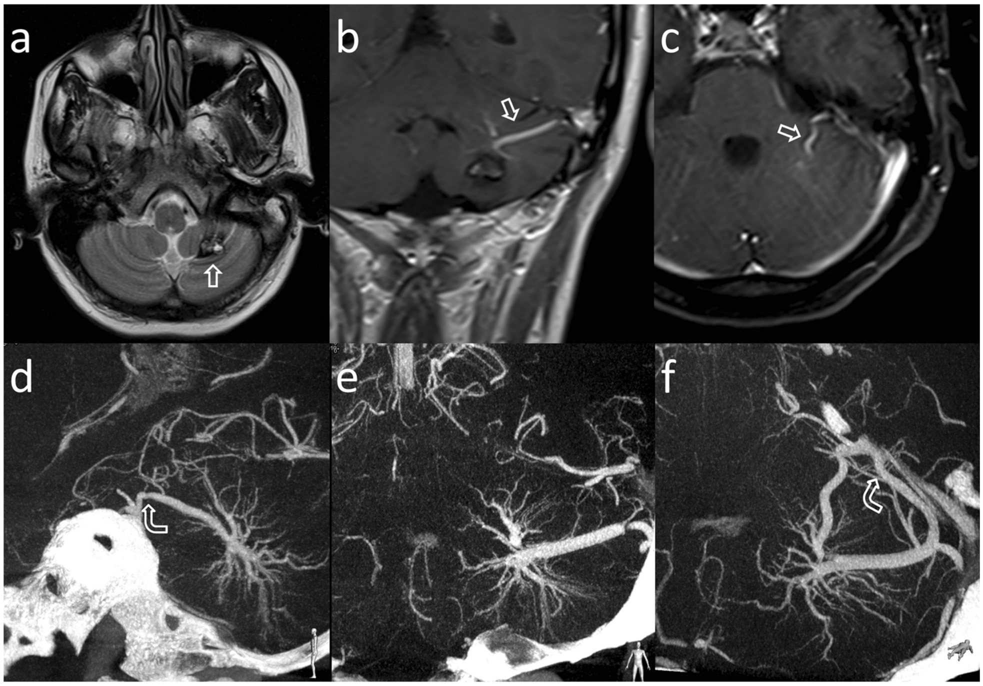

Fig. 2 A 32-year-old woman with severe headache harbouring an ICM in her left cerebellar hemisphere that is associated with a classic DVA seen on both CE-MRI and CE-CBCT. **(a)** Axial T2-weighted image shows an ICM (arrow) in the left hemisphere. **(b)** Coronal post-contrast T1-weighted image demonstrates an associated classic DVA (arrow) with few medullary branches. This image also shows that the draining vein of the DVA courses lateral side of the cerebellum. **(c)** Axial post-contrast T1-weighted image shows another draining vein (arrow) coursing anteriorly. **(d, e, f)** CE-CBCT images from different angles demonstrate the associated DVA and its numerous medullary branches with incomparable angioarchitectural details. **(d, f)** It can be easily noted that both draining veins have proximal-distal size discrepancies (curved arrows). Supplementary online video file for CE-CBCT is also available for further details and better understanding (Video 1)

Intra- and interobserver agreement

Intraobserver agreement for the presence or absence of associated DVAs was excellent for CE-MRI, κ =0.960 (95%CI: 0.881-1.000; $p < 0.05$). It was also excellent for CE-CBCT, κ =0.931 (95%CI: 0.796-1.000; $p < 0.05$).

Interobserver agreement for the presence or absence of associated DVAs was substantial for CE-MRI, κ =0.803 (95%CI: 0.639-0.967; $p < 0.05$). On the other hand, it was excellent for CE-CBCT, κ =0.810 (95%CI: 0.602-1.000; $p < 0.05$).

Discussion

In this study, we retrospectively investigated the added diagnostic value of CE-CBCT to CE-MRI (gold standard) for detecting associated DVAs in patients with sporadic ICMs for the first time in the literature. The overall diagnostic performance of CE-CBCT for detecting DVAs in patients with sporadic ICMs was higher than CE-MRI in many aspects, with promising intra- and interobserver agreement. The most noteworthy finding of this study was that CE-CBCT significantly improves the diagnosis as to the presence of associated DVAs especially in patients with negative CE-MRI studies, which might be particularly quite important for the patients who are surgical candidates.

The literature has somewhat perplexing imaging and surgical data as to the coexistence of DVAs and sporadic ICMs. In standard or routine MRI sequences, up to one third of the ICMs are associated with DVAs [10]. Meanwhile, a 7-Tesla susceptibility-weighted imaging (SWI) study reported a 100% association rate for the coexistence of ICMs and "local venous abnormalities". However, their definition of "local venous abnormalities" included variant I (classic type; 30%) and variants II-III (composed of single or multiple enlarged draining veins that do not fit in the classic DVA definition; 70%) [7]. So far, in the literature, the CE-CBCT appears to have the greatest rate (88%), which is about threefold higher, for classic DVA and ICM coexistence in patients with sporadic ICMs [8]. In the present study, the association rate in CE-CBCT was 83.9%, which is close to the previous results.

Regarding the CE-MRI in evaluation of DVA and ICM coexistence in patients with ICMs, the literature suffers from a scarcity of studies that evaluate its diagnostic performance compared to the other MRI sequences at same or different field strength (1.5-Tesla versus 3-Tesla versus 7-Tesla), or the other imaging modalities. The studies that we encountered usually focus on DVAs and their co-occurrence with ICMs in DVA patients and thus provide no comparable data. Even so,

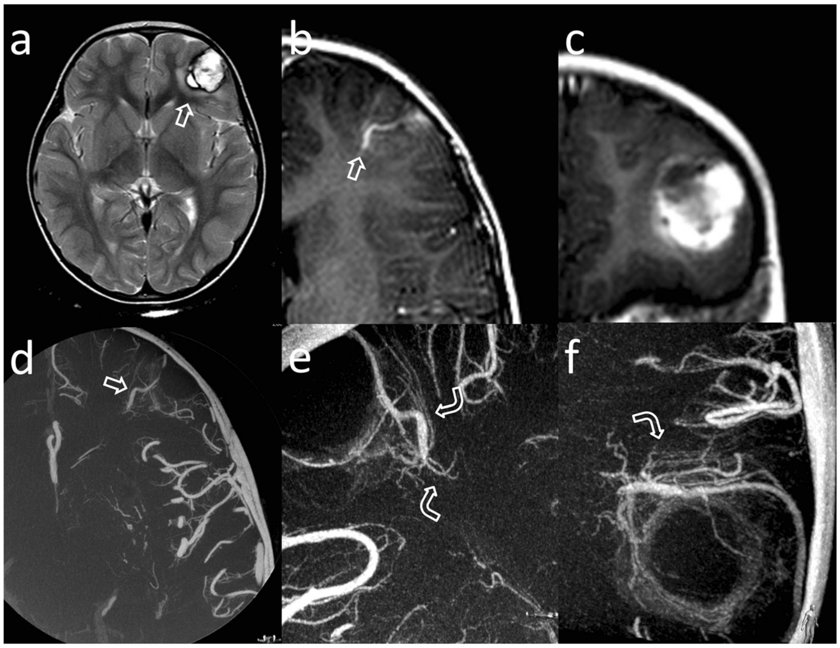

Fig. 3 A 3-year-old girl with epileptic seizures harbouring an ICM in left frontal lobe that is associated with a solitary or non-branching DVA on CE-MRI and classic DVA pattern on CE-CBCT. **(a)** Axial T2-weighted image shows an ICM (arrow) in the left frontal lobe and perilesional oedema. **(b)** Axial post-contrast T1-weighted image depicts a solitary or non-branching venous structure (arrow) representing a DVA. **(c)** There is no sign of DVA on post-contrast coronal T1-weighted image. **(d)** On CE-CBCT image with a relatively large field of view, there is an associated DVA (arrow) with a few branches at its tip. **(e, f)** CE-CBCT images obtained with a new reconstruction in a smaller field of view reveal numerous medullary branches of the associated DVA (curved arrows). Please note that there is a diameter discrepancy in the draining vein between its deep and superficial segments. Supplementary online video file for CE-CBCT is also available for further details and better understanding (Video 2)

seeking associated ICMs in patients with DVAs is another point of view to this matter and still gives us important insights. As such, in their seminal study conducted in patients with intracranial DVAs using CE-MRI as gold standard, Young et al reported that CE-MRI can reveal more DVAs than non-enhanced 1.5-Tesla MRI sequences like SWI can [16].

This study makes a major contribution to the research on the coexistence of ICMs and DVAs by demonstrating that nearly in half of the sporadic ICM patients with negative CE-MRI studies, an additional CE-CBCT scan might reveal an associated DVA as a new diagnosis. As regards the natural history of the ICMs that are associated with DVAs, several authors suggested that sporadic ICMs that are associated with DVAs have a more aggressive clinical course [1–6]. For instance, the association of ICM and DVA presents a higher risk of symptomatic haemorrhage than does the ICM alone. Furthermore, previous authors also suggested that the DVAs associated with ICMs should be preserved during excision of the ICMs to avoid possible complications such as venous infarction, because they drain normal neural parenchymal tissue [2, 10, 22–25]. Hence, evaluation of the venous angioarchitecture of the ICMs before surgery seems to be essential in the decision-making process. In this context, CE-CBCT might be a helpful method in detecting associated DVAs especially in patients with negative routine CE-MRI, providing useful data for neurosurgeons as to their absence or presence, precise localisation, and angioarchitecture as well. On the other hand, CE-CBCT has a few disadvantages, including radiation exposure and administering contrast medium, which should not be ignored in any case. In the light of our findings and considering its pros and cons, we suggest that patients, especially the surgical candidates with sporadic ICMs and no associated DVAs on his or her CE-MRI scans should be scanned with CE-CBCT. There are also only few studies about use of CT angiography along with perfusion for haemodynamic evaluation of DVAs but not regarding the association [26]. Although it is not systematic, our experience is that CE-CBCT with its ultra-high-resolution capabilities provides better assessment of DVAs than regular CT angiography. To reshape and improve our decision making on the matter, we are also in need of many more studies.

This study may change our perspective in DVAs as to their size spectrum. Apart from the DVAs with classical caput medusa formation, which are usually easily identified on standard 1.5- or 3-Tesla SWI or CE-MRI, they might be present in tiny branching forms that could not be definitively imaged with standard (1.5-Tesla CE-MRI or SWI) or even with certain advanced imaging modalities (7-Tesla SWI). Although it is not clear nowadays, future research might reveal their possible significance in natural history and treatment of ICMs.

Regarding the CBCT imaging technique, the raw images are obtained using conventional rotational angiographic

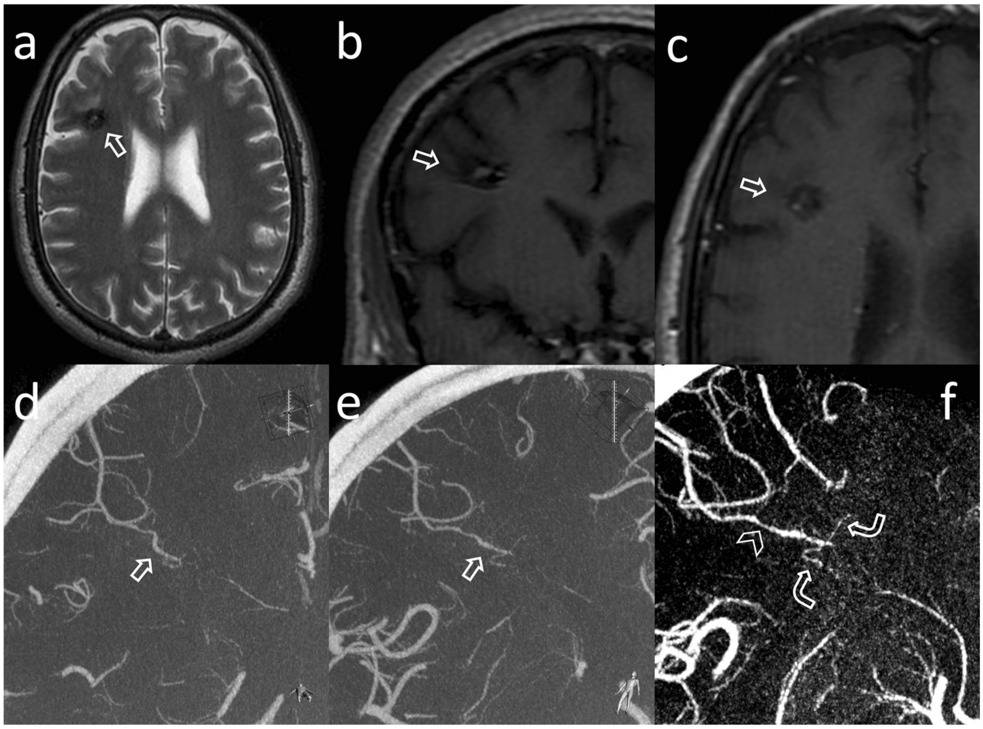

Fig. 4 A 54-year-old man with severe headache has an ICM in his right frontal lobe and an associated DVA that is seen only on CE-CBCT, not on CE-MRI. **(a)** Axial T2-weighted image shows a right-sided ICM (arrow) in the frontal lobe. **(b, c)** Coronal and axial T1-weighted images demonstrate no associated DVA around the ICM (arrows). **(d, e)** CE-CBCT images from various angles shows a DVA (arrows) with a distinct appearance compared to the adjacent normal venous vasculature. The DVA has a longer course compared to the adjacent normal venous vasculature, extending from the deep white matter region to the pial surface. **(f)** CE-CBCT image obtained with a new reconstruction in a smaller field of view reveals a proximal to distal diameter discrepancy (arrow head) at its proximal segment. It has a few medullary branches at its proximal tip (curved arrows). Supplementary online video file for CE-CBCT is also available for further details and better understanding (Video 3)

fluoroscopic frames in angiography suits, which is not diagnostic. Use of contrast material turns CBCT to a type of CT angiography. The raw data images are reconstructed in dedicated workstations in order to create CT-like cross-sectional images with isotropic voxels. The added reconstructions using certain soft tissue algorithms are necessary to increase the visibility of the vascular structures. Use of smaller cubic sample size (volume of interest) also increases the visibility and details of vascular structures, but the cost is decreased field of view.

Retrospective study design, relatively small patient population, lack of surgical observations, and being a large tertiary referral centre were the major limitations in the present study. Comparing a 3-dimensional isotopic modality with an MRI with 5 mm of slice thickness might be regarded as a limitation, but it should be kept in mind that the MRI protocol in this study represents the routine clinical practice. In the future, state of the art 3-dimensional CE-MRI with thinner slices would be a good option for prospective studies. We only presented a comparison with 1.5-Tesla CE-MRI and CE-CBCT. On the other hand, use of 3-Tesla CE-MRI for this comparison would be an interesting subject for future research because there is no relevant study on this. Small field of view (FOV) on CE-CBCT may be considered a technical limitation. Nevertheless, appropriate use of the FOV by placing the ICM to the location of interest minimises the possible drawbacks. Performing more than one scan in some patients was another important limitation to be considered. Motion-related artefacts or location of the ICMs around border-zones may require more than one scan, exposing the patient to more radiation and contrast agent doses. These aspects must be considered and weighed in clinical decision-making.

Conclusions

The CE-CBCT evaluation may be a useful imaging technique in sporadic ICM patients especially with negative routine CE-MRI in terms of detecting associated DVAs. In nearly half of the patients with no associated DVAs in CE-MRI, an additional CE-CBCT has a potential to improve the diagnosis, which might be of great importance particularly in surgical candidates. Nonetheless, these findings need to be confirmed with larger prospective and comparative studies.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Civan Islak.

Conflict of interest The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

Statistics and biometry One of the authors (Burak Kocak) has significant statistical expertise.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Study subjects or cohorts overlap Some study subjects or cohorts have been previously reported in authors' previous publication Kocak B, Kizilkilic O, Oz B, Bakkaloglu DV, Isler C, Kocer N, Islak C. Ultra-high-resolution C-arm flat-detector CT angiography evaluation reveals 3-fold higher association rate for sporadic intracranial cavernous malformations and developmental venous anomalies: a retrospective study in consecutive 58 patients with 60 cavernous malformations. Eur Radiol. 2017 Jun;27(6):2629-2639. doi: 10.1007/s00330-016-4595-9. Epub 2016 Sep 21.

Methodology
- retrospective
- diagnostic study
- performed at one institution

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