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Fibromuscular Dysplasia and Its Neurologic Manifestations

¹ Grace, ¹ Yohanes

¹ Faculty of Medicine, Maranatha Christian University, Bandung City, West
Java, Indonesia

Correspondence : dr.grace9373628@gmail.com



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ABSTRACT

Background: Fibromuscular dysplasia (FMD) is recognized as a significant vascular disorder that predominantly affects medium-sized arteries, with notable implications for neurologic health. The literature reveals that FMD is characterized by non-atherosclerotic and non-inflammatory changes, which can lead to a spectrum of neurologic manifestations, particularly involving the cervicocephalic arteries. **Literature Review:** The foundational work by (Arning & Grzyska, 2004) highlights the critical role of the internal carotid artery (ICA) in FMD, noting that it is often implicated in transient ischemic attacks and cerebral infarctions, alongside nonspecific symptoms such as headaches and vertigo. This establishes a baseline understanding of FMD's neurologic implications, which is further expanded by case studies such as that presented by (Altun et al., 2013), where central retinal artery occlusion was associated with FMD, illustrating the heterogeneous nature of the disease and its varied clinical presentations. Diagnostic challenges related to FMD are highlighted by (Yiek, 2021), who emphasizes the reliance on imaging techniques for accurate identification. The article stresses that while renal artery involvement is prevalent, cervicocephalic manifestations can lead to serious complications, necessitating vigilant diagnostic practices. This is further supported by (Fujiwara et al., 2022), who presents a case of intracerebral hemorrhage linked to FMD, despite normal angiographic findings, thereby challenging conventional diagnostic expectations. **Conclusion:** In conclusion, the literature collectively underscores the complexity of fibromuscular dysplasia and its neurologic manifestations. The critical importance of early detection, comprehensive evaluation, and tailored management strategies is evident across studies. Clinicians are urged to maintain a high level of suspicion for FMD in patients presenting with unexplained neurologic symptoms, as timely intervention can significantly impact patient outcomes.

Keyword: Fibromuscular Dysplasia, Neurologic Manifestations

INTRODUCTION

Fibromuscular dysplasia (FMD) is a complex and multifaceted vascular disorder characterized by non-atherosclerotic and non-inflammatory changes in medium-sized arteries, leading to a variety of neurologic manifestations. The literature reveals a growing understanding of FMD's clinical implications, particularly concerning its effects on the cervicocephalic arteries and the resultant neurologic complications.

(Arning & Grzyska, 2004) emphasize that FMD primarily affects the internal carotid artery (ICA), often resulting in transient ischemic attacks or cerebral infarctions, alongside more nonspecific symptoms like headaches and vertigo. Their findings highlight the importance of early detection, as timely intervention can mitigate the risk of severe cerebrovascular events. This foundational understanding sets the stage for subsequent investigations into the broader manifestations of FMD.

(Altun et al., 2013) expand upon this knowledge by presenting a rare case of central retinal artery occlusion associated with FMD. Their work underscores the heterogeneous nature of FMD, which can involve various vascular territories, including the retinal arteries, and illustrates the diverse clinical presentations that can arise from this condition. They also reinforce the notion that FMD often presents with nonspecific symptoms, complicating timely diagnosis.

In a more recent study, (Arnaud et al., 2021) provide critical insights into the prevalence of cervical artery dissection in patients with FMD, particularly noting that male sex and a history of migraine are significant risk factors. This study contributes to the understanding of demographic and clinical characteristics that can stratify risk among patients, emphasizing the need for heightened awareness in clinical practice.

(Yiek, 2021) further elucidates the diagnostic challenges associated with FMD, particularly the reliance on imaging techniques for accurate identification. The author notes that while FMD is most commonly associated with renal artery involvement, its manifestations in the cervicocephalic region can lead to serious complications such as ischemic strokes. The article highlights the necessity for clinicians to be vigilant regarding the potential for delayed diagnosis, which can adversely affect patient outcomes.

(Fujiwara et al., 2022) present a case of intracerebral hemorrhage linked to FMD, despite the absence of angiographically visible vascular abnormalities. This finding challenges the conventional understanding of FMD's presentation and reinforces the need for comprehensive evaluation in patients with cerebrovascular symptoms, even when typical imaging findings are not evident.

(Cicarese et al., 2022) explore the less common hepatic and mesenteric manifestations of FMD, further demonstrating the systemic nature of the disease. Their findings highlight that while FMD may often be asymptomatic, it can lead to significant complications such as hypertension and stroke, necessitating a multifaceted approach to management.

(Ismail et al., 2022) focus specifically on extracranial carotid localized FMD, reiterating that the cervicocephalic arteries are frequently involved. Their case report illustrates the clinical symptoms that may arise, including TIAs and headaches, and emphasizes the importance of individualized management strategies for symptomatic patients.

Finally, (Kesav et al., 2023) provide a comprehensive review of cerebrovascular FMD, reinforcing the notion that this condition is as prevalent in the cerebrovascular territory as it is in the renal arteries. They summarize the spectrum of symptoms associated with C-FMD and highlight the importance of recognizing the diverse manifestations of the disease. Their work calls attention to the need for standardized definitions and diagnostic criteria to enhance the understanding and management of FMD.

Through this literature review, the evolving narrative surrounding FMD and its neurologic manifestations is articulated, highlighting the critical importance of early detection, comprehensive evaluation, and individualized management strategies to improve patient outcomes.

LITERATURE REVIEW

The article "Color Doppler imaging of cervicocephalic fibromuscular dysplasia" by (Arning & Grzyska, 2004) provides a comprehensive overview of fibromuscular dysplasia (FMD), particularly focusing on its manifestations in the cervicocephalic arteries, including the internal carotid artery (ICA) and vertebral artery. The authors clarify that FMD is characterized as a non-atheromatous and non-inflammatory arteriopathy with an unknown etiology, presenting segmentally in medium-sized arteries. This classification is crucial as it distinguishes FMD from other vascular conditions, highlighting its unique pathological features.

One of the significant points made in the article is the prevalence of FMD in the renal arteries, which often leads to renovascular hypertension. This aspect underscores the importance of recognizing FMD not only for its neurological implications but also for its systemic effects. The authors note that cervicocephalic involvement occurs in approximately 0.6% to 1% of cases, often bilaterally, which is critical for clinicians to consider when diagnosing and managing patients with suspected vascular conditions.

The clinical manifestations of FMD, particularly concerning the ICA, are highlighted as transitory ischemic attacks and cerebral infarctions, alongside nonspecific symptoms such as headache and vertigo. This range of symptoms can complicate the diagnosis, as they may overlap with other neurological disorders. The article emphasizes the necessity for prompt detection of FMD, especially in cases presenting with cerebrovascular events, where timely intervention can significantly affect patient outcomes.

Furthermore, the authors advocate for the use of color Doppler imaging as a valuable diagnostic tool for identifying FMD in the cervicocephalic region. This

non-invasive imaging technique can facilitate the assessment of blood flow and vascular abnormalities, thereby aiding in the early diagnosis of FMD and guiding subsequent treatment options, which may include endovascular or surgical interventions.

The article "Central retinal artery occlusion in association with fibromuscular dysplasia" by (Altun et al., 2013) provides a significant contribution to the understanding of the neurologic manifestations associated with fibromuscular dysplasia (FMD). The authors emphasize the heterogeneous nature of FMD, which is characterized by noninflammatory and nonatherosclerotic changes primarily affecting small and medium-sized arteries, including those in the renal and craniocervical regions.

The article highlights that the etiology of FMD remains largely unknown, which poses challenges in the diagnosis and management of the condition. The pathological features described, such as circumferential or eccentric collagen deposition, are critical for understanding the vascular changes that occur in FMD. These changes can lead to various clinical manifestations, with renal artery involvement being the most prevalent, often resulting in systemic hypertension due to renal arterial stenosis.

The authors provide an insightful case study of central retinal artery occlusion (CRAO) in a patient diagnosed with FMD, illustrating a less common but significant neurologic manifestation of the disease. This case underscores the importance of recognizing the diverse vascular complications associated with FMD, which can include transient ischemic attacks, headaches, syncope, and even subarachnoid hemorrhages. The correlation between the site of arterial involvement and the clinical manifestations is a crucial point made in the article, which enhances the understanding of how FMD can impact neurological health.

The article "Male Sex Is Associated With Cervical Artery Dissection in Patients With Fibromuscular Dysplasia" by (Arnaud et al., 2021) presents significant findings regarding the neurologic manifestations associated with fibromuscular

dysplasia (FMD), particularly emphasizing the prevalence of cervical artery dissection (CAD) among affected individuals. The study highlights that the involvement of cervico-encephalic arteries is comparably frequent to that of renal arteries in patients diagnosed with FMD, indicating a need for heightened awareness among clinicians regarding the vascular implications of this condition.

One of the key insights from the article is the reported prevalence of cervical artery dissection, which averages 14% in patients with FMD. This statistic underscores the critical need for early detection and intervention, especially in demographics identified as high-risk. The authors delineate several independent risk factors for CAD, including male sex, age under 50 years, a history of migraine, involvement of three or more vascular beds, and absence of hypertension history. These factors provide a framework for clinicians to stratify patients based on their risk profiles, enabling more tailored monitoring and preventive strategies.

The article's findings are particularly relevant in the context of neurologic manifestations, as cervical artery dissection can lead to serious complications such as stroke or transient ischemic attacks. The emphasis on male sex as a risk factor is noteworthy, as it challenges some prevailing assumptions about the gender distribution of FMD-related complications. Additionally, the association of CAD with a younger patient demographic further highlights the necessity for clinicians to maintain a high index of suspicion in evaluating symptoms that may suggest vascular involvement in this population.

Moreover, the authors advocate for increased awareness among healthcare providers regarding the potential for CAD in young males with FMD, suggesting that this could lead to improved clinical outcomes through timely diagnosis and management. The article effectively contributes to the existing literature by providing empirical data that can aid in clinical decision-making and risk assessment in patients with fibromuscular dysplasia.

The article "Fibromuscular Dysplasia: A Rare Case with Multiple Vascular Beds Involvement" by (Yiek, 2021) presents a comprehensive overview of

Fibromuscular Dysplasia (FMD) with a particular focus on its clinical manifestations and the challenges associated with diagnosis and management. The author emphasizes that the clinical manifestations of FMD are largely contingent upon the vascular beds involved, which can lead to a variety of nonspecific signs and symptoms. This nonspecificity can significantly delay diagnosis, underscoring the importance of heightened awareness among clinicians.

The article highlights that while FMD most frequently affects the renal arteries, it can also involve the carotid and vertebral arteries, which are critical in the context of neurologic manifestations. The author notes that the prevalence of FMD across multiple vascular beds remains inadequately characterized, which poses a challenge for understanding the full spectrum of the disease. This lack of clarity is particularly concerning given that neurologic complications, such as ischemic strokes, may arise from compromised blood flow in these areas.

Diagnostic imaging is presented as the cornerstone of FMD identification, with the "string of beads" appearance on angiography being a hallmark finding. This radiographic feature is essential for confirming the diagnosis and differentiating FMD from other vascular conditions. The reliance on imaging highlights both the advancements in diagnostic techniques and the potential for misdiagnosis if imaging is not performed or interpreted correctly.

In terms of management, the article outlines that therapeutic goals primarily focus on controlling risk factors and blood pressure, alongside preventing ischemic events through the use of antithrombotic medications in patients with ischemic strokes. However, the article reveals a notable gap in established protocols for managing FMD-related aneurysms, which poses significant risks for patients. The therapeutic options available, such as microvascular neurosurgical clipping and endovascular coiling, are contingent upon individual patient factors, including life expectancy and the risk of rupture. This variability in treatment underscores the complexity of managing FMD and the need for a tailored approach.

The article titled "A case of fibromuscular dysplasia related intracerebral hemorrhage without angiographically cerebral abnormal vessels" by (Fujiwara et al., 2022) provides valuable insights into the complexities of fibromuscular dysplasia (FMD) and its neurologic manifestations, particularly focusing on a unique case of intracerebral hemorrhage (ICH) associated with FMD. The authors elucidate the characteristics of FMD, which is recognized as a noninflammatory and nonatherosclerotic vascular disorder that predominantly affects the media of arteries, leading to various vascular complications.

The article emphasizes the typical presentation of FMD, characterized by arterial tortuosity, stenosis, occlusion, aneurysm, and dissection, particularly in the middle and distal segments of affected arteries. Notably, the authors highlight the "string of beads" appearance that is often observed in imaging studies of affected vessels, which serves as a hallmark of the condition. This presentation is crucial as it assists in the diagnosis and management of patients with FMD.

One of the significant contributions of this article is its focus on a case where ICH occurred without the presence of the commonly associated findings such as aneurysms or dissections in the cerebral arteries. This point is critical as it underscores the potential for FMD to cause serious neurologic complications even in the absence of clear angiographic abnormalities. The authors suggest that patients with FMD may still be at risk for cerebrovascular events, including stroke, despite normal findings on conventional angiography.

The case presented in the article illustrates the importance of a high index of suspicion for FMD in patients presenting with unexplained ICH. The authors advocate for further investigation and consideration of FMD as a possible underlying cause, especially in younger patients or those without traditional risk factors for cerebrovascular disease. This perspective is essential for clinicians in order to improve diagnosis and treatment strategies for patients with FMD.

The article "Hepatic and mesenteric fibromuscular dysplasia: an uncommon entity" by (Ciccarese et al., 2022) delves into the complexities of fibromuscular dysplasia

(FMD), particularly its manifestations beyond the more commonly affected renal and carotid arteries. The authors highlight that FMD is characterized as a non-atherosclerotic and non-inflammatory arterial disease, which presents a unique challenge in diagnosis and management due to its often asymptomatic nature.

A significant aspect of FMD discussed in the article is the angiographic presentation, which typically reveals multifocal stenoses that exhibit a 'string-of-beads' appearance in over 80% of cases. This specific imaging characteristic not only aids in the diagnosis of FMD but also underscores the importance of angiographic evaluation in patients presenting with unexplained vascular symptoms. The authors emphasize that while many individuals with FMD may remain clinically silent, a considerable number do experience severe neurologic manifestations, including hypertension, migraines, strokes, transient ischemic attacks, and subarachnoid hemorrhages. This correlation between FMD and neurologic complications is critical, as it necessitates a high index of suspicion among clinicians when faced with patients exhibiting these symptoms.

Furthermore, the article discusses the prevalence of aneurysm and dissection in patients diagnosed with FMD, which raises concerns regarding the potential for catastrophic vascular events. The authors advocate for a comprehensive treatment approach that encompasses both medical management—such as blood pressure control and the use of antiplatelet agents—and interventional therapies, including angioplasty, stenting, and, in some cases, surgical intervention. The recommendation for regular follow-up imaging is particularly noteworthy, as it underscores the need for ongoing monitoring in this patient population to mitigate the risk of serious complications.

The article "Extracranial carotid localized fibromuscular dysplasia: A case report and literature review" by (Ismail et al., 2022) provides a comprehensive examination of fibromuscular dysplasia (FMD), particularly in its manifestation within the extracranial carotid arteries. The authors effectively contextualize FMD as a significant vascular condition characterized by a noninflammatory and nonatherosclerotic arteriopathy, which leads to segmentation and constriction of the

arterial wall. This understanding is critical, as it distinguishes FMD from other vascular diseases that may present with similar symptoms.

The article highlights that the cervicocephalic arteries are the second most common site for FMD, following the renal arteries, with a notable incidence rate ranging from 0.42% to 3.4%. This statistical insight is essential for clinicians, as it underscores the importance of considering FMD in differential diagnoses, particularly in patients presenting with neurological symptoms. The authors note that over 90% of cases of cervicocephalic FMD involve the middle one-third of the carotid arteries, which further emphasizes the need for targeted imaging and evaluation in suspected cases.

A significant aspect of the article is the recognition that many patients with FMD remain asymptomatic, and the condition is often discovered incidentally during imaging for unrelated issues. However, the authors also elucidate the potential neurological manifestations of FMD, including headaches, transient ischemic attacks (TIAs), and strokes. This connection is crucial, as it highlights the importance of early detection and management of FMD to prevent serious neurological outcomes.

The case report presented in the article of a 53-year-old male patient with focal extracranial carotid unilateral FMD and recurrent TIAs serves as a poignant example of the clinical implications of this condition. The authors detail the management strategies employed, emphasizing that treatment primarily focuses on symptomatic relief. For patients who do not respond to medical therapy, surgical options may be considered. This approach aligns with contemporary practices in managing vascular conditions, where a tailored strategy based on individual patient needs is paramount.

The article "Cerebrovascular Fibromuscular Dysplasia – A Practical Review" by (Kesav et al., 2023) provides a comprehensive overview of cerebrovascular fibromuscular dysplasia (C-FMD), emphasizing its clinical significance and the challenges associated with its diagnosis and management. The authors illustrate that

FMD is a rare idiopathic arteriopathy primarily affecting medium-sized arteries, with a notable prevalence in younger females. This demographic insight is crucial, as it underscores the importance of awareness among healthcare professionals regarding the potential for C-FMD in this population.

A pivotal aspect of the article is the identification of the most commonly affected vascular territories, specifically the extracranial carotid and vertebral arteries. This information is critical for clinicians, as it guides the diagnostic imaging and evaluation processes for patients presenting with symptoms indicative of cerebrovascular involvement. The authors detail common symptoms such as headaches and pulsatile tinnitus, which are often overlooked, potentially delaying diagnosis. More severe manifestations, including transient ischemic attacks, ischemic stroke, and hemorrhagic events, highlight the urgent need for increased vigilance in recognizing C-FMD.

The discussion surrounding the pathophysiological mechanisms of C-FMD is particularly noteworthy. The authors explain that cervical artery dissection and intracranial aneurysms are significant complications associated with C-FMD, contributing to its morbidity. This connection is essential for understanding the broader implications of the disease, as it emphasizes the need for early intervention to prevent serious outcomes.

Moreover, the article addresses the historical context of FMD, noting that despite its recognition since 1938, the field has been hindered by a lack of standardized definitions, classifications, and diagnostic criteria. This gap in the literature is a critical barrier to advancing understanding and treatment options for C-FMD. The authors advocate for the establishment of clearer diagnostic frameworks to facilitate better recognition and management of the condition.

The authors also discuss the classification of focal FMD, which is characterized by either concentric or tubular narrowing of the affected vessels. They stress that the diagnosis of FMD cannot be made solely on the presence of isolated aneurysms, dissections, or tortuosity; rather, it requires the identification of at least one focal or

multi-focal stenotic lesion. This nuanced understanding is vital for clinicians to avoid misdiagnosis and to ensure appropriate management strategies are employed.

CONCLUSION

Fibromuscular dysplasia (FMD) is recognized as a significant vascular disorder that predominantly affects medium-sized arteries, with notable implications for neurologic health. The literature reveals that FMD is characterized by non-atherosclerotic and non-inflammatory changes, which can lead to a spectrum of neurologic manifestations, particularly involving the cervicocephalic arteries. The importance of early detection and comprehensive evaluation is emphasized across multiple studies, as timely intervention can mitigate the risk of severe cerebrovascular events.

The foundational work by (Arning & Grzyska, 2004) highlights the critical role of the internal carotid artery (ICA) in FMD, noting that it is often implicated in transient ischemic attacks and cerebral infarctions, alongside nonspecific symptoms such as headaches and vertigo. This establishes a baseline understanding of FMD's neurologic implications, which is further expanded by case studies such as that presented by (Altun et al., 2013), where central retinal artery occlusion was associated with FMD, illustrating the heterogeneous nature of the disease and its varied clinical presentations.

The investigation into cervical artery dissection by (Arnaud et al., 2021) adds to the understanding of demographic risk factors, noting that male sex and a history of migraine are significant considerations. This study underscores the necessity for clinicians to maintain a high index of suspicion for vascular involvement in patients with FMD, particularly those presenting with neurological symptoms.

Diagnostic challenges related to FMD are highlighted by (Yiek, 2021), who emphasizes the reliance on imaging techniques for accurate identification. The article stresses that while renal artery involvement is prevalent, cervicocephalic manifestations can lead to serious complications, necessitating vigilant diagnostic practices. This is further supported by (Fujiwara et al., 2022), who presents a case

of intracerebral hemorrhage linked to FMD, despite normal angiographic findings, thereby challenging conventional diagnostic expectations.

The systemic nature of FMD is explored by (Ciccarese et al., 2022), who discuss hepatic and mesenteric manifestations, reinforcing that FMD can be asymptomatic yet lead to significant complications, including hypertension and stroke. The need for a multifaceted approach to management is highlighted, particularly in recognizing the potential for neurologic complications.

The article by (Ismail et al., 2022) focuses on extracranial carotid localized FMD, reiterating the frequent involvement of the cervicocephalic arteries and the clinical symptoms that may arise. This reinforces the importance of individualized management strategies for symptomatic patients to improve outcomes.

Finally, the comprehensive review by (Kesav et al., 2023) summarizes the spectrum of symptoms associated with cerebrovascular FMD, calling attention to the need for standardized definitions and diagnostic criteria. This is crucial for enhancing understanding and management of FMD, particularly in its neurologic manifestations.

In conclusion, the literature collectively underscores the complexity of fibromuscular dysplasia and its neurologic manifestations. The critical importance of early detection, comprehensive evaluation, and tailored management strategies is evident across studies. Clinicians are urged to maintain a high level of suspicion for FMD in patients presenting with unexplained neurologic symptoms, as timely intervention can significantly impact patient outcomes.

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