Moyamoya Syndrome may Result from Psoriasis

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Abstract

Objective: To analyze the relationship between psoriasis and Moyamoya syndrome, to explore the potential mechanism.

Methods: A case series retrospective study analyzed 4 patients confirmed as Moyamoya syndrome by imaging in our hospital from 2017 through 2019; all of them had long-term of psoriasis prior to the Moyamoya syndrome -related stroke onset. The age of psoriasis occurrence and duration, the time and type of Moyamoya syndrome -related stroke onset, blood tests, imaging features, treatment and clinical outcomes were analyzed.

Result: The average duration from psoriasis confirmation till the first-time of Moyamoya syndrome -mediated stroke onset was 17 ± 3.56 years. The average age of the initial stroke onset was 58.25 ± 11.52 years, included 3 cases of hemorrhagic and 1case of ischemic strokes. All the Moyamoya syndrome -related stenosis involved bilateral cerebral arteries, Suzuki grade III for 1 case, grade IV for 2 cases, and grade V for 1 case. Abnormal elevated plasma IL-6 were seen in 4 cases. 2 cases had abnormal elevated immunoglobulin E, and 2 cases had thrombocytosis. All the 4 cases underwent medication (antiplatelet agents and psoriasis control agents) instead of surgery. With an average follow-up time of 19 ± 12.35 months, 3 times of transient ischemic attack occurred in 3 patients, respectively and no hemorrhagic event occurred.

Conclusion: Psoriasis may be a potential risk factor of Moyamoya syndrome formation. Moyamoya syndrome should be screened when the psoriasis patients presented with neurological symptoms.

Introduction

Moyamoya disease (MMD) is a non-atherosclerotic cerebrovascular structural abnormality, which was firstly described by Japanese scholars Takeuchi and Shimizu in 1969, and characterized by a progressive stenosis or occlusion of the intracranial internal carotid arteries (ICAs) and their proximal branches, with subsequent abnormally formed collaterals without clear etiology, causing transient ischemic attack (TIA), infarction or hemorrhage in the brain. Moyamoya syndrome (MMS) refers to having the similar intracranial arterial presentation of MMD but with clear etiology, such as: atherosclerosis, autoimmune disease, meningitis, and so on. However, no report about the psoriasis-related MMS has been found up to now. Especially, no MMS-mediated cerebral hemorrhage in adult psoriasis was reported.

Psoriasis is a common chronic immune skin lesion with a global incidence of about 2–3% per year, often manifested as erythema and scales on the scalp and extremities of the limbs. Psoriasis will have many complications including autoimmune diseases, cardiovascular and cerebrovascular diseases, and diabetes. Previous study showed that psoriasis was an independent risk factor of stroke, the incidence of stroke onset in patients with mild or severe psoriasis were 1/4115 per year and 1/530 per year, respectively.

As we all known that MMS is a special subtype of intracranial arterial stenosis, herein, we analyzed the clinical characteristics and prognosis of MMS-related ischemic and hemorrhagic stroke in patients with psoriasis retrospectively, and also, analyzed the probable mechanisms of psoriasis-mediated MMS, so as to make a reference for proper diagnosis and early etiology treatment.

Materials And Methods

A total of 4 patients with long-term of continuous psoriasis were confirmed as MMS-induced ischemic and hemorrhagic stroke by imaging in our hospital from January 2017 through May 2019 were enrolled into this retrospective study. Psoriasis was diagnosed by the dermatologists according to their clinical symptoms and skin lesions; MMS confirmed by CT angiography (CTA), magnetic resonance angiography (MRA) or digitally developed angiography (DSA); MMS-induced intracranial hemorrhage or cerebral infarction were confirmed by computerized tomography (CT) or Magnetic Resonance Imaging (MRI).

The ages of initial psoriasis and MMS confirmation, the time and types of MMS-related stroke onset, laboratory examination, imaging results, treatment and outcomes were analyzed. All the 4 patients were followed up by outpatient clinic and telephone, the contents mainly focused on the recurrence of stroke or transient ischemic attack, epilepsy and the status of vascular revascularization.

This study was performed in accordance with the Ethics Committee of Xuanwu Hospital, Capital Medical University. All participants signed the consent form prior to entering into the study.

Results

2.1 Clinical characteristics

The 4 patients included 3 males and 1 female, aged from 42 to 71 years. All of them had long-term (the average time was 17 ± 3.56 years) of poorly controlled psoriasis prior to their MMS confirmation. Other concomitant disease included eczema for 1 case, well-controlled hypertension for 3 cases and mild hyperlipidemia for 1 case. All the 4 cases had not the family history of psoriasis. The subtype of MMS-induced stroke in this psoriasis case-series included 3 patients with hemorrhagic stroke and 1case of ischemic stroke. The stenosis-involved positions in all the 4 patients were bilateral internal carotid artery, including the Suzuki grade III for 1 case, grade IV for 2 cases and grade V for 1 case. All of the 4 cases underwent routine medication for both ischemic or hemorrhagic stroke control instead of surgery. Details were displayed in Table 1.
Table 1
Demographic characteristics

| Items                  | Gender | ages of psoriasis (age) | ages of MMS-related stroke (age) | duration of psoriasis (years) | duration of hypertension (years) | blood pressure at admission (mmHg) | suzuki grade | modified Rankin Scale |
|------------------------|--------|-------------------------|----------------------------------|------------------------------|---------------------------------|----------------------------------|--------------|----------------------|
| Case1                  | Male   | 30                      | 42                               | 12                           | -                               | 120/70                           | 0            | 1                    |
| Case2                  | Male   | 52                      | 71                               | 19                           | 3                               | 122/68                           | 0            | 0                    |
| Case3                  | Female | 30                      | 47                               | 17                           | 2                               | 140/88                           | 0            | 2                    |
| Case4                  | Male   | 35                      | 65                               | 30                           | 3                               | 190/100 ↑                        | 0            | 1                    |

Moreover, according to the inpatients database in our hospital, only the 4 cases of MMS out of the 202 cases of MMD and MMS in the past 4 years were with psoriasis. The incidence of psoriasis in this cohort was 1.9%, which was much higher than that of psoriasis in Chinese population (0.47%)\(^5\).

2.2 Blood results

All the 4 cases had abnormal elevated plasma IL-6. 2 cases had abnormal elevated immunoglobulin E, and 2 cases had thrombocytosis. The percentage of mononuclear cells was 9.8–10%, which was higher than the normal cutoff range (3–8%). The specific examination results are shown in Table 2 and Fig. 1.

Table 2
Data of blood tests

| Items                  | White blood cell | Neutrophils (4–10) X 10\(^9\)/L | Monocytes (0.1–0.6) X 10\(^9\)/L | Platelet (100–300) X 10\(^9\)/L | Interleukin-4 (0–3) pg/ml | Interleukin-6 (0–5.3) pg/ml | Immunoglobulin E (0–40) mg/L | Treg cells (CD4+) (2.86–7.74) % | Cholesterol (2.8–5.2) mmol/L | LDL cholesterol (1.6–3.4) mmol/L |
|------------------------|------------------|---------------------------------|----------------------------------|------------------------------|--------------------------|-----------------------------|-----------------------------|-------------------------------|-------------------------------|-------------------------------|
| Case1                  | 9.38             | 5.57                            | 0.63 ↑                          | 203                          | 1.09                     | 8.27 ↑                      | 90.8 ↑                      | -                             | 5.76 ↑                        | 4.15 ↑                        |
| Case2                  | 7.67             | 4.95                            | 0.51                            | 244                          | 1.22                     | 7.63 ↑                      | 68.9 ↑                      | -                             | 4.04                         | 3.18                         |
| Case3                  | 6.92             | 4.32                            | 0.5                             | 358                          | 3.43                     | 8.49 ↑                      | 17.8                        | 11.4 ↑                        | 4.88                         | 3.36                         |
| Case4                  | 9.4              | 7.5                             | 0.74 ↑                          | 338                          | 0.35                     | 8.86 ↑                      | 16.9                        | -                             | 4.84                         | 2.44                         |

Note: The arrows indicated that the results were over the normal cutoff value.

2.3 Imaging features

All the 4 cases with MMS-related cerebral arterial stenosis involved bilateral cerebral middle arteries in MRA or CTA maps with Suzuki grade III for 1 case, grade IV for 2 cases, and grade V for 1 case. Brain lesions included ischemic and hemorrhagic damages located at the area of the stenosis arterial territories on MRI/CT (Fig. 1, black arrows).

2.4 Treatment and outcomes

All the 4 patients underwent routine medication treatment of ischemic and hemorrhagic stroke control as well as some agents of psoriasis control. During follow-up time, 3 patients with severe psoriasis had recurrent transient cerebral ischemia events and all the symptoms and the mRS scores were improved by aspirin treatment. The average follow-up time was 19 ± 12.35 months. 4 patients were alive during the study.

Discussions

According to the inpatients database in our hospital, the incidence of psoriasis in this cohort was 1.9%, which was much higher than that of psoriasis in Chinese population (0.47%)\(^5\). Whereby, we suspect that there may be some relationship between psoriasis and MMS.

Psoriasis and atherosclerosis have similar histological and molecular in inflammation and immunity\(^6\). It is clear that psoriasis is not only resulting in skin lesions but also promoting a systemic immune process, for example, helper T1 lymphocytes and helper T17 lymphocytes play an important role in the development of psoriasis and atherosclerosis\(^6\).

In this study, all the 4 cases had the abnormal elevated plasma IL-6. 2 cases had abnormal elevated immunoglobulin E, and 2 cases had thrombocytosis (Table 2). Therefore, we speculate that the mechanism of psoriasis-mediated MMS may be that psoriasis activated chronic immune inflammatory...
process, which damaged cerebral arterial wall, resulting in arterial stenosis and further triggering stroke onset³.

Kazumata reported an 8-year-old female with psoriasis and MMS without MMS–related stroke onset⁷. The first case of MMS with psoriasis reported in China was an adult male in 2014⁸, the symptoms included dizziness with typical cerebral ischemia such as numbness and weakness in limbs. A meta-analysis showed that the risk of stroke and myocardial infarction increased 20% in patients with psoriasis⁹. Gelfand's study showed that the risk of stroke increased 44% in patients with severe psoriasis⁴. However, the two reports did not classify the stroke subtype in details.

Previous study reported that the abnormally high expression of IgG and S100A4 in intracranial vessel wall in patients with MMD revealed that MMD-related endometrium damage released IgG and recruited smooth muscle cells through the intima gap, resulting in the intimal thickening, the mechanism may be the same as that in MMS.

Studies also found that endothelial progenitor cells were mainly acted in the process of angiogenesis, while monocyte chemoattractant protein-1, tumor necrosis factor (TNF) and vascular endothelial growth factor were involved in the activation of endothelial progenitor cells¹¹–¹³. Keratinocytes, dendritic cells, and T lymphocytes mediate immune responses in psoriasis, in which cytokines IL-6, IL-17, IL-23, and TNF are directly involved¹⁴–¹⁶.

Although 3 out of the 4 cases have mild hypertension, which may also result in stroke, however, all of their hypertensions were well controlled. Whereby, the predominant risk factor for their arterial stenosis formation in this case series we considered was psoriasis-related MMS.

To our knowledge, this is the first report about psoriasis-related MMS complicated cerebral hemorrhage and infarction, and the probable mechanism of psoriasis-related MMS may involve immune damage. However, all the preliminary findings in this study still need further research in a cohort with large case number in Chinese.

**Limitations**

This is just a case series study, further well designed study with larger number of cases on the pathogenesis of psoriasis-related MMS in our team is underway, which may better explore the relationship and progress of psoriasis and MMS, which is of great significance for the MMS-related stroke management.

**Conclusions**

Psoriasis may be a potential risk factor of MMS formation. MMS should be screened when the psoriasis patients presented with neurological symptoms.

**Abbreviations**

MMD: moyamoya disease, MMS: moyamoya syndrome, MRI: magnetic resonance imaging, MRA: magnetic resonance angiography, CTA: computerized tomography angiography, DSA: digitally developed angiography, TNF: tumor necrosis factor, IL-6: Interleukin -6.

**Declarations**

**Ethics approval and consent to participate**

This study was approved by the ethic committee of Xuanwu Hospital, Capital Medical University and the affiliated Hospital of Jiujiang University, respectively. Patients who were prepared to participate in this study were asked to sign the written consent form by themselves or their legally authorized delegates.

**Consent for publication**

Written informed consent for publication was obtained from all participants.

**Availability of data and materials**

All data generated or analysed during this study are included in this published article.

**Competing interests**

The authors declare there is no conflicts of interest regarding the publication of this paper.

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Authors’ contributions

Dr. Zhiying Chen: Manuscript drafting and revision, data collection and interpretation
Dr. Xiaqing Yu, Xiaoping Yin, Linghua Liu, Jiayue Ding, and Kexin Jin: data collection and interpretation
Dr. Yuchuan Ding and Xunming Ji: manuscript revision
Dr. Ran Meng: Study concept and design, and manuscript drafting and revision

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