

**Progressive perianeurysmal edema preceding the rupture of
a small basilar artery aneurysm**

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A short title: Progressive perianeurysmal edema preceding aneurysmal rupture

Abstract

We herein report the first case of progressive perianeurysmal edema preceding the rupture of a small saccular aneurysm, without any intervention or intraluminal thrombosis.

A 71-year-old woman was incidentally noted to have a cerebral aneurysm (5 mm in diameter) at the lower basilar artery. Twelve months later, magnetic resonance (MR) imaging showed a T2-elongated area around a dome of the aneurysm buried in the brain stem, suggesting perianeurysmal edema formation. Interestingly, the edema progressed with the formation of a bleb, in addition to an increase in size of the aneurysm over the following 3-year period. The aneurysm eventually ruptured as a brain stem hemorrhage without any subarachnoid clots three days after the final check-up with MR imaging, by which a significant increase of edema formation with an increase in size of the aneurysm and a marked expansion of the bleb was observed.

These findings raise the possibility that bleb formation and an enlargement of a small cerebral aneurysm might also be associated with perianeurysmal edema and a subsequent aneurysmal rupture. In addition to the pulsatile flow and/or compression from the expanded aneurysm, local inflammation in the aneurysm wall may play an important role in such edema formation.

Keywords: bleb formation; cerebral aneurysm; magnetic resonance imaging; inflammation; perianeurysmal edema; rupture.

1. Introduction

Brain edema has been shown to develop around partially-thrombosed, relatively-large or giant aneurysms [1, 2]. Although the precise mechanism of such edema formation has not yet been clarified, previous reports have proposed several candidates for the etiological processes including a pulsatile blood flow [3], bleeding [2] or local inflammation [4] within an aneurysm wall. However, similar perifocal edema surrounding a small unruptured saccular aneurysm has only rarely been reported [5].

We herein present a unique case of progressive perianeurysmal edema preceding the rupture of a small unruptured saccular aneurysm, and discuss the mechanisms and clinical implications of this rare phenomenon.

2. Case Report

A 71-year-old woman was incidentally found to have a cerebral aneurysm arising from the lower basilar artery (*Fig. 1A*). The maximum size of the aneurysm was 5 mm in diameter. She rejected surgical treatment and was followed every six months by magnetic resonance (MR) imaging using a 1.0-tesla unit (Magnex Polaris; Philips Medical Systems, Netherlands). Twelve months later, a fluid-attenuated inversion recovery (FLAIR) image showed a T2-elongated area surrounding a dome of the

aneurysm, possibly thought to be perianeurysmal edema (*Fig. 2B*). The degree of edema gradually progressed with an increase in size of the aneurysm and the formation of a bleb (*Fig. 1, B and C, Fig. 2, B and C*). Three years after the initial diagnosis, the edema further increased with an increase in size of the aneurysm and a marked expansion of the bleb (*Fig. 1D, Fig. 2D*). However, she did not have any symptoms or neurological deficits, and she still refused to undergo either surgical treatment or cerebral angiography. Three days after this MR imaging, she suddenly developed left hemiparesis and a loss of consciousness. MR images and computed tomography (CT) scan demonstrated a brain stem hemorrhage without any subarachnoid clots (*Fig. 3, A, B and C*), probably due to the aneurysmal rupture.

The patient underwent endovascular coil embolization of the ruptured aneurysm (*Fig. 3, D and E*), and the postoperative course was uneventful. The left hemiparesis gradually improved, and she was discharged one month after the intervention.

3. Discussion

Despite recent advancements in the diagnosis and treatment of intracranial aneurysms, the mechanisms for formation, development, and subsequent rupture of aneurysms are still not well understood [6]. Saccular aneurysms tend to grow over years

[7], while serial angiographic studies have revealed that aneurysms can rapidly enlarge [8]. The aneurysm wall is subjected to increasing hemodynamic stress and often undergoes morphological changes before a rupture [9]. Vascular remodeling triggered by abnormal hemodynamic stress on the blood vessels could therefore play a role in developmental processes of these aneurysms [6]. Pathological examinations of ruptured aneurysms [9, 10] also suggest a possible role of inflammation in the remodeling of the walls, even in relatively-small aneurysms. However, we have no evidence to support this mechanism, even when using current imaging techniques in vivo.

Brain edema has been reported to develop around partially thrombosed aneurysms as well as large or giant aneurysms [1, 2, 11]. A pulsatile blood flow [3], bleeding within an aneurysm wall (from vasa vasorum) [2], an inflammatory process [4], and the expression of angiogenesis growth factors in the aneurysm wall [12] have also been proposed as candidates that may play a role in the development of such edema formation. We recently experienced unique cases of progressive vasogenic edema surrounding the large cerebral aneurysms extending widely into the brain parenchyma after incomplete coil embolizations [13]. Most of these reported aneurysms are large, giant, and/or partially-thrombosed. The serial MR images of our embolized cases

indicated that the edema might be associated with a recanalization or a regrowth of the aneurysm, thus suggesting that an aneurysm pulsing and/or an inflammation play important roles in perianeurysmal edema formation [13].

In the present case with a small aneurysm, the perianeurysmal edema also gradually progressed with the growth and bleb formation of the aneurysm for three years. This may suggest that even in small aneurysms, mechanisms similar to those with large, giant and/or partially-thrombosed aneurysms are involved in edema formation. Especially, local inflammation in the aneurysm wall may play an important role, because it is unlikely that a mass effect was the only mechanism as discussed in a recent report showing that the perifocal brain edema rapidly developed around a small unruptured aneurysm within an arteriovenous malformation [5]. The aneurysm in that report appeared to be too small to induce a mass effect causing obvious brain edema. As a result, the authors proposed another possible explanation, namely that vascular endothelial growth factor, known as a vascular permeability factor and an inflammatory mediator, may also play an important role in the formation of the aneurysm and perifocal edema [5]. These observations suggest that perianeurysmal edema indirectly reflect a change of milieu in and/or around the wall of a small aneurysm by chance. Our experience may lend support to the hypothesis that inflammatory mechanism(s) play a

role in both aneurysmal growth and rupture.

A remarkable increase of edema associated with the aneurysmal growth and bleb expansion was observed on serial FLAIR imaging just three days before the rupture, thus suggesting a rapid increase of a pulsatile flow, compression from the expanded aneurysm, and/or inflammatory process preceding the rupture. It seemed difficult to consider a minor leak or ischemic stroke for the changes in the MR imaging findings because the patient did not have any symptoms or neurological deficits despite the fact that the lesion presented in an eloquent area, although the possibility of such mechanisms cannot be totally ruled out. To the best of our knowledge, this is the first report to describe an observation of progressive perianeurysmal edema in vivo preceding the rupture of a small saccular aneurysm, without any interventions or intraluminal thrombosis. Since a part of the aneurysm had been buried in the brain stem, we might have indirectly observed the mechanical or biochemical processes of the wall leading to the aneurysmal rupture.

Ruptured saccular aneurysms commonly present as subarachnoid hemorrhage (SAH) but they also cause an intraparenchymal hemorrhage, an intraventricular hemorrhage, a subdural hemorrhage [14], and rarely present with an intraparenchymal hemorrhage and/or an intraventricular hemorrhage without a SAH [15]. In our case, the

aneurysm presented with an intraparenchymal hemorrhage without SAH because the bleb was buried in the brain.

4. Conclusion

We presented a case of progressive perianeurysmal edema preceding the rupture of a small basilar artery aneurysm which had been buried in the brain stem. These findings suggest 1) even a small unruptured aneurysm could cause perifocal brain edema as in previously reported cases with large, giant and/or thrombosed aneurysms; and 2) in addition to a pulsatile flow and/or compression from the expanded aneurysm, a presence of local inflammation might thus play an important role in a growth, bleb formation, and a rupture of small aneurysms. Our experience may shed some lights on the mechanism(s), other than a mass effect, regarding perianeurysmal edema formation which may result in an aneurysmal rupture.

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Figure Legends

Figure 1. MR angiography showing an aneurysm arising from the lower basilar artery

(A). Twelve months later, size of the aneurysm increased, and a bleb (arrows) appeared

(B). Thirty months later, size of the aneurysm further increased and the bleb expanded

(C). Thirty-six months after the initial diagnosis, MR angiography demonstrated the aneurysm to have grown larger than before and the bleb had also markedly expanded

(D).

Figure 2. Initial MR FLAIR image showing no brain stem lesions (A). Twelve months

later, FLAIR image revealed T2-elongated area surrounding the aneurysm dome (arrow)

(B). Thirty months later, the T2-elongated area (arrows) gradually progressed (C).

Thirty-six months after the initial diagnosis, the T2-elongated area progressed significantly (D).

Figure 3. MR FLAIR (A and B) and plain CT (C) images showing a brain stem

hemorrhage without SAH. A hematoma is in close contact with a dome of the aneurysm

(A), thus suggesting an aneurysmal rupture. Anteroposterior view of right vertebral

artery angiogram (D) demonstrated an aneurysm arising from the lower basilar artery,

with a marked expansion of the bleb (arrow). The aneurysm was completely embolized

(E).

Financial Disclosure

We have no financial support to disclose.

Acknowledgments

We wish to thank Nobutaka Horie and Junichi Kawakubo for their critical review of the manuscript and outstanding professional guidance.

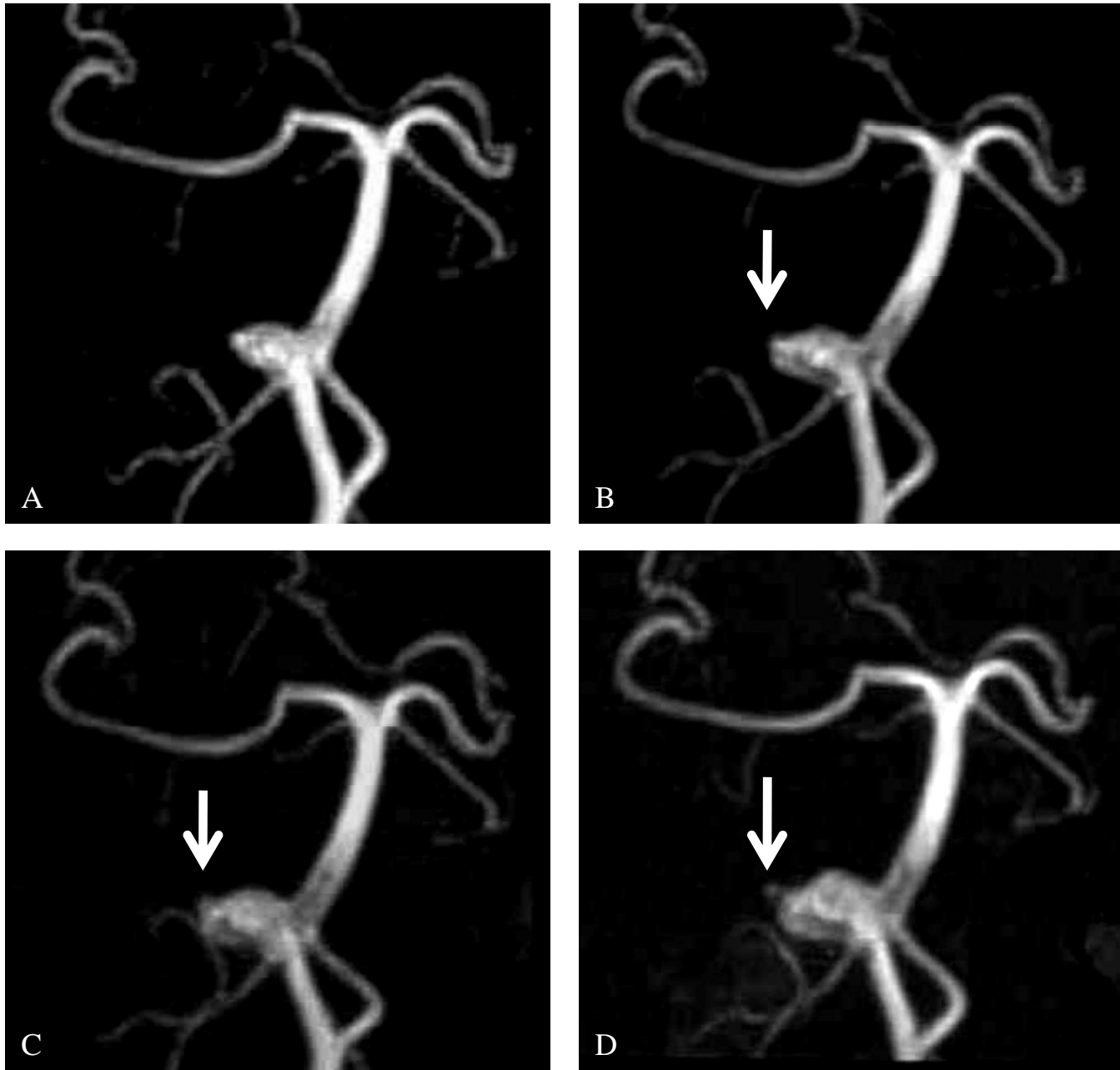


Fig 1.

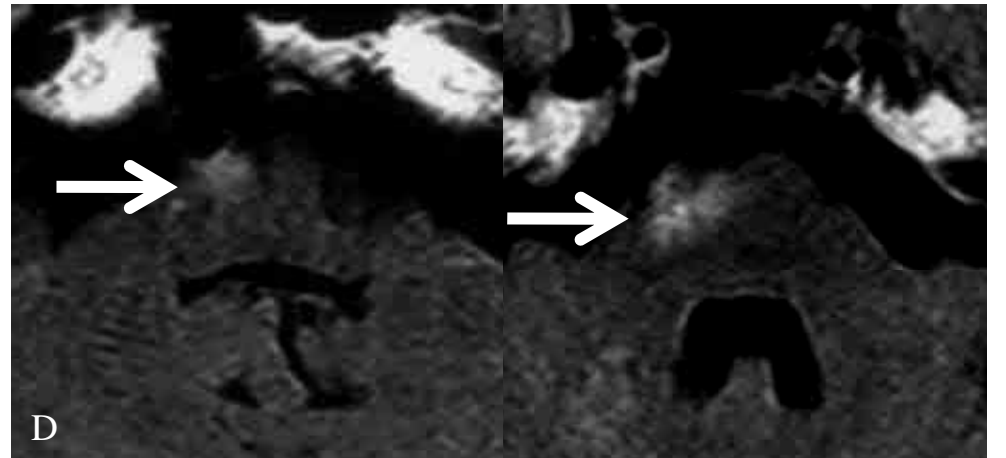
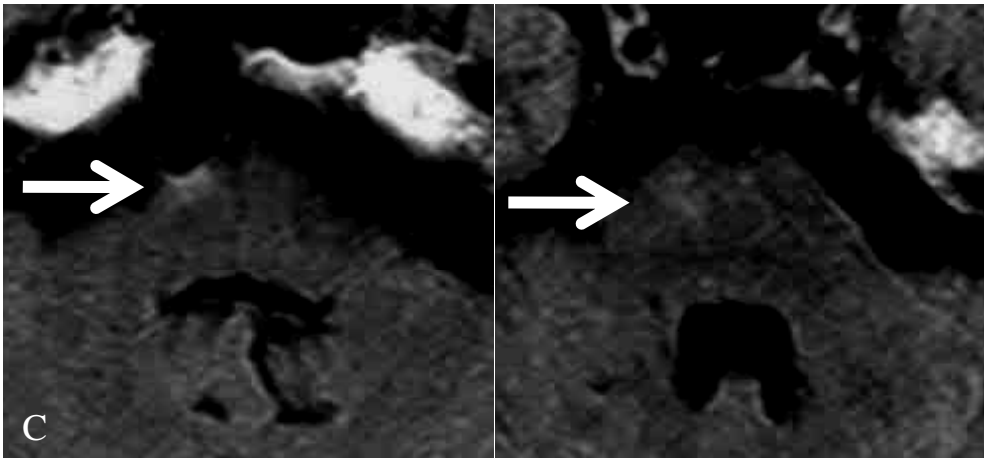
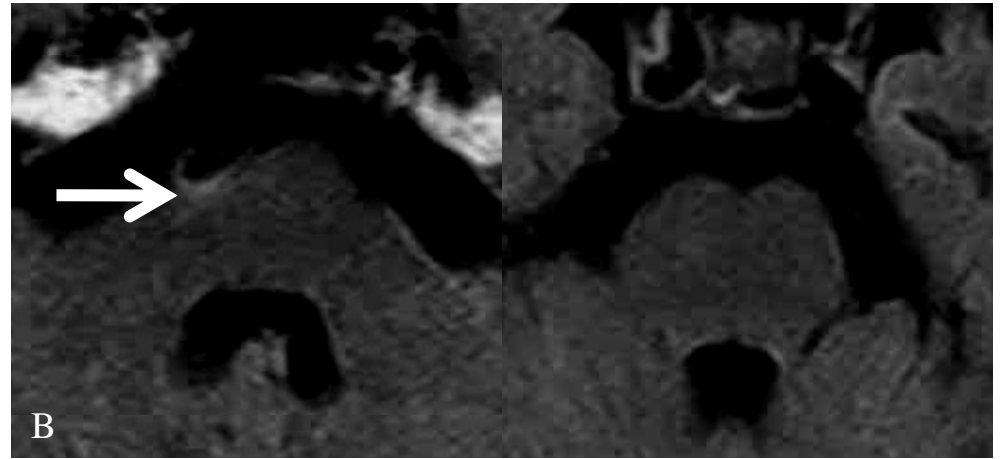
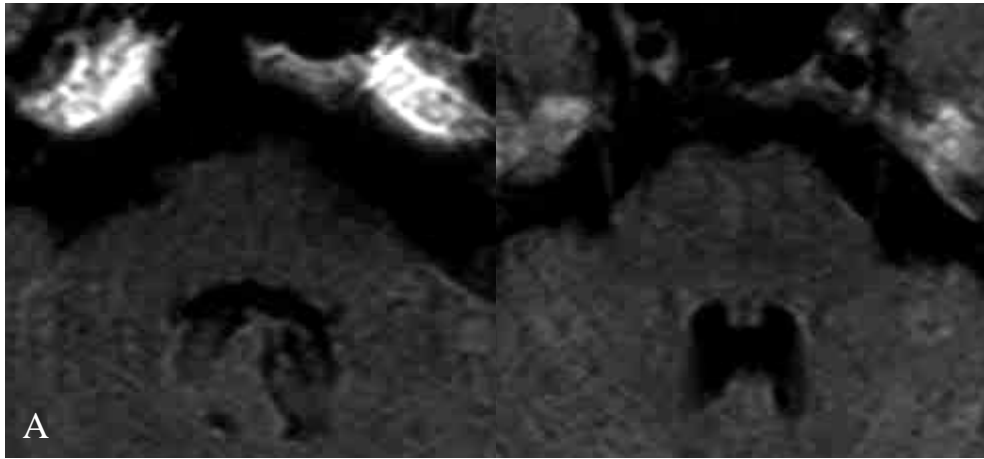


Fig 2.

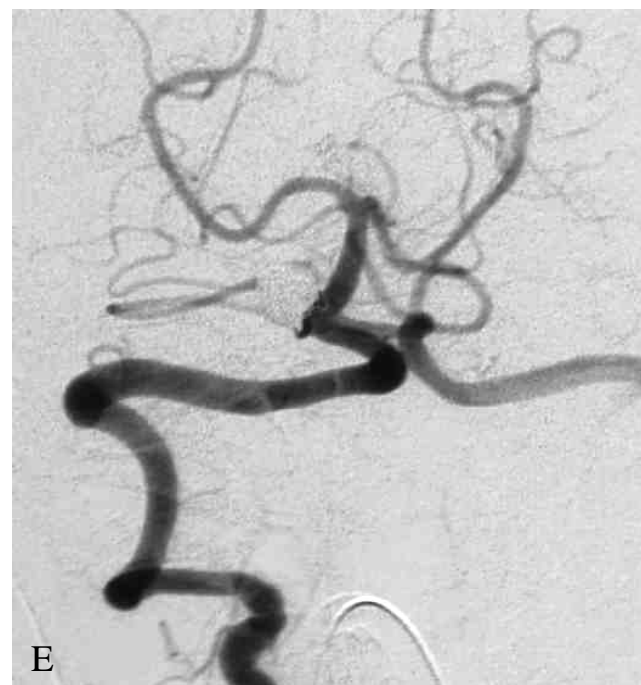
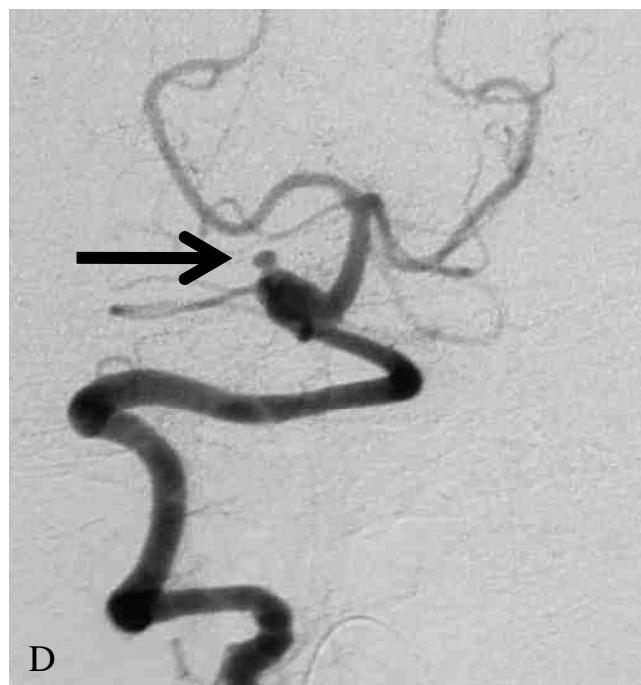
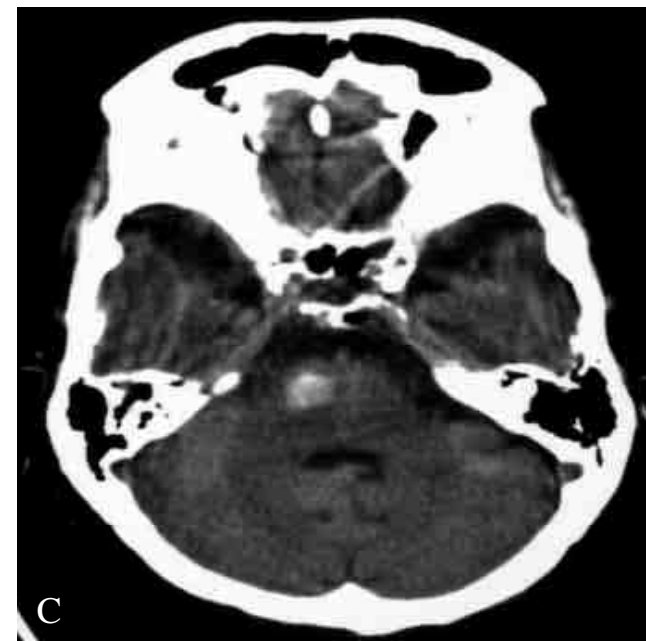
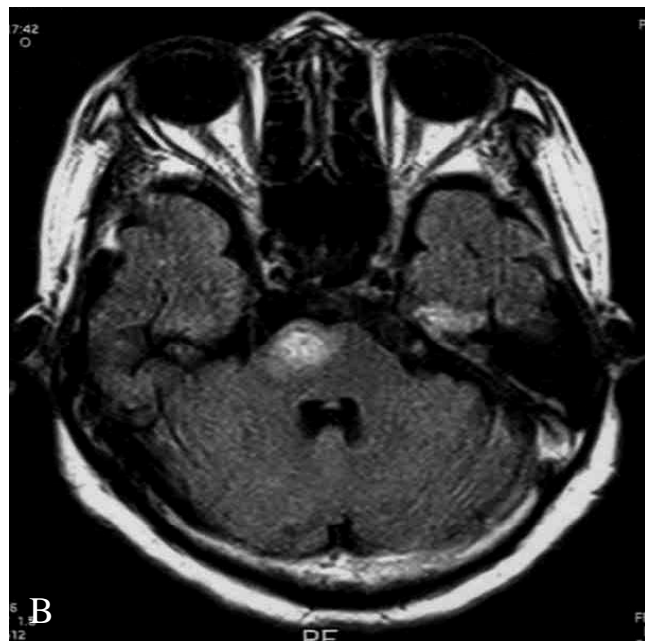
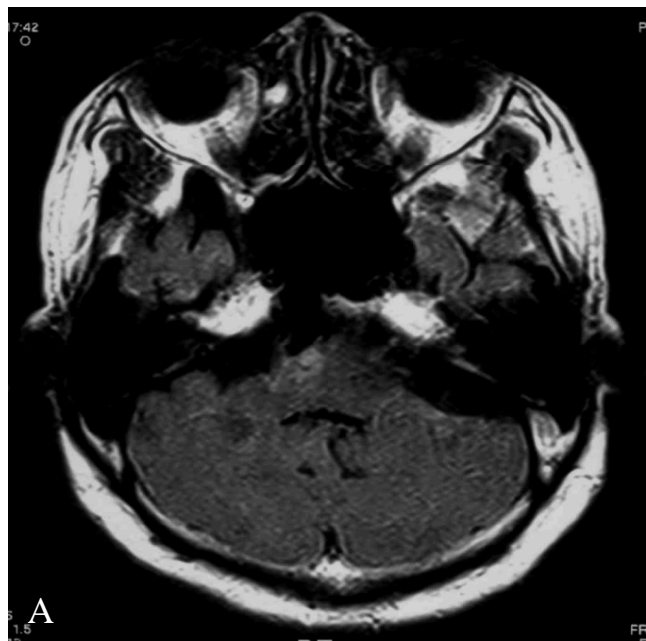


Fig 3.