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Multiple Infectious Intracranial Aneurysms in a Child with Acute Lymphoblastic Leukaemia - A Fatal Complication in a Highly Curable Disease

Yamini Krishnan[1*], S. Gazel[1], Shailaj Kurup[2] and V. P. Muralikrishnan[3]

[1]Department of Paediatric Oncology, MVR Cancer Centre and Research Institute, Calicut Kerala-673601, India.
[2]Department of Radiology, MVR Cancer Centre and Research Institute, Calicut Kerala,-673601, India.
[3]Department of Neurosurgery, MVR Cancer Centre and Research Institute, Calicut Kerala-673601 India.

Authors' contributions

This work was carried out in collaboration among all authors. Author YK wrote the case report and did the literature search of the manuscript. Author SG made the first draft of the manuscript. Author SK contributed to the writing of the manuscript and figures. Author VPM contributed to the neurosurgical aspects of the manuscript. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Multiple infectious intracranial aneurysms are rare in the paediatric population. This case report is of a child with acute lymphoblastic leukaemia who developed this fatal complication in induction therapy. The child succumbed despite aggressive medical management and surgical intervention. A high index of suspicion is required in the early diagnosis and treatment when a child presents with febrile neutropenia and intracranial haemorrhage.

Keywords: Lymphoblastic leukaemia; intracranial aneurysms; childhood malignancy.

**Corresponding author: E-mail: dryamini@mvrccri.co;*

1. INTRODUCTION

Intracranial aneurysms can be classified into infectious and non-infectious aneurysms. Infectious Intracranial Aneurysms (IIA) or mycotic aneurysms are focal dilatations of the cerebral vessels due to infection or inflammation. They constitute only 0.7-6.5% of all aneurysms occurring intracranially. Among paediatric intracranial aneurysms, IIA is around 15%. Most IIA occurs in the anterior circulation and the majority are solitary [1]. There is very little data on multiple IIA in children but a large adult series on IIA showed the incidence to be around 16% [2]. Most children present with either intraparenchymal or subarachnoid haemorrhage [1]. Though immunosuppression is the major factor involved in the development of IIA, the commonest aetiology is usually infective endocarditis.

We report a child with acute lymphoblastic leukaemia on induction chemotherapy with intraventricular haemorrhage as a presenting feature of multiple intracranial mycotic aneurysms.

2. PRESENTATION OF CASE

4-year-old girl presented to us with complaints of bilateral lower limb pain and pallor. On examination she was found to have hepatosplenomegaly and blood investigations done showed Hb-7g%, Total leucocyte count-3500cells/mm3 and platelet counts-35,000cells/m3. Bone marrow studies showed 93% blasts and flow cytometry was suggestive of CALLA positive, B-cell acute lymphoblastic leukaemia. The cytogenetic study did not reveal any specific abnormalities and CSF studies were normal.

She was started on ALL BFM IC 2009 protocol and Induction IA protocol (4 drug combination regimen with steroids, vincristine, daunorubicin, L-asparaginase) was completed without any major delay.

She had 3 episodes of febrile neutropenia during the 4 weeks of the protocol. Blood culture and sensitivity for the first febrile episode in the 2nd week showed Staphylococcus aureus for which she received gram-positive coverage and all repeat cultures during the rest of the febrile episodes were negative. After completion of the intensive phase, bone marrow showed remission and minimal residual disease was negative.
Immediately after she was started on Induction IB protocol, she developed high spiking fever, headache and abnormal posturing of the neck. CSF studies were negative and culture and sensitivity did not reveal any organism. MRI brain with contrast showed multiple tiny nodular enhancing lesions in subarachnoid space in contiguity with peripheral branches of bilateral middle and anterior cerebral arteries, distributed in both cerebral hemispheres which were consistent with aneurysms. .There were no infectious foci either in the orbits or sinuses (Fig. 1). In view of multiple lesions, CT chest and abdomen were done and it did not show any focus for septic emboli. Echocardiography was normal with no evidence of infective endocarditis. Blood cultures also grew no organism.

She was started on gram-positive and negative coverage with meropenem and vancomycin; along with antifungal coverage with voriconazole. On day 4 of admission, she developed hypertension, bradycardia and altered sensorium. CT brain was suggestive of massive intraventricular bleed with acute hydrocephalus (Fig. 2). An Ommaya reservoir was placed for CSF drainage and repeated CSF drainage was done and she had improvement in sensorium. But within a few days, she had deterioration of the sensorium and repeat CT brain showed massive fresh bleeds with hydrocephalus. CSF fluid culture at that time revealed Pseudomonas aeruginosa sensitive to meropenem. 3D CT angiogram showed a saccular aneurysm at the origin of the basilar artery (Fig. 3) and was increasing in size. Cerebral Digital Subtraction Angiogram (DSA) reconfirmed the aneurysm in the precoiling imaging (Fig. 4) and coiling of the same was done (Fig. 5). Post-procedure she had desaturation and was ventilated. The child also had features of raised intracranial tension and seizures. Given the prolonged delay in initiation of further chemotherapy, repeat bone marrow studies for assessment of disease status was done and the results showed leukaemic relapse.

One month after the initial detection of the mycotic aneurysms, the child became comatose and could not be revived.

3. DISCUSSION

Infectious aneurysms were described as mycotic aneurysms way back in the 1980s by Osler due to their resemblance to a mushroom [3]. The term mycotic aneurysm is a misnomer as the commonest causative organism is usually a bacterium rather than a fungus. Localised irreversible dilation of the blood vessel wall occurs due to invasive infective arteritis. In the

present-day clinical practice, the incidence of infective aneurysms has come down due to the prompt initiation of antibiotics.

Mycotic aneurysms are usually seen in major arteries, usually at branch points. The most common involved vessel is the femoral artery followed by the abdominal aorta. The other common site is the thoracoabdominal aorta and thoracic aorta [4]. Vessels of the peripheral limb and intracranial region are uncommon sites for aneurysm: rarest being the visceral vessels. Usually, these are single but fatal multiple aneurysms have been described in the literature [5,6]. Our child had multiple mycotic aneurysms in the cerebral vessels; largest in the posterior circulation - basilar artery; both of which are rare. In the case series by Kannoth et al, the commonest site for IIA was the carotid territory [2] which has been reiterated by Allen et al in whose series 78% of all IIAs were seen in the middle cerebral artery [7]. Basilar artery aneurysm was seen in 3 patients out of a series of 25 patients in the Kannoth et al study; all being adults. All the paediatric patients in their analysis had anterior circulation involvement [2]. The incidence of multiple vessel involvement has varied from series to series [8] but multiple mycotic aneurysms in children are limited to case reports [9,10].

Karsner in 1947 had described in detail the causation of a mycotic aneurysm. The most common aetiology is usually a septic emboli similar to infective endocarditis which was described by him as an intravascular variety. The second type is acquired by direct extension from an infective focus like sinusitis, osteomyelitis or post-operative infection. The least common type described is that which has no source detected and needs to be confirmed radiologically or pathologically [11]. The commonest contributing factor for the development of IIA is immunosuppression like malignancy, HIV, cirrhosis or post-transplant. Though in most case series on IIA, the majority of patients were post-infective endocarditis, rapidly growing aneurysms were seen in highly immunocompromised patients especially in those with HIV [2,7]. Meningitis and orbital cellulitis are other etiological factors in non-HIV patients. There are case reports of solitary aneurysms in intracranial and extracranial locations in children with acute leukaemia undergoing chemotherapy [12,13,14]. The present report of multiple IIAs in a child with acute lymphoblastic leukaemia is rare.

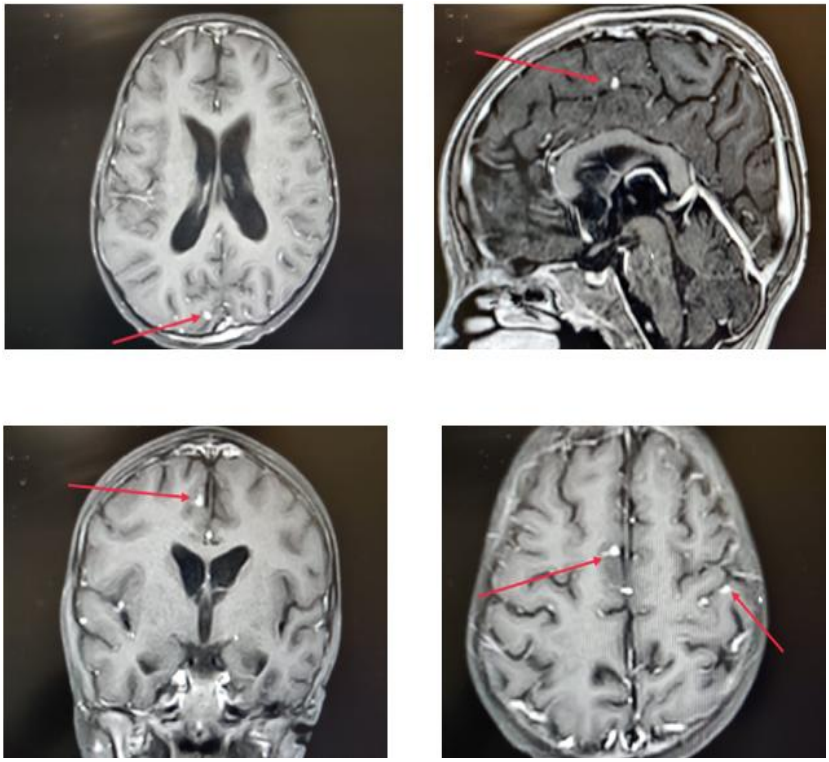

Fig. 1. MRI brain showing multiple mycotic aneurysms

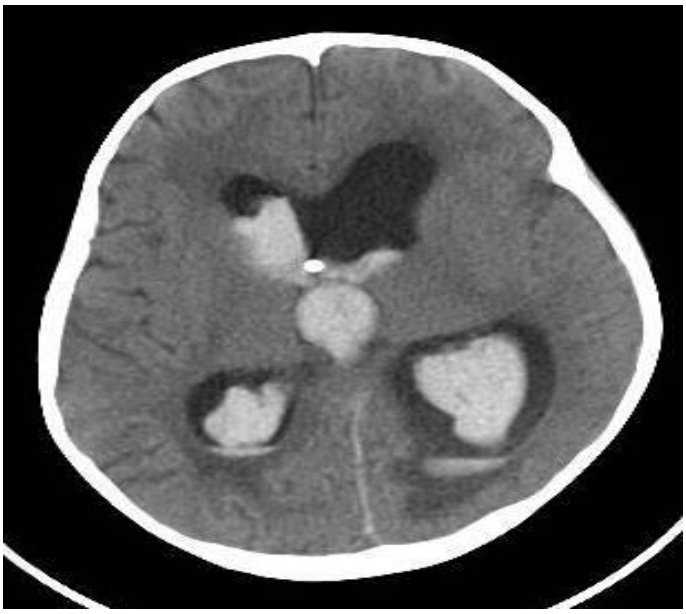

Fig. 2. CT scan brain showing intraventricular bleed

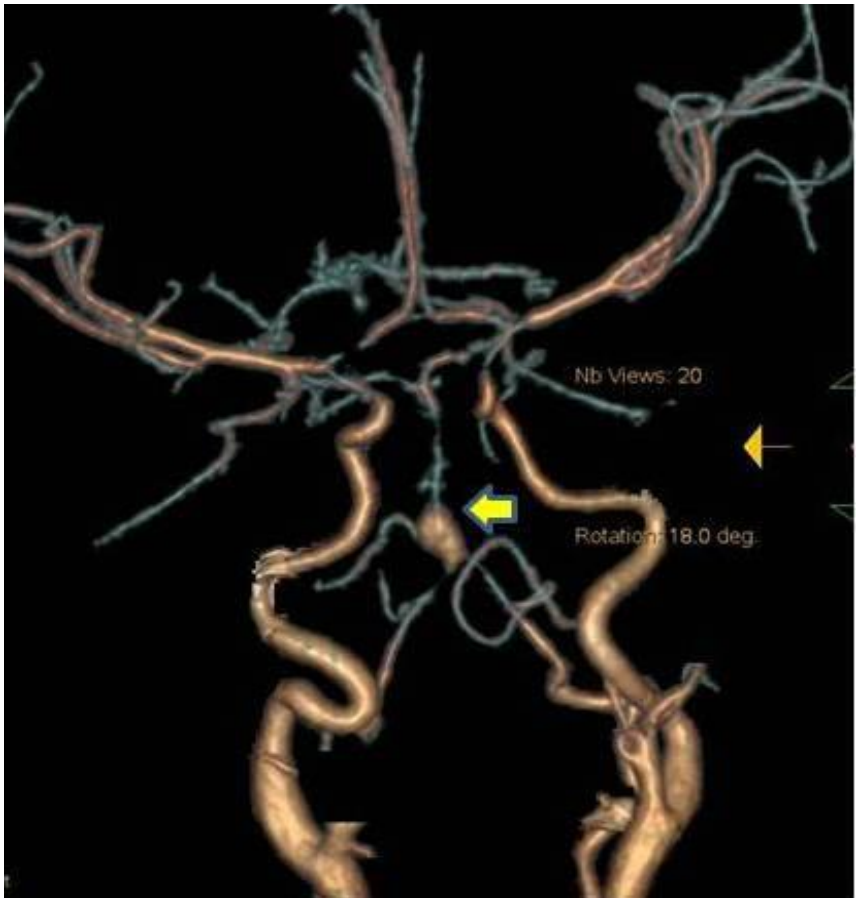

Fig. 3. Solid arrow showing proximal basilar artery mycotic aneurysm in 3D CT cerebral angiogram

Common clinical manifestation is very vague in the form of persistent fever, headache, vomiting, seizures and a very high index of suspicion is needed for early diagnosis. One of the major

fatal complications of an IIA is an intracranial bleed; the commonest site being either an intraparenchymal or a subarachnoid location. Further, IIA should be considered in any child with febrile neutropenia and intracranial haemorrhage. Our child had an intraventricular bleed which is an uncommon occurrence [15].

Though the culture yield in an IIA is low (25-40%), the commonest organisms implicated are Staphylococcus aureus and Streptococcus species. [7]. A large series by Oderich et al found Staphylococcus to be the most common organism, followed by E.coli in 43 cases of aortic aneurysm. Though rare, there have been fungal isolates of candida, aspergillus and mucor in many series [16]. In our child, the only isolate was Staphylococcus aureus, which probably was responsible for the condition.

Intracranial mycotic aneurysms can be evaluated with CT/MR or conventional angiography. The imaging characteristics of mycotic aneurysms may include focal vascular dilatation and sac-like outpouching from the vessel wall. A rapid change in size or shape over time may occur, and new aneurysms may appear at the follow-up of the angiographic imaging [17,15]. Most of the IIAs are peripherally located though a minority (20 - 33%) can be centrally located. Morphologically, these aneurysms are typically small, although rarely giant intracranial mycotic aneurysms have been described. They are typically fusiform (more common), saccular or sacculofusiform [18]. DSA is the gold standard imaging modality. The diagnosis of an infectious aneurysm is supported in our child by a history of systemic infection, multiplicity and rapid increase in size over time. Differential diagnosis in MRI includes berry aneurysm, nodular leptomeningeal deposits and vasculitis.

The overall mortality in various series has ranged from 12-40%. Patients with an aneurysm secondary to infective endocarditis in a series by Barrow et al have shown 100% survival as against a worse outcome (33% survival)in patients with meningitis and other causes [19]. Immunosuppression is another major risk factor for mortality. In a study by Allen et al, the authors have shown that lethality is highly variable and difficult to predict. The chance of an aneurysmal rupture is higher in larger lesions as against smaller ones (10mm vs 5mm); as well as the immune status of the individual [7]. Multiple IIAs have an invariably poor prognosis due to the difficulty in surgically treating the same as also because of the high chance of rebleed [9,20]. Oderich et al, in their series, have described extensive periarterial infection, staphylococcus aureus infection and aneurysmal rupture as variables associated with mortality. Our child had both multiple aneurysms as well as a severe immunosuppressed state; probably responsible for the poor outcome.

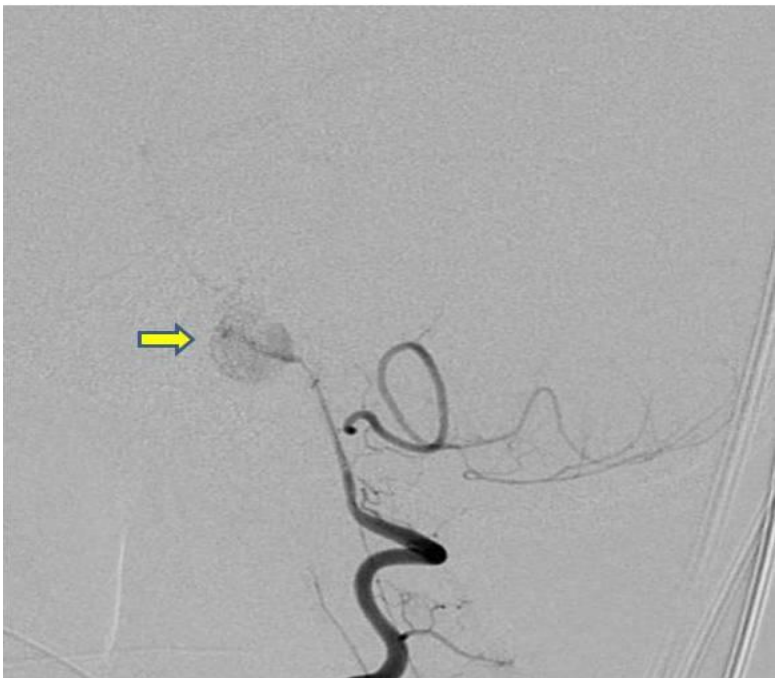

Fig. 4. Solid arrow showing aneurysm in the precoiling cerebral DSA

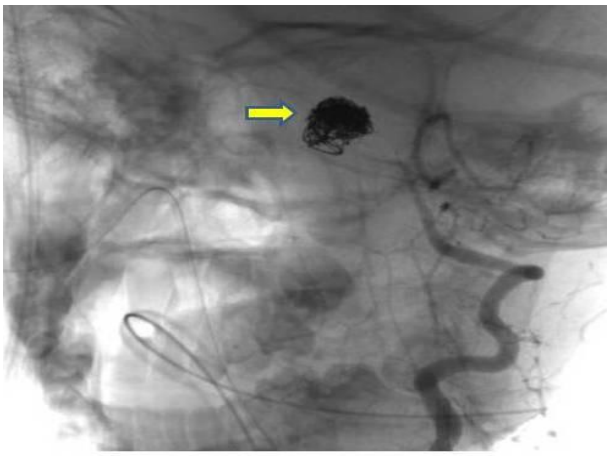

Fig. 5. Solid arrow showing post coiling aneurysm in the cerebral DSA

Many investigators have advocated prolonged antibiotic treatment for IIAs with a resolution rate of around 30% [21], but some have described an invariably poor outcome in the medically treated group as against patients who have undergone intervention [2]. The most preferred option in the present is endovascular coiling. Other surgical interventions include clipping, bypass procedures and excision of the aneurysm with vessel grafting. Rupture of the aneurysm, progression of size on antibiotic therapy, mass effect and presence of residual aneurysm on completion of medical management are indications for surgery. The decision to intervene depends on various factors like age, the health of the patient, characteristics, site and multiplicity of the aneurysm.

4. CONCLUSION

We report a case of multiple intracranial aneurysms in a 4-year-old girl with acute lymphoblastic leukaemia, which is a rare fatal complication in otherwise highly curable childhood malignancy. The detection of the same requires a high index of suspicion which ultimately affects the survival outcome.

CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline participant consent and ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Flores BC, Patel AR, Braga BP et al. Management of infectious intracranial aneurysms in the pediatric population. Childs Nerv Syst. 2016;32(7):1205-17.
2. Kannoth S, Iyer R, Thomas SV, et al. Intracranial infectious aneurysm: presentation, management and outcome. J Neurol Sci. 2007;256(1-2):3-9.
3. Osler W. The Gulstonian lectures, on malignant endocarditis. Br Med J. 1885; 1(1264):577–579
4. Parkhurst GF, Dekcer JP. Bacterial aortitis and mycotic aneurysm of the aorta; A report of twelve cases. Am J Pathol. 1955; 31:821-35.
5. Chen YF, Lin PY, Yen HW, et al. Double mycotic aneurysms of the ascending aorta. Ann Thorac Surg. 1997;63:529-31.
6. Fisk M, Peck LF, Miyagi K, et al. Mycotic aneurysms: A case report, clinical review and novel imaging strategy. QJM: An International Journal of Medicine. 2012; 105(2):181–188.
7. Allen LM, Fowler AM, Walker C, et al. Retrospective review of cerebral mycotic aneurysms in 26 patients: focus on treatment in strongly immunocompromised patients with a brief literature review. AJNR Am J Neuroradiol. 2013;34(4):823-827.
8. Rinne J, Hernesniemi J, Puranen M, et al. Multiple intracranial aneurysms in a defined population: prospective angiographic and clinical study. Neurosurgery. 1994;35(5):803-808.
9. Khormi YH, Tyndall RG, Tamber M. Malignant clinical course of mycotic

intracranial aneurysms in children: A review. Surg Neurol Int. 2020;11:71.
10. Müller BT, Wegener OR, Grabitz K, et al. Mycotic aneurysms of the thoracic and abdominal aorta and iliac arteries: experience with anatomic and extra-anatomic repair in 33 cases. J Vasc Surg. 2001;33(1):106-113.
11. Karsner HT. Acute Inflammation of Arteries. Springfield. III: Charles C Thomas Publishing. 1947;16.
12. Sahu KK, Yanamandra U, Dhawan R, et al. Fungal Mycotic Aneurysm in a Case of Acute Lymphoblastic Leukemia. Indian J Hematol Blood Transfus. 2016;32 (Suppl1):32-37.
13. Zingale A, Chiaramonte I, Albanese V, et al. Infected cerebral hemorrhage by ruptured infectious anterior communicating artery giant aneurysm in a patient with T cell acute lymphoblastic leukemia. Case report. J Neurosurg Sci. 1997;41(4):395-400.
14. Khera S, Simalti AK, Balasubramaniam D, et al. Rasmussen's aneurysm in a child with acute lymphoblastic leukaemia. BMJ Case Rep. 2020;13(6):e235399.
15. Shen G, Shen X, Pu W, et al. Imaging of cerebrovascular complications of infection. Quant Imaging Med Surg. 2018;8(10): 1039-1051.
16. Oderich GS, Panneton JM, Bower TC, et al. Infected aortic aneurysms: aggressive presentation, complicated early outcome, but durable results. J Vasc Surg. 2001;34 (5):900-908.
17. Larry M Baddour, Walter R Wilson et al. Infective endocarditis: Diagnosis, antimicrobial therapy and management of complications: a statement for healthcare professionals from the committee on rheumatic fever, endocarditis, and kawasaki disease, council on cardiovascular disease in the young, and the councils on clinical cardiology, stroke, and cardiovascular surgery and anesthesia. American heart association: endorsed by the infectious diseases society of America. Circulation. 2005;111 (23):e394-43420.
18. Wai-Kit Lee, Peter J, Mossop, et al. Infected (Mycotic) aneurysms: Spectrum of imaging appearances and management. Radio Graphics. 2008;28:1853–1868
19. Barrow DL, Prats AR. Infectious intracranial aneurysms: comparison of groups with and without endocarditis. Neurosurgery. 1990;27:562–72.
20. Vajda J. Multiple intracranial aneurysms: a high risk condition. Acta Neurochir. 1992; 118(1-2): 59-75.
21. Rice CJ, Cho SM, Marquardt RJ, et al. Clinical course of infectious intracranial aneurysm undergoing antibiotic treatment. J Neurol Sci. 2019;403:50-55.

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