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Approach to a Child with Bilateral Proptosis as a Rare Presentation of Acute Myeloid Leukemia

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Abstract

A 6-year-old girl presented with a 2-month history of sudden onset, painless, progressively increasing bilateral proptosis, palpable lymphadenopathy and skin pallor. A full blood count showed bicytopenia and the erythrocyte sedimentation rate (ESR) was raised. Computerized tomography (CT) scan showed bilateral lacrimal gland enlargement. The bone marrow biopsy was consistent with M2 acute myeloid leukemia (AML). The patient received symptomatic treatment and was sent to pediatric oncologist for induction chemotherapy and tumor lysis syndrome (TLS) protocol. Bilateral proptosis is a rare manifestation of several diseases. This case report emphasizes on the low threshold for hematological malignancies in the presentation of bilateral proptosis. Ophthalmologists should be cognizant of the unusual ophthalmic manifestations of haematological malignancies, as they are a diagnostic challenge but knowledge about the rare extramedullary manifestations of AML facilitates early diagnosis and thereby improves prognosis.

Categories: Ophthalmology, Pediatrics, Hematology
Keywords: *Haematological Manifestations, Pediatric Rare Diseases, Ocular Metastasis, Acute Myeloid Leukemia (Aml), Bilateral Proptosis*

INTRODUCTION

Acute Myeloid Leukemia (AML) is a hematological malignancy characterized by proliferation of immature myeloid cells (mainly blasts) which eventually replaces the healthy bone marrow, circulates in the blood and accumulates in other tissues of the body. The common manifestations of AML are due to suppression of normal hematopoiesis by the leukemic infiltrates [1].. In this case report, a diagnostic dilemma has been addressed in the form of extensive workup for sudden onset, rapidly progressing, bilateral proptosis which was later diagnosed as rare presentation of AML. Proptosis is a condition where the eye protrudes forward from the orbit. It is of utmost importance to differentiate proptosis from contralateral enophthalmos, microphthalmos and other causes of pseudoproptosis. The differential diagnosis of bilateral proptosis in pediatric age group are thyroid ophthalmopathy, idiopathic orbital inflammatory disease, metastatic tumors like neuroblastoma and Ewings sarcoma, erythropoietic and lymphoproliferative neoplasms like leukemia, lymphoma and histiocytic disorders like langerhan's cell histiocytes [2] Proptosis is a common symptom in various diseases affecting the structures around the eye socket. Evaluating proptosis involves detailed ocular and systemic history specific to the age group, performing extensive ocular exam, confirming the cause through peripheral smear, MRI, and bone marrow assessment, and conducting histopathological examination if necessary [3,4]. The problem addressed in this abstract is the uncommon occurrence of bilateral proptosis in a 6-year-old girl, which ultimately led to the diagnosis of M2 acute myeloid leukemia (AML). This case report highlights the diagnostic challenge faced by ophthalmologists in recognizing the atypical ophthalmic manifestations of hematological malignancies. By increasing awareness of these rare extramedullary manifestations of AML, early detection and subsequent treatment can be facilitated, ultimately improving the patient's prognosis.

Case Presentation

A 6-year-old girl presented to our hospital in the outpatient department with a 2-month history of slowly progressing bilateral protrusion of the eyes and masses in the orbits (Figure *1*, *2*). According to the mother there was sudden onset, gradually progressive, painless protrusion of the eyes. The mother did not notice any significant change in vision. She had no reported weight loss or gain, no flushing, sweating or any heat intolerance. There were no associated tremors or palpitations. She had no significant past history of any trauma or surgery (facial/ophthalmic). No reported systemic disease, no history of known cancer or any chemo-radio-therapy. There was no family history of proptosis. All other siblings were ophthalmologically and systemically normal. She was not taking any regular medications.

Figure 1: Bilateral Proptosis In A 6 Year Old Child, Frontal View

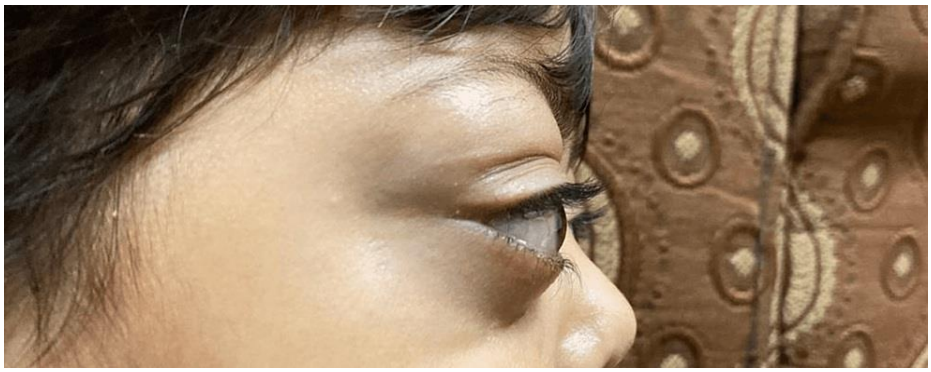

Figure 2: Bilateral Proptosis In A 6 Year Old Child, Lateral View

Her visual acuity was 6/12 with LEA symbols in both eyes, with no further improvement. The pupils were round, regular and reactive to light with no relative afferent pupillary defect (RAPD). Color vision and contrast sensitivity were normal. Visual fields were grossly normal. The extraocular movements were restricted in all gazes except in depression. The lacrimal glands were enlarged and palpable. The intraocular pressures were 30mm Hg in the right eye and 24mm Hg in the left eye. There was a subconjunctival haemorrhage in the superotemporal aspect of bulbar conjunctiva of the left eye. There were chorioretinal folds on the maculae of both eyes. Table *1* summarizes the ocular exam findings:

Table 1: Summary of Ocular Examination Findings

OCULAR EXAMINATION COMPONENTS	RIGHT EYE (OD)	LEFT EYE (OS)
VISUAL ACUITY	6/12 with LEA symbols	6/12 with LEA symbols
BEST CORRECTED VISUAL ACUITY	No further improvement	No further improvement
PUPILS	Round, regular, reactive to light; no RAPD	Round, regular, reactive to light; no RAPD
COLOR VISION AND CONTRAST SENSITIVITY	Normal	Normal
VISUAL FIELDS BY CONFRONTATION	Grossly unaffected	Grossly unaffected
EXTRAOCULAR MOVEMENTS	Restriction in all gazes except in depression	Restriction in all gazes except in depression
IOP	30mm Hg	24mm Hg
ADNEXA AND ORBITS	Enlarged, palpable lacrimal glands.	Enlarged,palpable lacrimal glands glands
CORNEA	Clear	Clear
CONJUNCTIVA	Subconjunctival haemorrhage in superotemporal aspect of bulbar conjunctiva in the left eye	
ANTERIOR CHAMBER	Deep and quiet	Deep and quiet
LENS	Clear	Clear
FUNDI	Chorioretinal folds on the macula	Chorioretinal folds on the macula

RAPD= relative afferent pupillary defect

Physical examination was notable for mild fever, pallor, cervical and preauricular lymphadenopathy. No facial asymmetry or scars were noted. Axial proptosis was present with no dystopia, not associated with lagophthalmos or corneal exposure. The lacrimal glands were enlarged and palpable. No bruit were heard over the orbit and no pulsations felt. The patient was not cooperative for examination with an exophthalmometer. Laboratory investigations were performed, the results of which are summarized in Table 2:

Table 2: Results of the Investigations

Investigations	Results	Units	Reference Ranges
RBCs	2.04	$x10^6$/uL	4-6
WBCs	7.79	$x10^3$/uL	4-11
Platelets	64	$x10^3$/uL	150-450
Hemoglobin	6.6	g/dL	11.5-17.5
LDH	684	U/L	91-180
ESR	120	mm at the end of 1st hour	0-15
CRP	0.3	mg/L	<1
Blood Urea	25.9	mg/dL	10-50
Total Bilirubin	0.29	mg/dL	0.1-1
ALT	14	U/L	10-50
ALP	135	U/L	<269
Creatinine	0.35	mg/dL	0.3-0.9
Blast cells	28% atypical cells (blasts)	%	<5
Cell Morphology	Anisocytosis	-	
Chest X-ray	Normal		

LDH= lactate dehydrogenase, ESR= erythrocyte sedimentation rate, CRP= c-reactive protein, ALT= alanine aminotransferase, ALP= alkaline phosphatase.

Bone marrow aspiration cytology confirmed 65% blast cells and acute myeloid leukemia (AML-M2).

Ocular investigations were performed which included optical coherence tomography retinal nerve fiber layer (OCT- RNFL) which showed thickening of the nerve fiber layer inferiorly in the right eye (Figure *3*). Fundus photographs showing chorioretinal folds on the maculae of both eyes (Figure *4*, *5*, *6*, *7*). CT brain showed bilateral lacrimal gland enlargement, likely lymphomatous masses (Figure *8*). In view of the confirmed diagnosis of leukemia, considering the financial constraints and the unstable clinical condition of the child, other forms of neuroimaging were deferred.

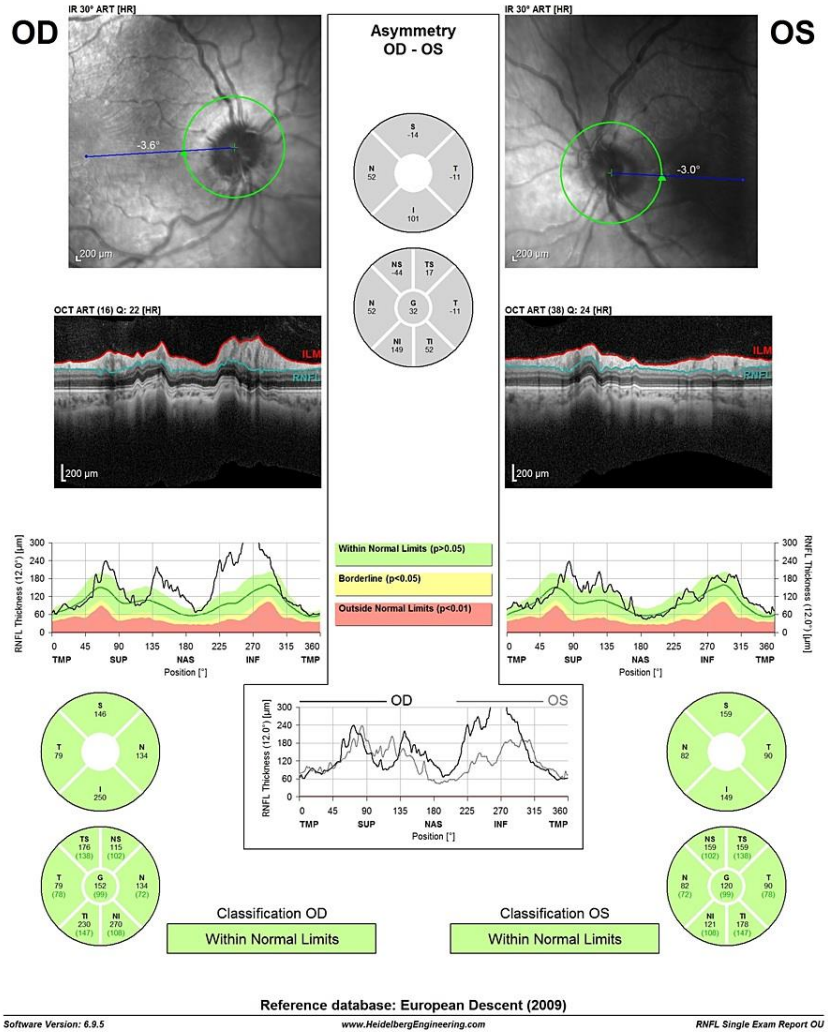

Figure 3: OCT-RNFL Showing Thickening of the Retinal Nerve Fiber Layer Infero-Temporally in the Right Eye

OCT-RNFL= Optical Coherence Tomography- Retinal Nerve Fiber Layer

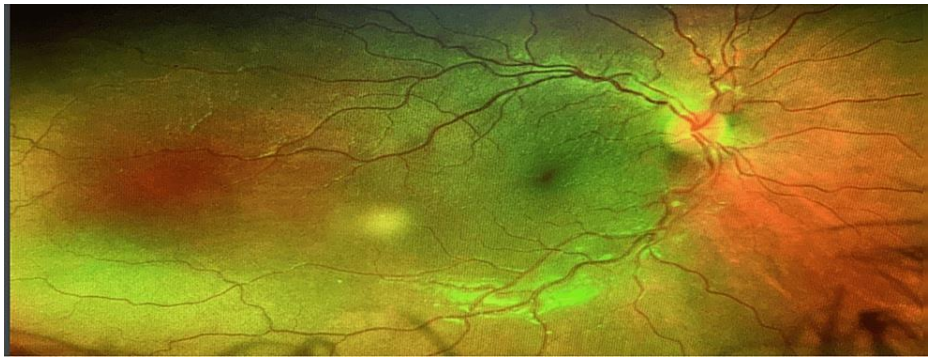

Figure 4: Fundus Photograph, Right Eye

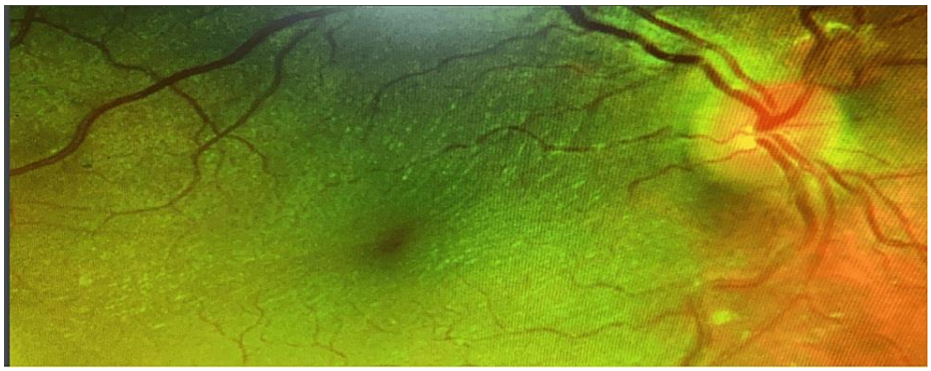

Figure 5: Fundus Photograph of Right Eye Showing Chorioretinal Folds

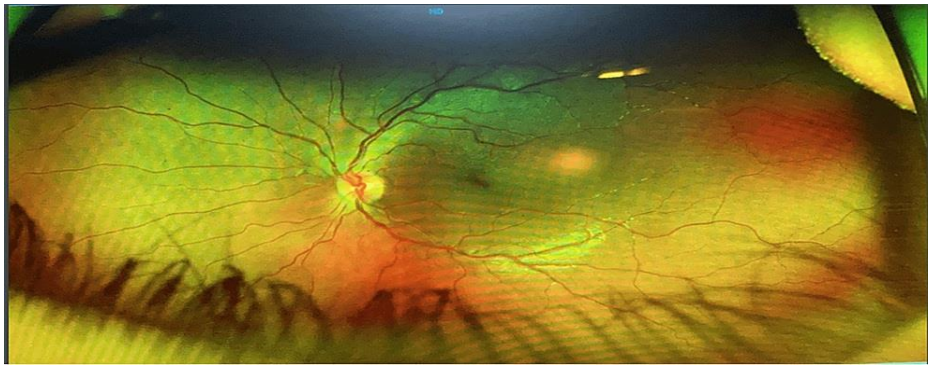

Figure 6: Fundus Photograph, Left Eye

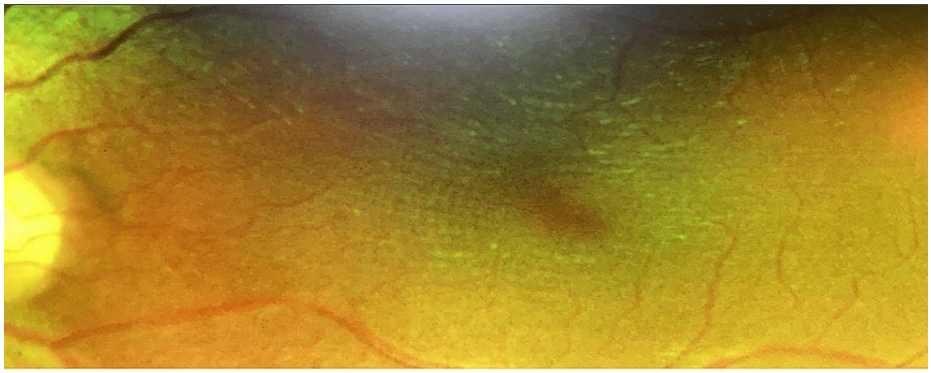

Figure 7: Fundus Photograph of Left Eye Showing Chorioretinal Folds

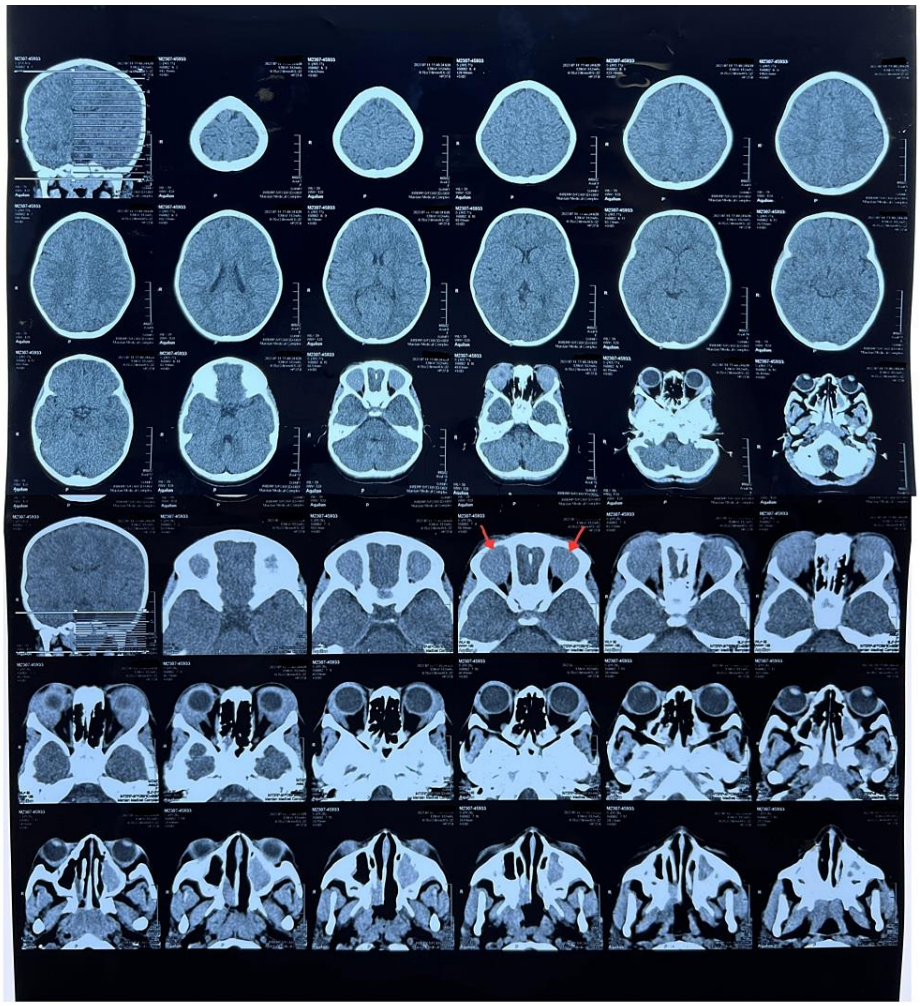

Figure 8: CT Brain Showing Enlarged Lacrimal Glands (Red Arrows)

Our patient was referred to the pediatric hematology and oncology department where she was started on induction chemotherapy and 1 month follow up showed subjective remission of the proptosis and improvement in visual acuity. As the optic discs of the patient showed no signs of compression (optic disc swelling/ optic atrophy) we expect good visual prognosis. This highlights the importance of early workup and timely management of bilateral proptosis. Ophthalmologists should be aware of the unusual ophthalmic manifestations of haematological malignancies, as they cause diagnostic dilemmas. Knowledge about the rare extramedullary manifestations of AML facilitates early diagnosis and thereby improves prognosis.

Discussion

Acute myeloid leukemia (AML) is a type of blood cancer where there is an abnormal and uncontrolled growth of immature myeloid cells, which are malignant versions of the normal myeloid cell lineages. These cells replace the normal bone marrow and spread to the other tissues of the body [5]. It is most common in children and young adults; the mean age being 7 years [5]. AML accounts for about 15% of all leukemias in children [4]. 'Granulocytic sarcoma' refers to

the aggregation of the leukemic cells in the extramedullary sites. It was previously called 'Green tumor' by Allen Burns due to the myeloperoxidase enzyme present in these cancerous cells and these represent only about 3% of the AML tumors [6]. They can involve skull, orbits, paranasal sinuses, sacrum, spine, sternum, and ribs. One rare presentation of these granulocytic tumors is as an orbital mass in AML [6].

The usual differential diagnoses to consider in the paediatric age group are dermoid cyst, retrobulbar hemangioma, retrobulbar hematoma, orbital cellulitis, orbital spread of retinoblastoma, pseudoproptosis due to enlargement of the globe or abnormalities of the craniofacial skeleton etc. Less common diseases are metastatic neuroblastoma, rhabdomyosarcoma and hematological malignancies such as leukemia and lymphomas. In our patient there was bilateral proptosis with enlargement of lacrimal glands bilaterally without any bony destruction.

AML has been reported as unilateral or bilateral proptosis as the presenting complaint [8,9]. The cause of proptosis in these cases can range from leukemic infiltrates to venous blockage including retrobulbar hemorrhage and orbital muscle infiltration. Unilateral or bilateral ptosis, involvement of the lacrimal glands, conjunctival masses, incomplete or complete uveal tract involvement are some other presentations of this disease [9]. Reduction in the visual acuity and limitation of the extraocular movements are seen in the vast majority of the cases. Peripheral smear is an important tool in diagnosing AML and gives a clue to diagnosis by showing immature blast cells and relative neutropenia. Complete neuroimaging was not done in our case except CT brain as the diagnosis was confirmed with bone marrow aspiration alone and there were financial constraints.

The treatment options with a good response in AML are chemotherapy or radiotherapy or both [10,11]. Nonetheless, stem cell transplant is the treatment of choice for providing disease-free survival for the patients [10]. Prognosis is related to the grade and spread of hematologic malignancy at the time of diagnosis.

A case like ours has been reported by Gupta et al. [2] in a 2-year-old child with bilateral proptosis and palpable mass in the superomedial aspect of both orbits, diagnosed as AML on aspiration cytology. Imaging studies were not performed in their case similar to ours.

In conclusion, a low threshold should be kept for AML in a child presenting with sudden onset, rapidly enlarging bilateral proptosis. For early diagnosis of AML, peripheral blood smear along with bone marrow aspiration should be performed, supported by radiological imaging in all the cases. The research gaps of our report include, late presentation, failure to perform complete proptosis examination due to which the objective improvement could not be assessed, loss of follow up after 1 month because of which prognosis of this particular patient could not be ascertained, incomplete neuroimaging due to poor financial status. These are the potential areas of research in the future. Further studies are needed to establish the relationship of time of presentation in bilateral proptosis with the prognosis of a patient in hematological malignancies needs to be studied.

CONCLUSIONS

Bilateral proptosis is an alarming symptom in children as it points out to the life threatening conditions. Therefore, meticulous work-up should be done for the early diagnosis and timely treatment as it can prove life saving for many children. Low threshold must be kept for leukemias/lymphomas in children with bilateral proptosis as sometimes it is the only presenting complaint. Ophthalmologists should be vigilant in diagnosing unusual ophthalmic manifestations of haemotological malignancies, as they are a diagnostic challenge but knowledge about the rare extramedullary manifestations of AML facilitates early diagnosis and thereby improves prognosis.

Additional Information

Disclosures

Human Subjects

Consent was obtained or waived by all participants in this study. Dr. Farooq Ahmad issued approval No.447/DME/KMC. Dr.Shafiq Tanveer, TMO (Department of Ophthalmology) MTI KTH Peshawar (Principal Investigator) has been, on the 2nd August, 2023given approval by the IREB of the Khyber Medical College/Khyber Teaching Hospital for the following case report: 'Approach to a child with bilateral proptosis as a rare presentation of Acute Myeloid Leukemia' During the whole work, all personal information of patients/subjects should be kept confidential. If you make any substantial change in the case report, you will need to inform the IREB for formal approval.

Conflicts of Interest

In compliance with the ICMJE uniform disclosure form, all authors declare the following:

Payment/Services Info

All authors have declared that no financial support was received from any organization for the submitted work.

Financial Relationships

All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other Relationships

All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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