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Acute haemothorax and pleuropulmonary blastoma: Two extremely rare complications of extralobar pulmonary sequestration

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ABSTRACT

Extralobar bronchopulmonary sequestration (eBPS) is a congenital lung malformation characterized by non-functional lung tissue with no connection with the bronchial tree, receiving systemic blood supply and covered by its own visceral pleura. It is mostly asymptomatic, however it can rarely get complicated with infections and neoplastic degeneration. Its management is still debated: many authors suggest observation for asymptomatic cases and intervention only in case of symptoms, others advocate surgery even in asymptomatic patients. Pleuropulmonary blastoma (PPB) is a rare malignant sarcomatous neoplasm, representing the most common primary lung malignancy in children. Typically, PPB is associated with congenital pulmonary airway malformation (CPAM). eBPS is rarely associated with PPB. We report a case of a previously healthy three-year-old boy presented to our emergency room with massive hemothorax after a low-energy chest trauma. Imaging revealed active thoracic bleeding by an anomalous artery arising from the celiac tripod, and an irregular mass in the lower right hemithorax. After performing biopsy, pathologic examination revealed a PPB. The patient underwent four cycles of chemotherapy before surgery. The operative findings revealed a right supradiaphragmatic extralobar mass, with no communication with the bronchial tree, strictly adherent to the right middle lobe. After mass excision, histological analysis confirmed the diagnosis of PPB type 2. The patient underwent postoperative chemotherapy. No recurrence nor metastasis were noted during the current follow-up. DICER-1 research revealed biallelic mutation on the tumor and on the surrounding normal tissue. We reviewed the literature concerning PPB and BPS. Based on these data, we would recommend intervention even in case of asymptomatic eBPS.

1. Introduction

Bronchopulmonary sequestrations (BPS) are congenital lung malformations characterized by nonfunctioning embryonic lung tissue with no connection with the bronchial tree, receiving systemic blood supply. They can be either intralobar (iBPS), when included in the

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lobar pleura, or extralobar (eBPS), when covered by their own pleura [1].

Even if BPS are mostly asymptomatic, they can complicate either during pregnancy or after birth. Prenatally, BPS can develop pleural effusion determining mediastinal shift and fetal hydrops [2]. Postnatally, they can compress the surrounding normal parenchyma leading to recurrent infections and can also lead to high output cardiac failure. Rare life-threatening complications include haemothorax and neoplastic transformation [3].

Consensus is reached on the treatment of symptomatic BPS. Regarding asymptomatic lesions, the majority of authors agree on surgery for iBPS, due to the high incidence of complications. On the contrary, eBPS may remain asymptomatic throughout life and the risk of complications is lower than in other malformations [1,4,5]. Therefore the management of eBPS is still controversial, varying from active follow-up to excisional surgery or embolization [6].

The occurrence of malignant transformations within BPS is rare. Neoplasms arising from BPS are mostly presented in adulthood and usually develop from iBPS. The most frequent degeneration is carcinoma [7]. Pleuropulmonary blastoma (PPB) is an extremely rare childhood mesenchymal neoplasm, which stems from lung, pleura or both locations. Germline mutation of DICER-1 is believed to be the cause of most PPBs [8]. The association of PPB with congenital lung malformations [9,10] is known, mainly with congenital pulmonary airway malformations (CPAM). Association between eBPS and PPB in childhood is rarely described [11,12].

We report a case of PPB as a plausible complication of undiagnosed extralobar sequestration.

2. Case report

A previously healthy 3-year-old boy presented to the emergency room of a peripheral Centre for respiratory distress after a low-energy chest trauma due to an accidental fall. Chest X-ray and CT scan showed massive right hemothorax. Hemoglobin's level was 14,4g/dl. He was then transferred to our pediatric emergency referral Centre. Upon arrival, the patient was tachypnoic with decreased breath sounds on the low right hemithorax. After one hour hemoglobin was 12,2 g/dl. Tranexamic acid was administered, and a 16 Ch chest tube was urgently placed: 550 ml of blood were drained. No blood transfusions were needed. Urgent CT angiogram revealed active thoracic bleeding by an anomalous artery arising from the celiac tripod, and an irregular mass in the lower right hemithorax. A venous vessel appeared to arise from the mass, draining in the right inferior pulmonary vein (Figs. 1, 2).

An urgent embolization of the anomalous vessel was performed through transfemoral access, under general anesthesia. The anomalous artery was selectively catheterized and coiled with three micro-spirals. This procedure succeeded to arrest the bleeding (Fig. 3). The patient was then extubated and no postoperative complications occurred.

After four days, a total body CT scan confirmed the presence of an irregular, unevenly vascularized mass (8.5 × 9.0 × 7.3cm) in the right lung, compressing the lower and upper lobes. (Fig. 4) Nodular pleural thickening was detected in the lower mediastinal pleural. No adenopathies, nor lesions in the left lung or metastatic disease were noted.

On the same day, accordingly with the oncologists, a biopsy of the mass was carried out through a mini-thoracotomy. The mass appeared tough and thickened and multiple pleural and perimediastinic adhesions were found.

Pathologic examination revealed a PPB with prevalent chondrosarcomatous solid elements. The patient was then referred to Istituto Nazionale dei Tumori of Milan (INT), a referral pediatric oncologic centre, where he underwent four cycles of neoadjuvant chemotherapy with Ifosfamide, Vincristine, Actinomycin-D and Doxorubicin (IVADO regimen) according to the European Cooperative Study Group for Paediatric Rare Tumors (EXPeRT) recommendations [13], with no side effects. At re-staging, a significant decrease of the tumor size was evident (from 12 × 9 × 7 cm to 5 × 4 × 4 cm), but no clear separation was visible between the mass and pleura,

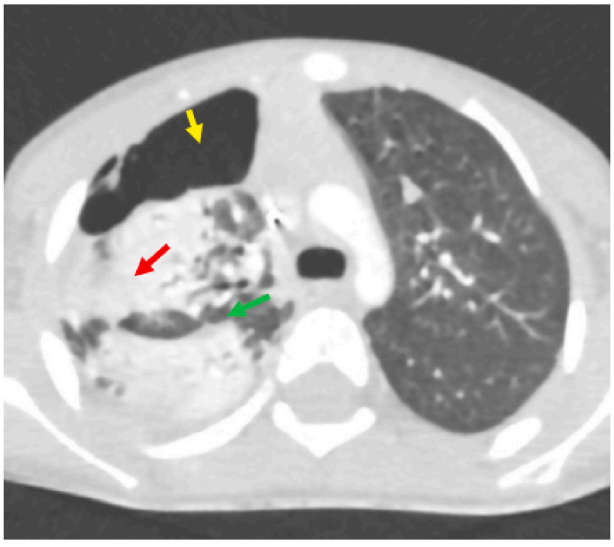

Fig. 1. First chest CT scan showing a massive hemothorax (yellow arrow) and a heterogenous mass in the right lung; solid part of the mass (red arrow); cystic part of the tumor (green arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

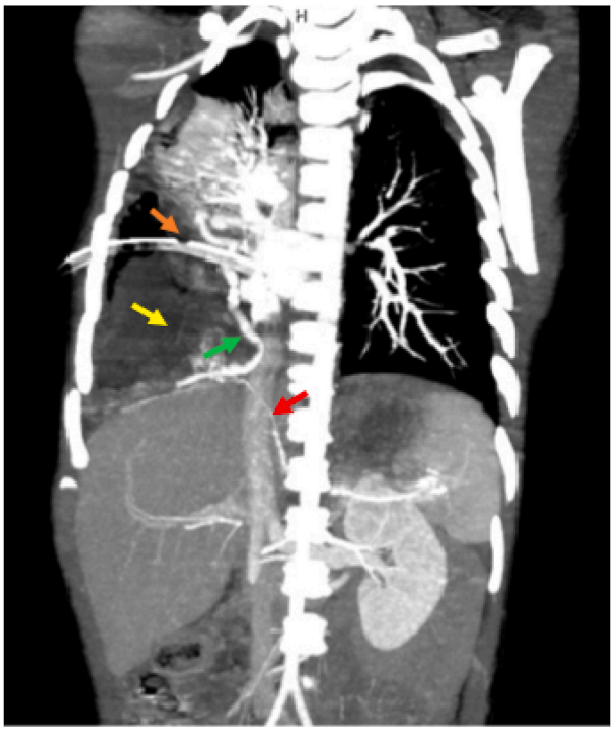

Fig. 2. Chest CT scan showing an anomalous artery arising from the celiac tripod (red arrow); venous vessel arising from the mass, draining in the right inferior pulmonary vein (green arrow); drain tube (orange arrow); hemothorax (yellow arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

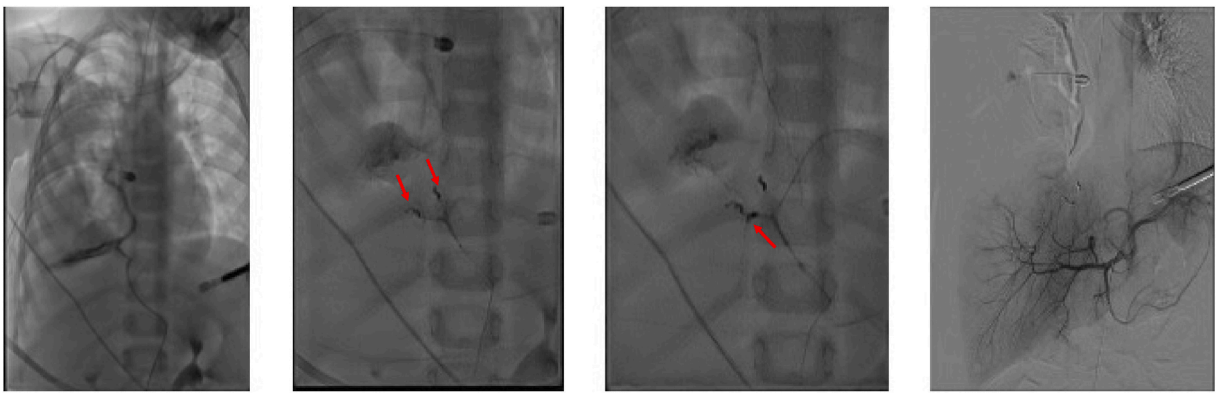

Fig. 3. The anomalous artery was selectively catheterized and coiled with three micro-spirals (red arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

diaphragm and pericardium.

After a multidisciplinary assessment carried by surgeons, oncologists, radiologists and pediatricians, surgical resection was planned at our Centre. The surgical plan comprised massive resection of the neoplasia to achieve tumor-free margins, with radical demolition involving diaphragm, pericardium and ribs, in case of their infiltration.

A right lateral muscle sparing double thoracotomy at 5th and 8th intercostal spaces was performed under general anesthesia, with the support of a 30° optic. A supradiaphragmatic extralobar mass was found, with no communication with the bronchial tree, strictly adherent to the right middle lobe. (Fig. 5) No signs of pericardial involvement were found. The artery supplying the mass was not visible, probably due to the previous embolization. The right hemidiaphragm appeared infiltrated. Intraoperative histological examination of diaphragmatic pleura described the presence of atypical elements. The surgery consisted of: *en bloc* mass removal with a minimal atypical resection of the middle lobe (Fig. 6); stripping of the diaphragmatic pleura with partial right hemidiaphragmatic excision; mediastinal and parietal subtotal pleurectomy; reconstruction of the right hemidiaphragm with a double layer polyester prosthesis; chest tube positioning (Fig. 7)

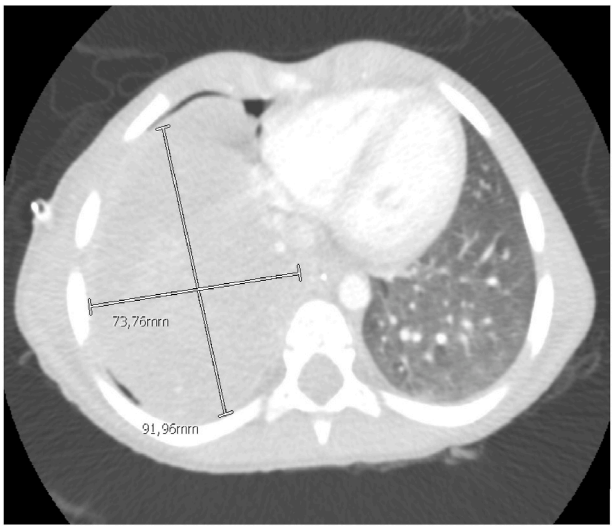

Fig. 4. CT scan confirming the presence of an irregular vascularized mass (8.5 × 9.0 × 7.3cm) in the lower right hemithorax.

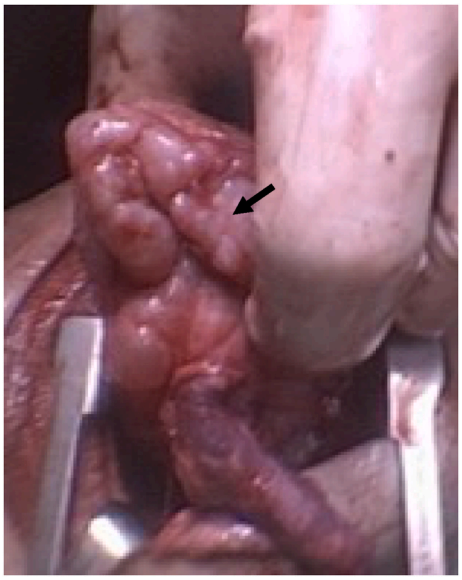

Fig. 5. Tumor characterised by a hard lesion with multiple cystic components (black arrow).

Grossly, the tumor consisted of a hard lesion with multiple cystic components. Pathology confirmed the diagnosis of solid and cystic pleuropulmonary blastoma type II (Dehners histological Classification) with predominantly chondrosarcomatous component, areas of necrosis and focal blastomatous areas (<5%). Resection margins were tumor-free.

No post-operative complications occurred and the patient was extubated after two days with no need for further ventilator respiratory support. Chest X-ray showed complete re-expansion of the right lung. The treatment was then completed with five chemotherapy cycles with Ifosfamide, Vincristine, Actinomycin-D (IVA regimen).

Four months after surgery, a control chest CT showed no residual disease. No signs nor symptoms of disease were noted during the three months follow-up after completing chemotherapy. DICER-1 research revealed biallelic mutation on the tumor and on the surrounding normal tissue.

3. Discussion

BPS are congenital lung malformations characterized by systemic blood supply and no communication with the bronchial tree, accounting for 0.15–6.4% of all congenital pulmonary anomalies. eBPS comprise 25% of BPS, differing from iBPS for their systemic venous drainage and their own visceral pleura. Typically, eBPS lies between the lower lobe and the diaphragm, it is left-sided and

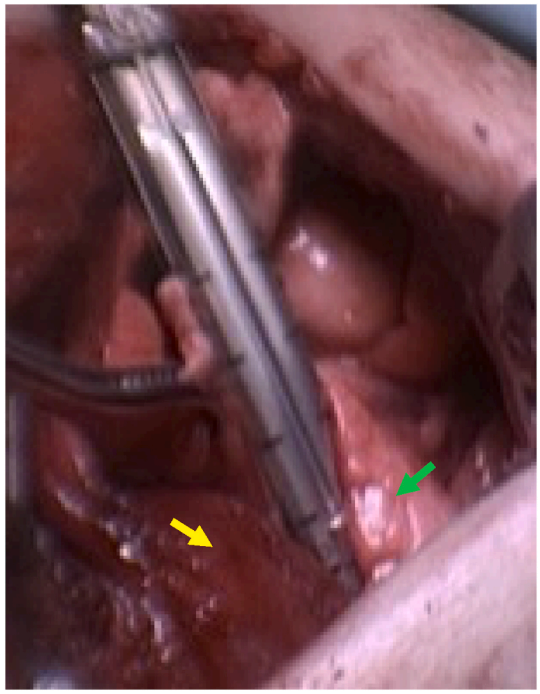

Fig. 6. Minimal atypical resection of the middle lobe was performed; the mass (yellow arrow) appeared strictly adherent to the middle lobe (green arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

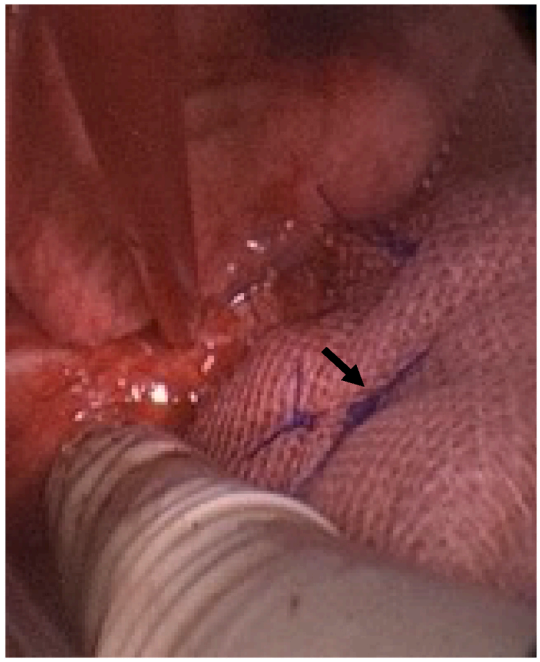

Fig. 7. Reconstruction of the right hemidiaphragm with a double layer polyester prosthesis (black arrow).

occupies the posterior-basal thoracic segment [6]. In more than 80% of cases, the eBPS arterial supply comes from the thoracic or abdominal aorta, in 15%, the feeding artery arises from another systemic artery, and, in 5% it is from the pulmonary artery [14]. Unlike the iBPS, eBPS may remain asymptomatic throughout life and less frequently present with respiratory symptoms such as cough, cyanosis, recurrent infections and rarely hemorrhage [15].

Nowadays most of BPS are detected prenatally, by routine ultrasound at 20 week's gestation. Three-dimensional Doppler

ultrasonography is used to distinguish BPS from other fetal lung lesions, thanks to the identification of the aberrant systemic vascular supply. Additionally, magnetic resonance imaging (MRI) is slightly superior in identifying the vasculature of the mass [6,16].

Despite this, missed diagnoses are still possible: in these cases, BPS may be detected incidentally during life or when symptoms appear [5,6].

In our case, the patient had no prenatal diagnosis and remained asymptomatic for three years. His first manifestation was respiratory distress due to a massive, life-threatening haemothorax after a low-energy trauma.

In literature few cases of eBPS presenting with haemothorax are described: according to Higashidate et al., only 11 cases have been reported, 6/11 cases being below 18 years of age. Among these, only one patient (8 year-old) had massive pleural effusion after a blunt trauma. On the contrary, torsion of the vascular pedicle was the most common etiology in the other cases. Torsion causes venous, lymphatic and finally arterial vessel congestion with consequent intraparenchymal hemorrhage and infarction [17].

In our case, we speculate that the chest trauma has been the main reason of the massive bleeding, based on the sudden onset of symptoms, unlike the cases of vascular torsion.

Higashidate et al. reported no need for emergent treatment: the timing from clinical presentation to surgery ranged from one day to two months [17].

In our case, the mass kept bleeding after the placement of chest tube, therefore, an emergency embolization of the anomalous vessel was performed successfully. We believe that interventional angiography is the safest and most rapid therapy in case of massive hemothorax. Indeed, another case of embolization procedure used to control massive bleeding from an iBPS was previously described [18].

In literature, as far as we know, only three cases of massive hemothorax in eBPS requiring urgent management were described: one in a 34-year-old man on anticoagulant therapy, one in an otherwise healthy 15-year-old young man, and one in a 50-year-old healthy man after workout. In all of these cases the patients underwent an explorative thoracotomy, which lead to bleeding control and to eBPS resection [15,19,20].

Another singular aspect of our case was that neoplastic degeneration had already appeared at the time of diagnosis: pathological findings after biopsy revealed PPB. This is an uncommon finding: compared with other types of congenital pulmonary malformations, BPS have a low risk of neoplastic transformation [7,21,22] and in eBPS transformation is even rarer than in iBPS [22,23].

The most frequent form of neoplasm associated with eBPS is carcinoma [7]. Only few cases of hamartomas and hemangiomas are reported in literature [9,22,24]. Most of these cases concern adults [23].

Our literature search yielded only one pediatric case of sclerosing haemangioma arising within eBPS in a 2-year-old girl [25]. Concerning PPB in pediatric age, we found only two cases arising within an eBPS in a 2-year-old girl [11] and in an 8-months-old female [12]. In both cases, respiratory symptoms were the first manifestation of the tumor: one of the patients had repeated respiratory infections, the other one had intermittent tachypnea. Both patients were treated with thoracotomy and resection of the mass. DICER-1 mutation analysis was not carried out.

PPB is an extremely rare sarcomatous malignant pediatric tumor, although it is the most common primary pulmonary pediatric neoplasm [8]. This is an aggressive tumor with metastatic disease at presentation in approximately 20% of cases, and mortality rate of 40% [26]. Genetic forms have been identified in the majority of cases; according to the International Pleuropulmonary Blastoma Registry [27], the association of PPB and DICER-1 loss of function mutations is reported in approximatively 66% of recorded cases. Accordingly, all patients with a diagnosis of PPB should be screened for DICER-1 mutations [8]. In our case, germline DICER-1 mutation research showed a biallelic mutation, leading to oncogenesis.

Three pathological types of PPB are recognized according to Dehners histological Classification [22]: type I is a cystic lesion; type II is characterized by both cystic and solid elements, and type III is completely solid. Low-grade PPB may be asymptomatic, however, most of children presents with symptoms like cough, chest pain, pneumonia and hemoptysis [26]. In our case, the patient was asymptomatic before chest trauma, which was the revealing event that led to the diagnosis of PPB. We assumed that without this complication, the diagnosis would be delayed, and consequences would be severe.

According to the management algorithm proposed by the EXPeRT Group, our patient underwent up-front biopsy followed by neoadjuvant chemotherapy, considering the chemosensitivity of PPB, the tumor size, and the importance of complete tumor resection as a major prognostic factor [8,13].

Originally, in our case, the surgical plan consisted in an open approach to achieve an extrapleural pneumonectomy with resection of the pleural surfaces, pericardium, phrenic nerve, diaphragm and the last ribs, offering local control and negative margins [8]. But intra-operatively, we found an extralobar mass only partially adherent to the inferior margin of the middle lobe, without pericardium involvement. Therefore, we were able to remove the tumor and pleural surfaces with minimal atypic resection of middle lobe and partial resection of right emidiaphragm. Then pathologic examination confirmed tumor-free resection margins.

PPB has historically been described in association with CPAM types 1 and 4, instead, the association between sequestration and PPB is less described.

The management of eBPS is still debated, many authors suggest observation for asymptomatic cases and intervention only in case of symptoms. In contrast, the risk of infections, the eventual compression of the surrounding lung parenchyma and the potential malignant transformation have been reported by authors who advocate surgical treatment even in asymptomatic patients [4,11].

Our case would suggest two extremely rare complications of an unknown eBPS: potentially life-threatening hemothorax and neoplastic degeneration. Therefore, although it is rare, we would recommend to consider the risk of these complications in the management of asymptomatic eBPS.

Consequently, we recommend intervention even in case of asymptomatic eBPS because of different reasons: difficulties in distinguishing iBPS, which are more commonly symptomatic and predisposed to neoplastic degeneration, from eBPS, only by imaging;

significantly better prognosis when treating an early cystic PPB as compared to a solid PPB; prolonged and invasive follow-up with high radiologic exposure in case of conservative management, with the risk of missing degeneration when adopting a six-month interval between imaging studies. The emotional burden and anxiety of the prolonged follow-up on the family should also be considered [28]. Instead, elective surgery is an effective strategy, considered safe and feasible if carried out within the first year of life, allowing less extensive lung resection due to fewer parenchyma inflammation and considering the lung regeneration achievable for the first months after birth [29].

Moreover nowadays, the development of minimally invasive surgery allows less pain, shorter hospitalization with low complication rates [6,30,31].

Finally, we strongly recommend DICER1 testing for asymptomatic patients with lung cysts that are considered for a non-operative management [8].

Consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient

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Authorship statement

All authors attest that they meet the current ICMJE criteria for Authorship

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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