Thoracoscopic obliteration of the left atrial appendage in paediatric protein S deficiency and neurological complications – prophylaxis of thromboembolic stroke

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Abstract

We present a case of minimally invasive surgical thoracoscopic obliteration of an abnormal left atrial appendage in a child with the diagnosis of protein S deficiency syndrome and dilative cardiomyopathy, who previously suffered a peripheral thrombosis with disabling stroke and underwent thrombolytic/anticoagulation treatment. The procedure we introduced was aimed at reducing the risk of further thromboembolic complications. We followed the concept of a prophylactic procedure to reduce the risk of another, potentially more disabling stroke in patients after neurological incidents, which is not unique, e.g. closure of patent foramen ovale or carotid endarterectomy.

The digital shape pathological structure of the entire LAA was thoracoscopically doubly ligated with endoscopic loops that were inserted through a separate puncture of the thorax, without complications. There was left a limited margin of the LAA under the area of exclusion because of potential hazard of turning down of the interatrial groove with coronary flow disturbances in the coronary arteries. Short- and mid-term follow-up was determined by intensive physiotherapy for improvement of neurological deficits after previous stroke.

Thoracoscopic obliteration of the LAA proved to be a feasible option that can be introduced clinically in the future as an additional minimally invasive palliative procedure in the complex prevention of thromboembolic stroke in paediatric patients.

Key words: paediatric cardiac surgery, left atrial appendage, dilative cardiomyopathy, protein S deficiency, thoracoscopy, stroke prevention.

Streszczenie

Przedstawiamy raport z leczenia metodą mało inwazyjnego torakoskopowego zamknięcia nieprawidłowego uszka lewego przedsionka u dziecka z zespołem niedoboru białka S i kardiomiopatii rozstrzeniowej, po przebytym wcześniej udarze mózgu z niedowładem, leczonym trombolitycznie i antyagregacyjnie. Wykonany zabieg miał na celu zmniejszenie ryzyka kolejnych powikłań zakrzepowo-zatorowych w przyszłości. W wyborze strategii postępowania kierowaliśmy się racjonalną zasadą możliwie najmniej inwazyjnej procedury interwencyjnej, ograniczającej ryzyko kolejnego, prawdopodobnie bardziej rozległego udaru, podobnie jak prewencyjne zabiegi endarterektomii tętnic szyjnych lub zamknięcia przetrwałego otworu owalnego u dorosłych pacjentów po udarach mózgu.

Uszko lewego przedsionka o patologicznym palczastym kształcie, zostało torakoskopowo dwukrotnie podwiązane z zastosowaniem niezależnych pętli endoskopowych, wprowadzonych metodą oddzielnego nakłucia klatki piersiowej, bez powikłań. Pozostawiono niewielki margines niezamkniętego uszka lewego przedsionka ze względu na ryzyko zawężenia gałęzi okalającej lewej tętnicy wieńcowej. W okresie średnio odległej obserwacji nie wystąpiły nowe powikłania neurologiczne, dziewczynkę poddano intensywnej rehabilitacji celem usprawnienia niedowładu po przebytym udarze mózgu.

Torakoskopowe zamknięcie uszka lewego przedsionka okazało się skuteczną opcją możliwą do zastosowania klinicznego jako dodatkowa mało inwazyjna procedura w objawowym kompleksowym leczeniu zapobiegającym kolejnym mózgowym powikłaniom zatorowo-zakrzepowym u dzieci.

Słowa kluczowe: kardiochirurgia dziecięca, uszko lewego przedsionka, kardiomiopatia rozstrzeniowa, zespół niedoboru białka S, torakoskopia, prewencja udaru mózgu.

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Background

The haemodynamic utility of the left atrial appendage (LAA), an additional chamber arising from the anterolateral surface of the left atrium, which provides accessory volume in normal atrial systole, is thought to be minimal. On the other hand, the left atrial appendage is the source of most emboli in the systemic circulation accompanying contractility disturbances, that cause peripheral thromboembolic complications, including lethal strokes [1]. The risk of LAA thrombus is greater in patients with additional problems leading to stagnancy of blood in the atria, such as atrial fibrillation (AF) or congestive heart failure (CHF), as well as any systemic disease that predisposes to intravascular clot formation. Previous studies in the cohort of adult patients with atrial fibrillation have proved that over 90% of atrial clots appear in the LAA, and left atrial clots are responsible for over 90% of thromboembolic strokes in the AF group [1]. Similarly, patients with heart failure in the course of cardiomyopathies, who are potentially predisposed to atrial arrhythmias with AF, are at higher risk of LAA clot and resultant implications for the systemic circulation. Patients with various forms of thrombophilia, including protein S deficiency (PSD) syndrome, are at higher risk of life-threatening thrombosis, which seems to be additionally magnified by the potential of clot formation in the lumen of a pathological left atrial auriculum.

The pathophysiology and treatment of thromboembolic complications in children with heart failure appear similar to those observed in the adult population, but an additional troublesome factor influencing the therapy is intolerance to anticoagulation/antiaggregation medication. The risk of arterial emboli in paediatric patients, with their most disabling complications of central nervous system origin, especially if there are accompanying non-cardiac risk factors (thrombophilia), needs prophylaxis and treatment. Herein we present minimally invasive additional palliative surgical treatment which we introduced in a child with the diagnosis of protein S deficit and dilative cardiomyopathy (DCM), who previously suffered peripheral thrombosis with disabling stroke and underwent thrombolytic/anticoagulation treatment prior to thoracoscopic obliteration of an abnormal left atrial appendage (TOLAA) aimed at reducing the potential for risk of thromboembolic complications.

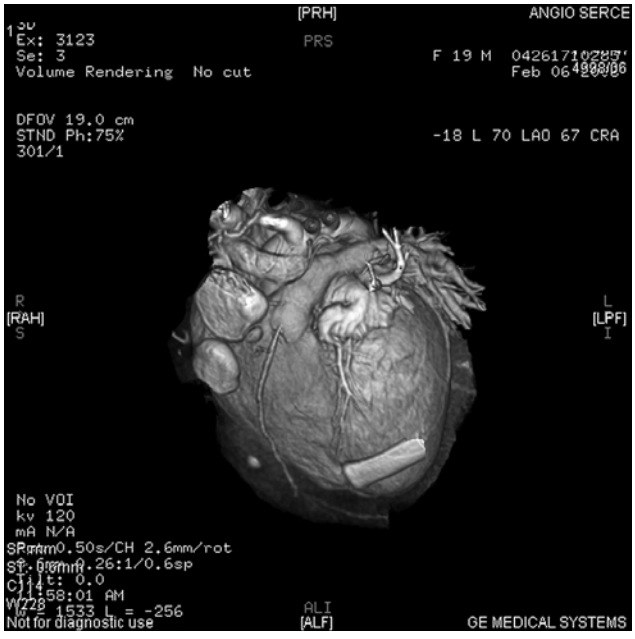

Fig. 1. Angio-CT scan that shows pathologically elongated and dilated LAA with lacunar peripheral segments and hypertrophied lacunar walls

Case report

The female child M.M., age 2 years, body weight 14.5 kg, 85 cm, was admitted to the Department of Cardiothoracic Surgery, Children's Memorial Health Institute, Warsaw, Poland (IPCZD) with the diagnosis of dilative cardiomyopathy and LAA pathology, with periodical presence of thrombi in the lumen of the auriculum, with susceptible myocarditis and protein S deficiency. The child before admission suffered ischaemic stroke of the right hemisphere with left partial paralysis, innominate vein and femoral artery thrombosis, and symptoms of heart failure deterioration. The echocardiography examination showed the presence of a large, fresh thrombus in the lumen of an enlarged left atrial appendage, with concomitant enlargement of the left ventricle and impaired contractility of the heart. The left ventricle ejection fraction (LVEF) was diminished to 30%, with grade 2 mitral and tricuspid insufficiency. The peripheral Doppler showed right femoral artery and innominate vein thrombosis. Intravenous thrombolytic therapy was administered immediately with recombined plasminogen activator (Actylise, Boehringer Ingelheim, EU). In the next 24 hours the child improved her neurological status, with residual symptoms of weakness of the left leg and arm muscle, and the LAA thrombus was dissolved. The continuation of intravenous heparin therapy resulted in recanalization of the left femoral artery and innominate vein. Transoesophageal echocardiography (TEE) showed pathology of the LAA, with enlarged volume and impaired contractility, lacunar and spongy wall structure, which was confirmed in the computer angio-tomography (Fig. 1). These imaging techniques enabled calculation of the digital shape LAA pool as a percentage of the entire left atrial body, which was recorded as 55%. After primary rejection of aspirin (ineffective in PSD syndrome) the girl was referred for chronic oral anticoagulation therapy with acenocoumarol, with great efforts to maintain the INR ratio between 2 and 3. Physiotherapy aimed at treatment of neurological impairment was introduced in the paediatric scheme. In the coagulation system laboratory investigations elevated activity of protein C was found (191%, norm: 70% to 140%), and decreased free protein S antigen (Ellis method, 55%, norm: 70% to 130%). Coagulation tests of both biological parents were carried out, and reduction of protein S antigen was confirmed in both individuals, which proved the monozygous form of the protein S deficiency syndrome. After the analysis the child was referred for thoracoscopic minimally invasive obliteration of pathological LAA.

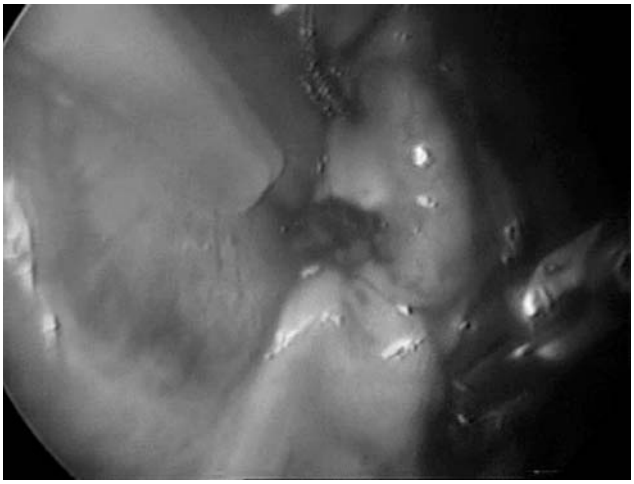

Fig. 2. The LAA gently grasped through the loop of the suture was obliterated with two endoscopic loops in its middle and basal segments. The pericardium was opened over the phrenic nerve and pulled downward for better exposure

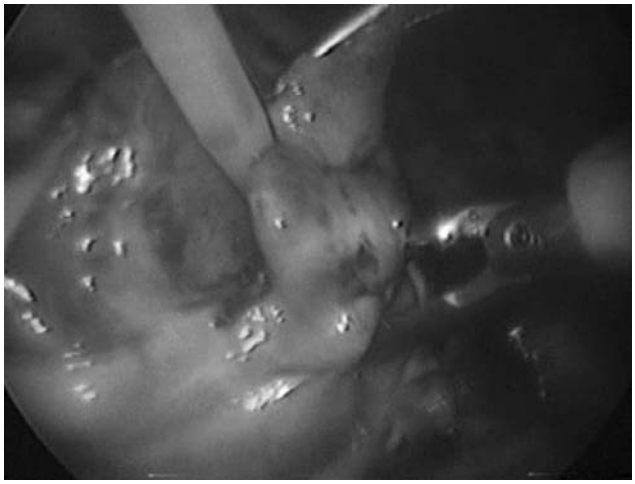

Fig. 3. There was left a safe margin of the LAA under the area of exclusion because of potential risk of turning down of the interatrial groove with LCx coronary artery

The procedure

The child was prepared for thoracoscopy in a typical manner; anticoagulation therapy with acenocoumarol was replaced with heparin before the operation. The thoracoscopy was carried out in modified general anaesthesia with selective intubation of the right main bronchus. The girl was placed on the operative table in a classic position suitable for left anterior thoracotomy, with oblique elevation of the left thorax. Three paediatric 5 millimetre soft expandable thoracic ports (5 mm Cannula with Radially Expandable Sleeve, Tyco, EU) were installed under control of the endo-camera (Videocamera 884 TE, Stryker, USA). Insufflation of 5 mmHg carbon dioxide was carried out (40 Light Flow Insufflator, Stryker, USA), with satisfactory collapse of the left lung and good exposure of the left side of the pericardium. The thoracoscopic instruments were introduced to the thorax (Stryker Q 5000, USA). The pericardial sac was opened longitudinally starting from the area of the pulmonary artery, parallel and above the left phrenic nerve to protect the nerve from injury or paralysis with electrocautery or extensive tension. The pericardial incision was prolonged both cephalad and to the right ventricle. The lower margin of the pericardial window was pushed downwards, which gave good exposure of the LAA and the interatrial groove with the circumflex branch of the left coronary artery (LCx). The manoeuvres over the LAA were very gentle to avoid its additional trauma, in view of the expected fragility and potential for mobilization of residual micro-clots. With continuous monitoring of ECG and systemic pressures the digital pathological structure of the entire LAA was doubly ligated with endoscopic loops (Surgitie Loop 2-0, Auto Suture, USA), which were inserted through a separate puncture of the thorax (Fig. 2). There was left a limited margin of the LAA under the area of exclusion because of potential risk of turning down of the interatrial groove with coronary flow disturbances in the LCx artery (Fig. 3). After the final haemostasis we left a pericardial window to evacuate effusions and prevent a tamponade. A chest tube was inserted, sparing the anterior port incision. The other incisions were closed in layers with cosmetic sutures and sterile dressing. The child was extubated immediately on the operating table after the procedure without complications. The girl in a stable condition was transferred to the postoperative care unit, with continuation of recovery in cardiac surgery and cardiology units.

The ECG screening showed no symptoms of ischaemia or arrhythmia. In the postoperative echocardiography and TEE complete obliteration of the LAA was found with no fresh clots over the exclusion line as well as no puckering of the LA wall dome. The contractility of the heart was similar to that observed preoperatively, with improvement in further controls. The heparin was exchanged for acenocoumarol to be continued for the next six months because of treatment of protein S deficiency as guidelined, and stopped. The child left the institution for outpatient postoperative rehabilitation 29 days after the procedure. Present mid-term follow-up time (18 months) is free of any neurological or thromboembolic events. The child is free of any anticoagulants and has improved her neurological condition.

Discussion

The function of LAA is still not fully understood and its physiological significance has been studied in several trials [1]. The most important role of LAA is as the site of release of atrial natriuretic factor (ANF), which has natriuretic, vasodilatory and diuretic properties. The analysis of LAA in animal models showed the role in water intake regulation in hypovolemia (mechanisms dependent on ANF and its prohormones concentration and release), determination of haemodynamic response to volume or pressure overload and regulation of cardiac output, the lack of which may promote heart failure [2]. Many studies have shown the association between LAA dysfunction, mainly in AF, and previous systemic embolic

events with primary cerebral thromboembolism. Moreover the SPAF III study demonstrated prospectively the role of LAA malfunction for future embolic events [3]. Anatomical abnormalities of the left atrial appendage, such as LAA hypertrophy and dilation with its enlargement in the course of congestive heart failure and dilative cardiomyopathy, cause structure-dependent dysfunction with flow patterns that predict clot formation. Nevertheless, the multilobed structure of a healthy, but naturally enlarged LAA, which is in fact a "blind sac", may predispose to local thrombosis and systemic embolization in abnormal blood flow or clotting path pathologies.

Protein S deficiency is a genetic trait classified in the group of clotting disturbances that predispose to venous clots. The exact role of genetic protein S deficiency (PSD) in arterial thrombosis and thromboembolic complications (stroke, heart attack, peripheral artery clots) is unclear, but there are some new reports that suggest the disease could play a role [4, 5]. In the clotting process protein S serves as a cofactor of protein C, which inactivates the active form of factors V and VIII, enabling the conversion of factor II (prothrombin) to the active form (thrombin). According to genetic studies of protein S and its function, at a special risk of arterial thrombosis are homozygous patients with prothrombin gene mutation, like the patient and her family we presented above. In our case the clinical manifestation of PSD was bilateral venous and arterial thrombosis, with clot evidence either in the left atrial appendage or in the femoral artery. Because the child had no left-to-right shunt, there was clear coincidence between the LAA clot and subsequent ischaemic stroke.

Echo imaging enables easy visualization of the left atrium, but more precise visualization of the LAA is possible only in TEE. The left atrial spontaneous echo contrast or "smoke" is known as the precursor of the atrial thrombus in TEE, so we needed the angio-CT technique to prove the evidence of the clot and abnormal structure of the appendage and its walls [4]. Both these techniques were used to diagnose the presence of the thrombus in an abnormal structure of the LAA, which was the basis for systemic thromboembolic complications in our patient [7].

Anticoagulation therapy with acenocoumarol (and optionally warfarin), although highly effective in protection against ischaemic stroke in high-risk patients, is associated with significant risk of dangerous bleeding, with the most disabling intracranial haemorrhage [8]. At a higher risk of another stroke are those patients who demonstrated previous thromboembolic complications of cardiac origin and haematological complications with contraindications for anticoagulation therapy [1].

There are still a great many patients, including children and young adults, in whom the anticoagulants are poorly tolerated, with great efforts to maintain the balance between the therapeutic effects of acenocoumarol, and minimal risk of side effects while treated continuously as recommended. The options for patients illegible for acenocoumarol are: abandon the therapy and accept the risk of thromboembolic complications, therapy of lower dosage or antiaggregation treatment with aspirin [8]. The last option was *a priori* excluded as an ineffective in the case of our patient with PSD syndrome, which does not prevent the child having another stroke.

We finally considered that if the left atrial appendage could be obliterated safely in a minimally invasive technique, the risk of another central nervous system incident should be lessened with relatively low side effects and discomfort of the procedure. The final decision to proceed with thoracoscopic appendage obliteration in the child was easier because of, apart from the anatomical indications, the following features:

1. Medical failure and troubleshooting anticoagulation therapy with acenocoumarol requiring the international normalized (INR) ratio over 2 (between 2 and 3).
2. The presence of additional risk factors such as prior embolic episode with neurological deficits and recent congestive heart failure deterioration.
3. Transoesophageal echocardiography showing no atrial clot in the LAA while on the procedure.

The concept itself of a prophylactic procedure to reduce the risk of further stroke in patients after neurological incidents is not so unique, e.g. closure of patent foramen ovale or carotid endarterectomy in adult patients. Surgical exclusion of LAA was a well established, safe and easy procedure at the time of open heart surgery of different indications, which required direct vision extracardiac ligation, intracardiac plication or amputation with a stapling device. Minimally invasive techniques were successfully adopted for thoracoscopic LAA obliteration in adults, but to the best of our knowledge are rare so far in the paediatric population [9].

Minimally invasive thoracoscopic interventions are attractive surgical options for paediatric patients (e.g. patent arterial duct closure (PDA), vascular rings division, thoracic interventions, thymectomy). Accordingly thoracoscopy for LAA obliteration could be performed as an independent procedure, without any intracardiac invasion or the need of cardiopulmonary bypass. Apart from the reduction of operative trauma, TOLAA provide the obliteration of LAA with necessary gentle manipulation to avoid mobilization of micro-clots undetectable in preoperative imaging [9]. In the presented case we used two forthcoming endo-loops for complete closure of the LAA, starting from the peripheral ligature. The arguments were to avoid aggressive tension at the basal segment of the auriculum to minimize the risk of a tear. Another was to diminish the risk of long-term clot formation after the TOLAA if there is a smooth surface with no puckering of the remaining atrial dome at the base of the obliterated appendage.

The position typical for left anterior thoracotomy enabled precise manipulation with thoracoscopic tools in a small paediatric pleural cavity and improved visualization following the golden rule of trigonal position of thoracic ports. Selective intubation and insufflation with carbon dioxide (CO_2) under the pressure of 5 mmHg provided effective lung collapse with good exposure of the left pericardium, without haemodynamic deterioration while on the table. The left phrenic nerve was easy to identify, which provided direct incision of

the upper segment of the pericardium to avoid its injury. The second key point was the left circumflex coronary artery (LCx) in the atrioventricular groove, which should be carefully identified before the ligation of LAA in a manner to avoid any tension over the coronaries and surrounding tissues. After the final haemostasis with cautery the left pleura was drained in a typical manner via the anterior incision, previously for expandable port installation. The skin over mini-incision wounds was closed with cosmetic absorbable sutures.

The postoperative TEE proved the complete exclusion of the appendage with no clot in the remaining segments of the left atrium, as indicated. However, prolonged medical therapy was necessary because of PSD, according to haematological considerations, for the next 6 months after the procedure. Therefore acenocoumarol was continued with the therapeutic INR ratio maintained over 2 during the time and stopped, with adequate physical rehabilitation to improve neurological deficits.

Conclusions

In summary, the presented case of thoracoscopic obliteration of the LAA appears to be a feasible option that can be introduced clinically in the future as an additional minimally invasive surgical procedure in the complex prevention of thromboembolic stroke in paediatric patients. The patients we expect to gain a benefit are children with LAA dysfunction and potential for thrombus formation as well as systemic arterial thromboembolism. This coincidence of clinical features could appear as an effect of anatomical variation of the LAA structure and pathological anomalies in the course of congestive heart failure with hereditary clotting disturbances, both with a risk of atrial arrhythmias or intraluminal appendage clots.

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