PARADOXICAL EMBOLISM

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A paradoxical embolus is one that arises in the systemic veins or right side of the heart and crosses into the systemic arterial circulation through such a communication as a septal defect. The diagnosis may be established by finding the embolus caught in transit through the opening, or in other cases a presumptive diagnosis may be made: here it is necessary to demonstrate a source of emboli in the systemic venous system, an abnormal communication between the venous and arterial circulations, systemic arterial emboli, and the absence of an embolic source in the pulmonary veins, left heart, or systemic arteries. Johnson reviewed the published material in 1951 and collected 40 verified and 46 presumptive cases. Two more verified cases are reported here and the recent reported cases are reviewed.

CASE REPORTS

Case 1. A 50-year-old man was admitted to the Manchester Royal Infirmary for an abdomino-perineal resection of carcinoma of the anal canal. Post-operatively he became breathless and cyanosed. He had suffered from chronic bronchitis for seven years but now responded poorly to broncho-dilator drugs, oxygen, and digoxin. In addition to airway obstruction he now had pulmonary crepitations, triple rhythm, and an enlarged liver. Five weeks after the operation he complained of a sudden stabbing and cramping pain in his chest, lost consciousness, and died six hours later.

At necropsy the heart showed dilatation of all chambers. An elongated piece of thrombus, branched at one end, was lodged in a patent foramen ovale, about 3 cm. lying loose in each atrium (Fig. 1). No other thrombus was seen in the heart, and the myocardium and coronary arteries were normal. Both main pulmonary arteries and many of their branches contained coiled thrombus. The lungs showed oedema and congestion but no obvious infarction. There was thrombosis of both femoral veins and the prostatic venous plexus. The left kidney contained a small recent infarct, and the liver showed chronic venous congestion. No residual tumour was found, the operation wounds had healed well, and a pelvic colostomy was patent.

Microscopically there was no reaction to the emboli in the largest pulmonary arteries, but other pulmonary emboli were completely penetrated by fibroblasts and capillaries. The bronchi showed chronic inflammation, goblet cell proliferation, and squamous metaplasia, and there was moderate emphysema. The other macroscopic findings were confirmed.

Case 2. A man aged 50 was admitted to Manchester Royal Infirmary in a semi-conscious state having been found collapsed in the street. While walking along the road he had suddenly lost the use of his left arm and leg. He sat down, but overbalanced and remembered nothing more. On examination he had a left hemiplegia, pulmonary oedema, and expiratory rhonchi. A systolic murmur was heard in the mitral and aortic areas. The blood pressure was 185/110 mm. Hg, and an electrocardiogram showed left bundle-branch block. For many years he had had difficulty in breathing, and three months previously he had suffered an acute attack of breathlessness which lasted four days. Three similar attacks had occurred since. Four days after admission his blood pressure fell suddenly to 90/50 mm. Hg, but soon recovered to 180/100 mm. Hg. Eleven days after admission he suddenly became very breathless and died within a few minutes.

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FIG. 1.—Case 1. The heart opened from behind, showing a thrombotic embolus lodged in the foramen ovale and extending into both atria.

At necropsy there was a right cerebral hæmorrhage, with slight brown staining of the surrounding brain tissue. The heart weighed 480 g. and showed hypertrophy of the left ventricle. The myocardium otherwise appeared normal, as did the endocardium and heart valves. The coronary arteries and aorta showed minimal atheroma. Extending into both atria there was an elongated branched thrombus 8 cm. in length gripped at its mid-point by the margins of the foramen ovale. The lungs showed slight congestion and emphysema, and the bronchi contained tenacious mucus. Both pulmonary arteries and their branches contained thrombotic emboli, some adherent to the wall. There was thrombosis of the left deep calf veins. Both kidneys, but especially the right, were reduced in size by coarse scars which had a flattened base. Other organs were normal.

Histological examination of the lungs showed many small areas of congestion and hæmorrhage but no necrosis. There was early organization of some emboli, slight emphysema, and the mucous gland and goblet cell hyperplasia of chronic bronchitis. The renal scars showed the changes of chronic pyelonephritis. Other gross findings were confirmed.

DISCUSSION

Cases of paradoxical embolism additional to those reviewed by Johnson are listed in Tables I and II. Verified cases now number 54 and presumptive cases 56. In almost all the abnormal communication is a patent foramen ovale. Valvular competence of the foramen provides no protection, for the embolus passes from right to left. A ventricular septal defect or a patent ductus arteriosus should present an equal opportunity for paradoxical embolism, but there are only two reports of emboli traversing a ventricular septal defect (Birch, 1945; Richards and Cohn, 1954) and one of embolism of the ductus (Fruhling and Marcoux, 1953). This is presumably because these conditions are much rarer than a patent foramen ovale, especially at the average age of the verified cases of paradoxical embolism (53 years). Scammon and Norris (1918) found the incidence of anatomical patency of the foramen ovale in the general adult population to be 28 per cent.

TABLE I
EMBOLUS *IN SITU* IN FORAMEN OVALE

Author	Age (yr.) and sex	Primary condition	Source of embolus	Pulmonary condition	Site of other paradoxical emboli	Notes
Robinson (1950) ..	77 M	Operation for benign prostatic hypertrophy	Right femoral vein	Pulmonary emboli and infarction	None	Thrombus 10 cm. long
Bigelow (1953) ..	69 M	Ureterolithotomy	? Right calf veins	Pulmonary emboli and infarction	Recent renal infarct	Thrombus 3.5 cm. long
Elliott and Beamish (1953) Case 1	66 M	Gastrectomy for duodenal ulcer	Femoral veins	Pulmonary emboli and infarction	None	Thrombus 10 cm. long
Case 2	24 F	Puerperal sepsis	Left common iliac, left hypogastric, and right femoral veins	Pulmonary infarcts	Septic hepatic and renal infarcts; paradoxical air embolism to cerebral vessels and coronary arteries	Thrombus 5.3 cm. long
Fruhling and Marcoux (1953) Case 1	55 M	Tabes; syphilitic aortitis; carcinoma prostate	Iliac veins	Pulmonary embolus	None	Thrombus 5 cm. long
Case 2	58 F	Phlebitis and pulmonary infarct	Left femoral veins	Pulmonary embolus and infarct	Recent cerebral embolus and infarct	Thrombus 8.5 cm. long
Case 3	67 F	"Asystolic"	Not stated	Pulmonary embolus	Recent renal infarcts	Thrombus 7 cm. long
Case 4	65 F	Pyometra; operation for subacute appendicitis	Not stated	Pulmonary embolus and infarct	None	Thrombus 2 cm. long
Case 5	75 M	Cardiac asthma; ? hypertensive; chronic bronchitis	Not stated	Pulmonary embolus and infarct	Recent splenic infarct	Thrombus 4.5 cm. long
Case 6	8 days F (pre-mature)	Pyrexia, vomiting; superior sagittal sinus thrombosis	? Umbilical vein	Pulmonary embolus	None	Paradoxical embolus (2.5 cm. long) in ductus arteriosus
Soloff and Zatuchni (1956)	49 F	Obesity	? Leg veins	Pulmonary emboli	Renal infarct	Thrombus 5 cm. long
Zettner (1959)	55 F	Hypertension; old cerebral and myocardial infarction	Not identified	Pulmonary thrombosis	No recent infarcts	Two separate thrombi knitted together, measure 32 cm. in all
This paper Case 1	50 M	Resection of carcinoma of anal canal	Femoral veins	Pulmonary emboli	Recent renal infarct	Thrombus 6 cm. long
Case 2	59 M	Cerebral hæmorrhage	Left calf veins	Pulmonary emboli	None	Thrombus 8 cm. long

Given a source of emboli and a veno-arterial communication, paradoxical embolism also requires the reversal of the normal pressure gradient from left to right. The usual cause of this is pulmonary hypertension due to antecedent pulmonary emboli. Pulmonary emboli or infarcts were present in 83 of 101 cases in which the lungs are described. Most of those in which there was no evidence of pulmonary emboli had other lung disease, such as pneumonia, tuberculosis, or emphysema, but in the cases of Jacobi, Kenler, and Silverman (1934) and Anderson (1946) the lungs and their vessels appeared quite normal. Porter (1941) suggested that in such cases the embolus may first block the tricuspid valve by coiling over it and then pass through the foramen ovale when the right atrial pressure exceeds that in the left.

Emboli caught in the foramen ovale have usually been regarded as no more than an interesting confirmation that paradoxical embolism may occur, and death has usually been attributed to a final massive pulmonary embolus. Elliott and Beamish (1953), however, believe that when present the foramen may provide an important safety valve in cases of pulmonary embolism and that plugging of this gap by a further embolus may often be the terminating factor.

TABLE II
PRESUMPTIVE PARADOXICAL EMBOLI

Author	Age (yr.) and sex	Primary condition	Source of emboli	Pulmonary condition	Sites of paradoxical emboli	Notes
Anderson (1946) ..	42 F	Hysterectomy for metropathia	Not stated	Lungs and pulmonary arteries normal	Aorta; recent infarcts in spleen and kidney	Foramen ovale slit-patent
Ross and Sprague (1948)	69 M	Operation for benign prostatic hypertrophy	Left deep femoral vein and prostatic plexus	Pulmonary emboli and infarction	Renal arteries	Foramen ovale admitted pencil
Richards and Cohn (1954)	51 M	Ventricular septal defect, "cyanose tardive"	Thrombosed pulmonary artery aneurysm; left popliteal vein	Infarction of right lung	Splenic, renal, superior mesenteric, and popliteal arteries	Ventricular septal defect 2.5 x 2 cm.; foramen ovale slit-patent
Sauer (1955)	29 F	Childbirth	Not identified	Pulmonary emboli	Middle cerebral and internal carotid arteries	Foramen ovale admitted 0.6 cm. probe
Keeley (1957)	69 F	Ligation of thrombosed varicose saphenous vein	Left internal iliac vein and inferior vena cava	Pulmonary emboli	? Leg and cerebral arteries; (leg amputated; head not examined)	Foramen ovale 1 cm. diameter
Horlick (1961) ..	39 F	Thrombophlebitis	Deep calf veins	Pulmonary emboli	Aortic bifurcation	Patient recovered
De Swiet (1962) ..	23 F	Childbirth	Not stated	Pulmonary infarction	Left subclavian and middle cerebral arteries	Patient recovered
Blanck and Olanders (1963) Case 1	60 M	Pulmonary tuberculosis	Left calf veins	Pulmonary emboli	Right coronary artery	Foramen ovale admitted pencil
Blanck and Olanders (1963) Case 2	62 F	Operation for hernia	Right calf veins	Pulmonary emboli	Left coronary artery	Foramen ovale admitted pencil
McCall (1963) ..	53 F	Pharyngitis; ? varicose veins	Femoral veins	Pulmonary emboli	Left carotid, left femoral, and both renal arteries; infarction of spinal cord	Foramen ovale admitted pencil

Paradoxical embolism has almost always been diagnosed at necropsy, but Thompson and Evans (1930), Porter (1941), Horlick (1961), and De Swiet (1962) were able to make the diagnosis in life. Their four patients all survived. The clinical diagnosis is based upon evidence of systemic venous thrombosis and arterial embolism in the absence of such cardiovascular disease as myocardial infarction, mitral stenosis, atrial fibrillation, or bacterial endocarditis.

Attention has so far been confined to thrombotic emboli but paradoxical emboli consisting of other material, such as fragments of liver and cerebellar tissue, shrapnel, and air, have been reported. Metastatic tumours and abscesses are more difficult to accept as having derived from paradoxical emboli, because small intermediate foci in the lungs or transpulmonary passage can never be fully excluded. However the association of cerebral abscess with congenital heart disease suggests that this may be due to paradoxical emboli bypassing the normal filtering mechanism of the pulmonary capillary bed (Abbott, Lewis, and Beattie, 1923). Tyler and Clark (1957) found the incidence of cerebral abscess fairly constant (2%) in all forms of congenital heart disease in which it is anatomically possible for venous blood to reach the systemic circulation without passing through the lungs.

SUMMARY

Two cases of thrombotic embolus arrested in a patent foramen ovale are described. Both were middle-aged men who also had pulmonary emboli. Reports of 52 similar cases have been published. As well as venous thrombosis and an abnormal vascular communication, reversal of the normal left-to-right pressure gradient is required, and the usual cause of this is antecedent pulmonary

embolism. The communication is usually a patent foramen ovale, but ventricular septal defects and the ductus arteriosus have been involved. Clinical diagnosis is rare.

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