

How common is cholesterol embolism?

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Abstract

Histological sections of spleen and both kidneys from 372 necropsies were examined for the presence of cholesterol emboli. These were identified in nine (2.4%) cases and the clinical histories of these cases were reviewed. All the subjects with cholesterol emboli were older than 60 years and eight out of nine were male. Lesions of differing ages were found in individual cases, suggesting that the process of embolism was recurrent. Two of the cases had undergone arteriography procedures in the month before death and, if these were excluded, then the incidence of "spontaneous" cholesterol embolism was 1.9%. This incidence is much lower than that of previously published studies and may be due to a lower incidence of cholesterol embolism in Britain compared with North America or a decrease in incidence over the past two decades. In three of the subjects with cholesterol embolism the cause of death could be related to systemic atherosclerosis, but in the other six cases there was no apparent correlation between the finding of cholesterol embolism and the cause of death. The clinical relevance of the histological finding of cholesterol embolism can only be assessed in conjunction with clinical information.

Embolisation of cholesterol crystals from ulcerated atherosclerotic plaques is well known. Disseminated cholesterol emboli may produce a systemic illness^{1,2} with livedo reticularis of the lower limbs^{3,4} and splinter haemorrhages of the nails⁵; the features may mimic polyarteritis nodosa.^{6,7} Cholesterol embolism has also been documented as a cause of renal failure,^{8,9} acute pancreatitis,¹⁰⁻¹² gastrointestinal haemorrhage,^{13,14} bowel strictures^{15,16} and spinal cord infarction.¹⁷ It can occur spontaneously but is also seen as a complication of aortic surgery,¹⁸ balloon angioplasty,¹⁹ and various angiographic procedures,²⁰⁻²² including aortography,²³ left heart catheterisation,²⁴⁻²⁶ renal arteriography²⁷ and mesenteric angiography.²⁸ Some reports have suggested that embolisation may be facilitated by thrombolytic treatment^{29,30} which may prevent thrombus forming over ulcerated plaques; discontinuation of treatment may reverse the symptoms.³¹

Panum published one of the first descriptions of the pathology of cholesterol embolism in 1862³² and since then there have been several more comprehensive reports,³³⁻⁴³ but few of these studies examine the

prevalence of cholesterol embolism. Flory examined histological sections from 267 necropsies and found that 3.4% of the cases had cholesterol emboli³³; all these cases had been selected because the necropsy had shown "advanced arteriosclerosis" in the aorta. Other series with selected cases coming to necropsy include one restricted to subjects older than 60 years³⁷ and another on subjects who had had arteriographic procedures.⁴² Maurizi *et al* looked at 100 consecutive necropsies and found that four contained cholesterol emboli in the lower extremities,⁴⁰ but this is a North American study and was performed 23 years ago so it may not be relevant to a British population today.

Some estimate of the prevalence of cholesterol embolism is useful in the interpretation of biopsy specimens: a single cholesterol embolus in a vessel of a renal biopsy specimen would be of little relevance if such embolism was common, but if cholesterol embolism was rare then it would have to be regarded as a possible cause of the renal dysfunction. Preston *et al* reported 14 cases of cholesterol emboli in a series of 334 renal biopsy specimens from patients older than 65 years,⁴⁴ but all these patients had renal failure before biopsy. Disseminated cholesterol embolism has been recognised as the cause of disease after identification in biopsy material^{45,46} but these patients had clinical features, such as livedo reticularis, which provided confirmatory evidence. This study aimed to examine a large, apparently unbiased, sample of histological specimens taken at necropsy to produce an estimate of the current prevalence of cholesterol embolism in Britain.

Methods

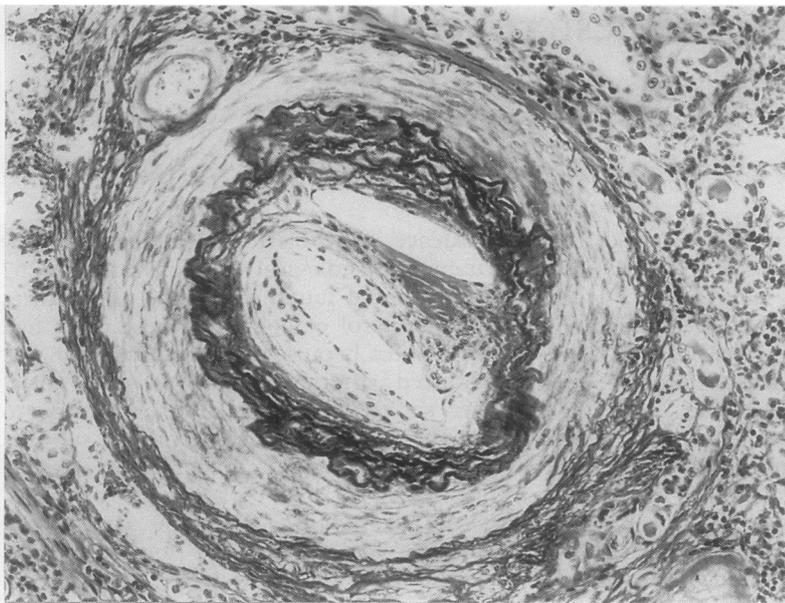
The histological material from all necropsies performed at the Royal Hallamshire Hospital between 1987 and 1990 was reviewed. Cases with a slide of the spleen and each kidney were used in the study. The haematoxylin and eosin stained slides of these organs were screened at a final magnification of $\times 100$ for the presence of cholesterol emboli using the histological features described by Kennedy⁴³ as criteria for identification. In cases where cholesterol emboli were found the slides were re-examined, the number of lesions was recorded, and assessment of lesional age was made using the features described by Flory³³ and Snyder and Shapiro.³⁹ The external diameter of all vessels containing cholesterol emboli was measured. The clinical history of all positive cases was reviewed, together with the cause of death stated after necropsy.

The age and sex of all subjects coming to

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Fibrous tissue surrounding two cholesterol-crystal-shaped clefts in the lumen of an artery in the kidney (elastic van Gieson).

necropsy was recorded. The age distribution of the total necropsy population was compared with those necropsies with histology using the Mann-Whitney U test; the sex distribution of these two groups was examined using the χ^2 test.

Results

Necropsies ($n = 1838$) were performed during the study period on 1038 men (56%) and 800 women (44%) with a mean age of 66.5 years (range 10-99 years). Three hundred and seventy-two of these necropsies had slides of the spleen and both kidneys; 212 (57%) were from men and 160 (43%) from women with a mean age of 66.4 years (range 17-92 years). Cholesterol emboli (figure) were identified in nine cases (2.4% of those cases with appropriate histological material). The age distributions of these populations are given in table 1. There was no significant difference

Table 3 Number of lesions of different ages

Case No	Recent lesions (<3 days)	Giant cell lesions (3-6 days)	Fibrotic lesions (>6 days)
1	4	0	2
2	1	1	1
3	0	0	1
4	0	0	4
5	2	0	0
6	0	0	4
7	0	0	3
8	5	0	6
9	1	0	0
Total	13	1	21

($p > 0.5$) between the age or sex distributions in the group of necropsies with appropriate histology compared with all the necropsies. Tables 2 and 3 summarise the results in the positive cases. The median external diameter of vessels containing cholesterol emboli was 166 μm (range 71-536 μm). The two cases with antemortem angiography had each had left heart catheterisations four weeks before death.

Discussion

This is a retrospective study and so there are potential problems with bias in the sample of necropsies which had appropriate histology available. The selection of histological material was made by individual pathologists with no agreed sampling protocol, so it is possible that the cases with two slides of kidneys and one of spleen differed from the overall population of necropsies, but there was no significant difference in the age or sex distribution of the two populations. The causes of death in the two groups could not be compared as no suitable analytical framework could be devised.

Much of the data from this study confirm the features of cholesterol embolism reported previously.³³⁻⁴¹ Most (8/9) of subjects were male and all were older than 60. Lesions of differing ages were found in individual cases, suggesting that the process of embolism was recurrent. It was not possible to grade the degree of aortic atheroma from the subjective evaluation available in the necropsy reports, but most descriptions included the presence of

Table 1 Age distribution of study populations

Population	Number of cases in age division (years)							
	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89
All necropsies	29	56	54	107	224	457	533	333
With renal and splenic histology	4	9	12	26	50	87	115	61
With emboli	0	0	0	0	0	3	5	1

Table 2 Details of cases with cholesterol emboli

Case No	Age (years)	Sex	Number of emboli		Angiography?	Thrombolytic treatment	Cause of death
			Kidneys	Spleen			
1	62	M	5	1	N	N	Carcinoma of bladder
2	66	M	0	3	Y	N	Myocardial infarction
3	67	M	1	0	Y	N	Myocardial infarction
4	70	M	1	3	N	N	Carcinoma of bronchus
5	71	M	1	1	N	N	Myocardial infarction
6	73	M	1	3	N	N	Pulmonary embolism
7	77	M	0	3	N	N	Subarachnoid haemorrhage
8	79	M	8	3	N	N	Obstructive uropathy
9	81	F	1	0	N	N	Multiple injuries

extensive ulcerated atherosclerotic plaques.

The overall prevalence of cholesterol embolism in the kidneys and spleen in this study (2.4%) is lower than that found in the study by Maurizi (4%).⁴⁰ That study included biopsy specimens of the lower extremities which could have increased the number of cases detected, but 24 of the 25 cases had cholesterol emboli in the kidneys, 15 had emboli in the spleen, and all cases had emboli in either the kidneys or spleen. The prevalence in subjects 60 years and older in this study (3.4%) is much lower than the 17.6% reported by Gore,³⁷ a North American series performed 30 years ago. In Gore's study 12 of the 13 cases had emboli in the kidneys and 10 had emboli in the spleen. Two of the positive cases in this study had had left heart catheterisation four weeks before death, this is well recognised inciting factor for cholesterol embolism.²⁴⁻²⁶ If these cases are excluded then the prevalence of "spontaneous" cholesterol embolism in this study is 1.9%, which is lower than that of previous studies, and may indicate a lower prevalence of cholesterol embolism in Britain compared with North America or a decrease in prevalence over the past two decades. This low prevalence might suggest that cholesterol embolism in biopsy material is a clinically important finding, but the causes of death in this study do not support this. Three of the subjects died with myocardial infarction, and the cholesterol embolism could be regarded as a marker of severe atherosclerosis; the other deaths were from a variety of causes with no apparent relation with cholesterol embolism.

The main conclusion of this study is that cholesterol embolism is rare, even in selected populations such as subjects older than 60, but its clinical importance can be assessed only in conjunction with other clinical information.

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