CASE REPORT

Human coronary morphology after β radiation brachytherapy of in-stent restenosis

P H Grewe, T Deneke, C Hanefeld, K-M Müller


This case report discusses the human coronary morphological findings 18 hours after brachytherapy (β radiation) of an in-stent restenosis. Brachytherapy produced aseptic inflammation of the periadventitial connective tissue integrating the vasa vasorum in the acute phase. The stent neointima eight months after stenting and acutely 18 hours after radiation consisted of the same cellular components as human stent neointima of specimen not additionally treated with radiation. No evidence of necrosis or excessive fibrotic alterations of the arterial vessel wall have been found.

Intravascular radiation has been introduced as an effective therapy for in-stent restenosis. The histomorphological changes induced by the combination of mechanical force caused by angioplasty and ionising radiation have not been well described. Structural changes have only been studied systematically in animal models. Only one case report exists on the cellular morphological findings after γ radiation of an in-stent restenosis obtained from atherectomy material.

In this paper human coronary morphological findings 18 hours after brachytherapy (β radiation) of an in-stent restenosis are discussed.

CASE REPORT

A 61 year old woman with symptomatic coronary one vessel disease underwent stenting of a severe right circumflex (RCx) artery stenosis eight months before death. Unstable angina pectoris led to a diagnosis of in-stent restenosis one day before death which was redilated using a 2.75/15 mm cutting balloon followed by β radiation brachytherapy (Novoste Beta Cath System, 60 mm, 2.55 min radiation time, 18.4 Gy dose, 2 mm away from radiation source).

Eighteen hours after angioplasty, directly after withdrawing the arterial sheath, angina reoccurred and blood pressure dropped to 70/30 mm Hg and heart rate dropped to below 30 beats/min. Pericardial effusion was excluded by echocardiography and re-coronary angiography was initiated. During preparation, acute irreversible cardiac arrest and electromechanical discoupling was found. Emergency angiography revealed occlusion of the RCx distal to the region treated by brachytherapy. Actilysis therapy and one hour cardiopulmonary reanimation were unable to resuscitate the patient.

Signs of an old compact cardiac infarction scar with increased connective tissue were found on the lateral wall of the left ventricle. During postmortem angiography of the excised heart the RCx stent was identified.

A new adherent thrombus was detected in the region of the intervention (fig 1). Eight months after implantation the stent neointima was found to be dissected by many longitudinal dissections caused by the cutting balloon. An ulcer-like defect of the stent neointima was found 1 mm proximal to the stented, and now redilated, area (fig 1).

Proliferating myofibroblasts (smooth muscle cells) were found to be the major cellular component in the region of the stent neointima. Eighteen hours after intervention factor VIII positive cells (endothelial origin) can be detected on the luminal side of the stent neointima. CD3 positive T lymphocytes and CD68 positive macrophages accumulated in the stent neointima eight months after implantation.

In the region that was irradiated severe polymorphic inflammatory cellular infiltration was documented on the peri-adventitial side but no infiltration was seen in the arterial media or the vasa vasorum (fig 2). The aggregation of inflammatory cells was only visible in the region treated with β radiation and not in any of the regions proximal or distal, or in regions of the left anterior descending coronary artery. No

**Figure 1** Thrombus detected in the region of the intervention.

**Figure 2** Irradiated region showing severe polymorphic inflammatory infiltration on the peri-adventitial side but no infiltration in the arterial media or vasa vasorum.
necrosis of the vascular wall or oedematous swelling was seen as a consequence of the severe radiation necrosis.

DISCUSSION

Ionising radiation has effectively been applied in controlled studies as an adjunctive therapy option for de novo coronary stenosis and in-stent restenosis. As early as the beginning of the 1990s endoluminal radiation in atherosclerotic lesions was studied in animal models. In addition to experimental dosimetric studies, the morphology of tissue reaction on endoluminal radiation therapy was documented.

In our case, necropsy revealed thrombotic occlusion of the coronary vessel segment, which had been treated by brachytherapy, as the cause of acute myocardial infarction occurring one hour before death. The documented reactions of the vessel wall on intraluminal radiation in this reported case are comparable to the findings of animal studies. As shown in animal models brachytherapy leads to mild to severe aseptic inflammation of the peri-adventitial connective tissue, secondarily incorporating the vasa vasorum in the acute phase. Fajardo and colleagues found vasculitis of the vasa vasorum 28 days after radiation using a $^{32}$P source. In 14% of the animals studied, inflammatory reaction of the peri-adventitial tissue was documented eight months after brachytherapy. This polymorphic inflammatory response seems to smoulder for months and produces peri-adventitial scarring with occlusion of some vasa vasorum. Integrating our findings it seems as if the perivasal inflammatory reaction after brachytherapy may influence chronic vessel wall remodelling.

In this case report, the stent neointima 18 hours after radiation consisted of the same cellular components as human stent neointima of specimens not additionally treated with radiation. Eighteen hours after coronary angioplasty and brachytherapy, factor VIII positive endothelial cells were found remaining on the vascular lumen. This has not been documented in human specimens so far, indicating that the endothelial lining is not completely destroyed during angioplasty. This case displays no evidence of significant necrosis or excess fibrosis in the media which is comparable to animal studies with applied dosages between 7–56 Gy.

Implying differences in animal models, lack of an endothelial coverage of the vascular segment treated with radiation can be postulated.

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