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Evidence for macrophage-mediated defluorization of a Teflon vascular graft

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Polytetrafluoroethylene (PTFE) is a common biomaterial used for vascular grafts because it is regarded as a nondegradable material with good healing characteristics and a low complication rate, even as a long-term implant. XPS-investigation of a ruptured arterial PTFE-prosthesis with formation of a false aneurysm revealed loss of fluorine at the area of rupture, whereas fluorine was found in the morphologically intact areas in normal concentrations. Because macrophages, found in large number at the ruptured and degraded area, are capable of producing hydroperoxide radicals, it is assumed that the present case is an example of macrophage-mediated defluorization with subsequent rupture of the PTFE-prosthesis.

1. Introduction

Polytetrafluoroethylene (PTFE), which is regarded as nondegradable biomaterial, is widely used for arterial grafts [1–3]. The host reaction on the implanted material is composed of a mild inflammation, consisting of macrophages and some giant cells adjacent to the prostheses followed by an external collagenous capsule [4]. At the luminal site only a thin fibrin film was found. The complications most often reported are thrombosis, infections, and false aneurysms and less often, prosthetic dilatation [4–7]. The formulation of false aneurysms and prosthetic dilatation suggest that some degradation of the biomaterial may be possible. Therefore, a currently observed case of prosthetic rupture with formation of a false aneurysm was investigated morphologically and by X-ray photoelectron spectroscopy analysis for elemental composition of the biomaterial, giving strong evidence for defluorization of PTFE.

2. Materials and methods

2.1. Case report

A 64-years-old male patient haemodialysed for chronic renal failure due to glomerulonephritis for 11 years was presenting with an aneurysmatic dilatation of the arterial part of his artriovenous prosthesis on the left arm. The prosthesis (6 mm Gore-Tex^R – standard graft), which had been implanted for four years, was removed and replaced by a new one. Follow up to date has been without complications.

2.2. Morphological investigation

The explanted material together with the adherent tissue was fixed in 10% formaline and embedded in paraffin. 5 μm sections were cut and stained with hematoxylin and eosin (H&E) and elastica van Giesson (EvG), and examined by light microscopy. Representative areas of intact and severely degraded regions were marked for XPS-investigation.

2.3. XPS investigation

2.3.1. Principle

X-ray photoelectron spectroscopy (XPS) is a surface-sensitive method which determines the elemental composition except for hydrogen and helium, and the chemical states of the elements, e.g. the method distinguishes between differently bonded carbons like aliphatic (–CH2–), oxygen, and fluorine bonded carbon in the outermost layers (information depth is about 50 atomic layers).

This surface analytical method is based on the photoelectrical effect. The sample is irradiated with photons of known energy and the emitted electrons (so-called photoelectrons) are discriminated according their kinetic energy. The kinetic energies of the emitted electrons are characteristic of the elements and their chemical surrounding (binding states). With the help of the known excitation energy of the photon ($h\nu$) and the measured kinetic energy of the photoelectrons (E_{kin}), the binding energy of the electrons (E_{bin}) ejected from an element and the corresponding electron level

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can be calculated:

$$E_{bin} = h\nu - E_{kin} \quad (1)$$

2.3.2. Experimental

XPS investigations were performed using a SSX-100 X-probe spectrometer (Surface Science Instruments, Mountain View, CA, USA), which uses a monochromatic aluminium–potassium X-ray source (1486.6 eV). For all samples a spot size of 1000 μm was used, and an electron flood gun set at 24 eV to minimize charging effects. The survey spectra were measured with a pass energy of 150 eV and the elemental spectra with 25 eV. All binding energies were referenced by setting the maxima of the C 1s hydrocarbon photopeak of the samples of 285.0 eV. The acquisition times of the spectra were kept short (1 scan), since the embedding material (paraffin) was strongly outgassing in the vaccum chamber.

3. Results and discussion

Morphological investigation reveals a rupture of the PTFE prostheses with formation of an aneurysm with a fibrous wall. At non-degraded sites a fibrous capsule was found adjacent to the fibrous material. The space between the individual fibres of the material was filled with an amorphous material, probably proteins and some collagen fibres (Fig. 1). These healing characteristics are in agreement with the literature, where the formation of an external collagenous capsule in association with a chronic inflammation have been described, beginning after the first month, increasing in thickness with time and with the intensity of inflammation [4]. However, large interindividual differences in the healing of identical prostheses were observed as well as differences in infiltration of different areas of the same prosthesis [4].

Complications in the use of PTFE for vascular grafts are mainly thrombosis, infection, and false aneurysm as described in the present case. At the margins of the fibrous wall of the aneurysm the individual fibres of the prosthesis were disarranged and appeared reduced in number. In this area an intense inflammation, rich in macrophages and some multinucleated giant cells, was visible (Fig. 2). The defect in the prosthetic material observed and other reports of prosthetic dilatation suggest that degradation of PTFE may occur. Although GUIDOIN *et al.* [8] did not detect any chemical degradation of explanted PTFE for periods of up to 6.5 years using electron spectroscopy for chemical analysis (ESCA), and found only slight changes in the surface composition by increasing contact angles and the occurrence of specific bands within the FTIR-spectra, which were related to lipid and/or protein absorption, we performed a comparative analysis of the morphologically degraded PTFE with the intact PTFE areas.

The survey spectra of the intact and degraded prothesis are shown in Fig. 3. The intact material reveals 1s photolines of carbon, oxygen, and fluorine at binding energies of about 285, 532, and 689 eV. The C 1s

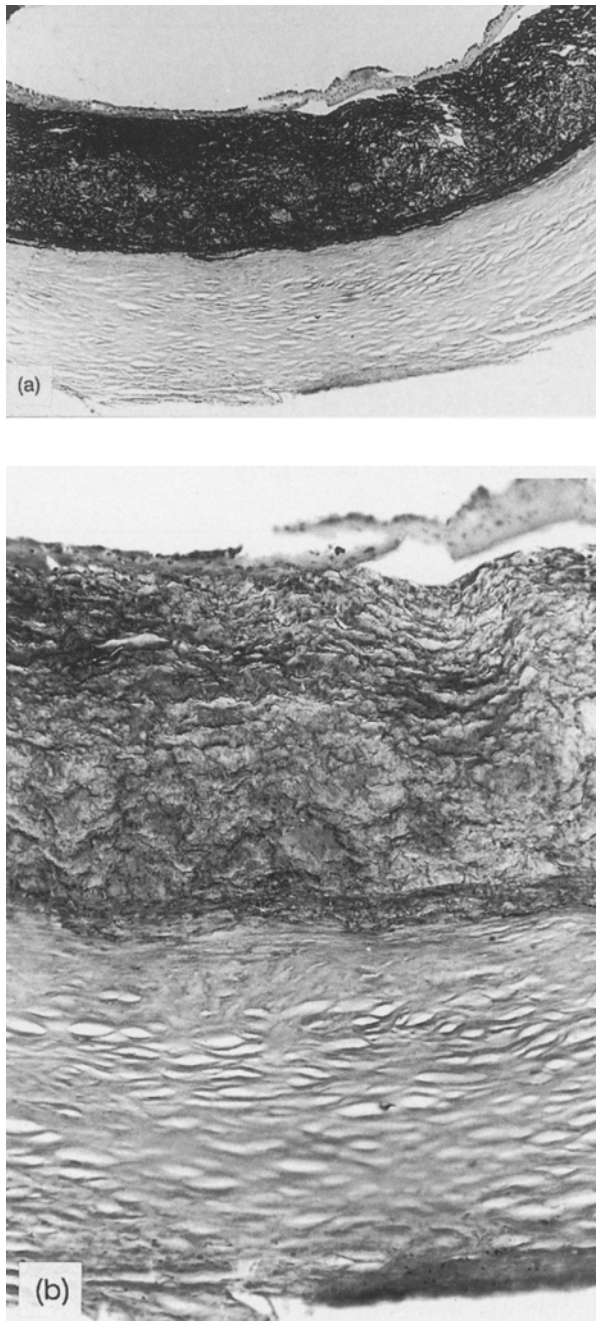

Figure 1 (a) Non-degraded area of the explanted prosthesis with a fibrous capsule (H&E) × 100. (b) Increased magnification × 400.

line is divided in a $-CH_2-$ and a $-CF_2-$ photoline because of the strong chemical shift of the $-CF_2-$ group compared to aliphatic carbon. The detection of the F 1s as well as the $-CF_2-$ line proves that the intact material is PTFE. The presence of a stronger aliphatic carbon– than –C–F– line results possibly from an excitation of the embedding material paraffin. In addition to the above mentioned photolines, nitrogen (N 1s) and silicon (Si 2s and Si 2p) can be determined. The detection of a significant amount of fluorine, a higher amount of oxygen, and the presence of nitrogen and silicon indicate decomposition of PTFE and adsorption of protein residues as well as silicon contamination at the surface of the prothesis. Table I shows the elemental composition of both samples. Fig. 4 illustrates the energy range of the C 1s photoline in more detail. While in the spectrum of the intact

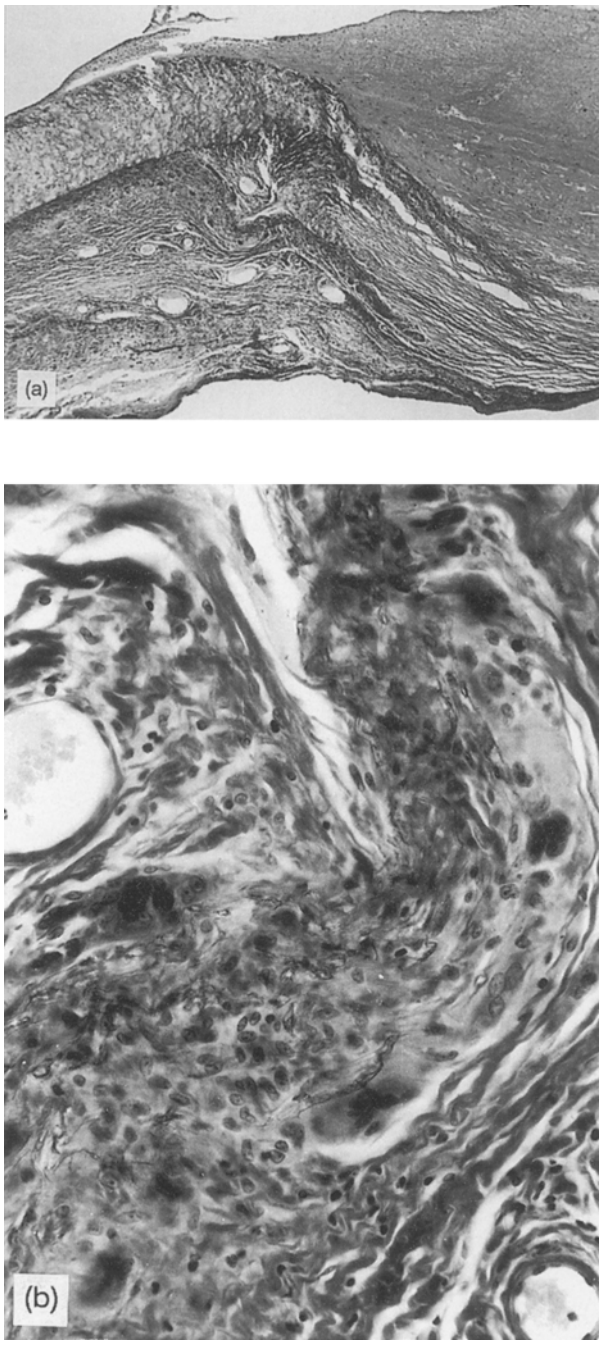

Figure 2 (a) Degraded area with abundant macrophages and some multi-nucleated giant cells (H&E) × 100. (b) Increased magnification × 1000.

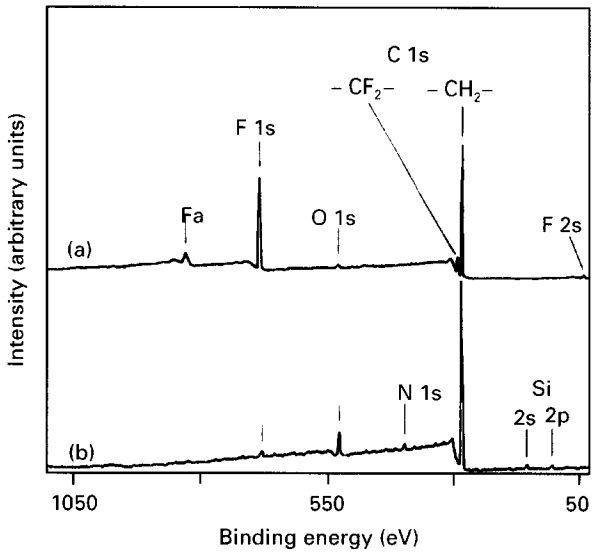

Figure 3 Survey spectra of the (a) intact and degraded (b) prothesis.

TABLE I Elemental composition of intact of degraded PTFE

Element	Intact	Degraded Prothesis
C	78,1	86,8
O	1,5	5,8
F	20,4	1,1
N		2,8
Si		3,5

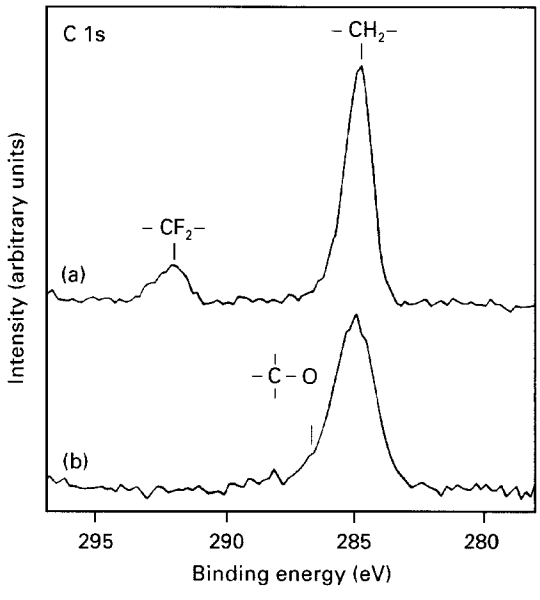

Figure 4 C1s spectra of the (a) intact and (b) degraded prosthesis.

sample the $-CF_2-$ photoline (binding energy: 292.1 eV) is clearly detected near aliphatic carbon (285.0 eV) the spectrum of the degraded sample reveals only an aliphatic and a C–O-bonded carbon (286.6 eV).

These data provide strong evidence that the loss of fluorine is the reason for the prosthetic defect. The presence of a large number of macrophages at the degraded PTFE site suggests a connection between defluorization and inflammation. Macrophages produce, as nonspecific cytotoxic agents, reactive oxygen products [9]. Although not proven as yet, it is an interesting hypothesis that macrophage-mediated oxygen radicals may cause such effects. The reason for the focal macrophage stimulation is unclear. However, some studies revealed bacteria on the luminal surface without a granulocytic inflammatory reaction [4, 7, 10, 13], however, they can stimulate macrophages. By light microscopy we did not find bacteria, but this does not exclude their presence because the detection rate of bacteria with light microscopy is low compared with other methods like scanning electrone microscopy [4]. Furthermore, local chronic inflammation of soft tissue as a complication of repeated puncture could cause macrophage accumulation and activation. Another possibility is surface differences of

the biomaterial causing local activation. More experimental data concerning surface characteristics of biomaterials and radical production of macrophages are necessary to understand these mechanisms.

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