Actinic arteritis of subclavian artery. Case report and literature review

Arterite actínica de artéria subclávia. Relato de caso e revisão de literatura

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Abstract

Several complications may occur as a consequence of adjuvant radiotherapy for cancer. One of these complications is actinic lesions of the subclavian artery in patients undergoing radiotherapy for breast cancer; however, there are few reported cases. In the present case report, we describe a case of right subclavian artery occlusion in a patient undergoing radiotherapy for breast cancer. Occlusion was treated by means of conventional artery bypass with interposition graft with polytetrafluoroethylene (PTFE). Our extensive review of the literature revealed 12 reported cases showing the different treatment options performed. We concluded that actinic arteritis of the subclavian artery is an uncommon condition; however, its presence should be considered in all patients with upper limb ischemia who underwent radiotherapy.

Keywords: subclavian artery; radiation effects; breast cancer.

Resumo

Diversas são as complicações possíveis da radioterapia na adjuvância do tratamento de neoplasias. Lesões actínicas de artéria subclávia em pacientes submetidos a este tipo de tratamento para neoplasia de mama são complicações conhecidas, porém com poucos relatos de casos publicados. No presente relato, descrevemos um caso de oclusão de artéria subclávia direita em paciente submetida à radioterapia para tratamento de neoplasia de mama, tratada com a revascularização convencional, com interposição de enxerto de politetrafluoretileno (PTFE). Na revisão da literatura realizada, foram encontrados doze casos descritos que evidenciaram diferentes opções terapêuticas. Concluímos que a arterite actínica de artéria subclávia é uma doença incomum, entretanto sua hipótese deve ser aventada em todos os pacientes com isquemia de membro superior já submetidos a tratamento de radioterapia.

Palavras-chave: artéria subclávia; efeitos de radiação; câncer de mama.

Introduction

The effects of radiation on human tissues have been extensively studied because radiotherapy is one of the therapeutic options in the treatment of several malignant tumors. One of the well-known adverse effects of radiation is the injury to healthy tissue in areas close to malignant tumors due to radiotherapy.

Breast cancer has a high mortality rate among women: it is the second most frequent type of cancer in the world

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and the most common in the female population[1]. Radical breast cancer treatment, particularly when complemented by radiotherapy, is knowingly responsible for substantial morbidity of the limb in the same side affected by the disease. Lymphatic system lesions, venous thrombosis of axillary and subclavian veins and limiting scar retraction are well-known complication reported in the medical literature. A severe and little known complication that may affect these patients is critical ischemia of an upper extremity due to arterial injury[2,3].

In oncology, arterial stenosis as a complication of radiotherapy is very rare, although reported in experimental studies that found evidence of it[4]. In major publications,[2,3,5] histological lesions due to radiation are not specific and are often associated with risk factors of atherosclerosis. Several types of lesions have been described, such as ruptures, aneurysms, occlusions, stenosis and thrombosis[5].

Although reports of arterial occlusive lesions after radiotherapy are found in the literature,[5] few series have been described considering the broad use of this treatment. The involvement of the subclavian artery in patients that underwent adjuvant radiotherapy for the treatment of breast cancer is rarely discussed in publications[6,7]. We describe a case of right subclavian artery occlusion in a patient that underwent radiotherapy for the treatment of cancer in the right breast. We provide evidence of the physiopathology of this disease and describe possible indications of treatment based on our extensive review of the literature.

Case report

A 68-year-old patient presented with reversible cyanosis and pain when the right arm and forearm were at rest. Symptom onset was three months earlier: the first sign was pain to move the upper right extremity, which worsened progressively. There were no palpable pulses in the right upper extremity, but the other pulses in the contralateral upper and lower extremities were normal.

The patient had hypertension and was an ex-smoker (10 pack/year). Twenty years before, she had undergone varicose vein stripping with bilateral removal of saphenous veins. Twelve years before she had a diagnosis of invasive ductal carcinoma with lymph node involvement. The patient underwent radical mastectomy and axillary lymph node dissection. She received six cycles of adjuvant chemotherapy using the cyclophosphamide, methotrexate and 5-fluorouracil (CMF) regimen and radiotherapy over the breast and the thoracic wall at a total dose of 5000 cGy divided into 25 fractions. The supraclavicular and axillary lymph node chains were also irradiated anteroposteriorly. She underwent hormone therapy with 20 mg/day tamoxifen for five years after surgical treatment.

After the diagnosis of critical arterial insufficiency of the right upper extremity, the patient underwent arteriography, which revealed occlusion of the subclavian artery in its middle third and brachial artery refill at the proximal third, with no signs of concurrent atherosclerosis (Figure 1). She underwent CT angiogram scanning, which did not reveal any local anatomic anomalies and confirmed arterial occlusion (Figure 2). Based on these findings, the hypothesis of actinic arteritis of the right subclavian artery was raised based on the fact that radiotherapy had been applied to that site.

As subclavian artery occlusion was extensive, surgery was the treatment chosen, with the interposition of an arterial graft of the subclavian artery to the brachial artery using a 6-mm PTFE prosthesis because the two internal saphenous arteries had already been removed. A right supraclavicular and longitudinal brachial approach was used. End-to-side anastomoses were constructed with prolene 6.0 in the arterial regions where there were no changes. Surgery was uneventful, and the patient was discharged on the fifth postoperative day without any complaints and with a palpable radial pulse. Ninety days after the surgery, outpatient follow-up of the patient showed that she had no complaints and that there was good perfusion of the extremity. Control CT angiogram did not show any abnormalities (Figure 3).

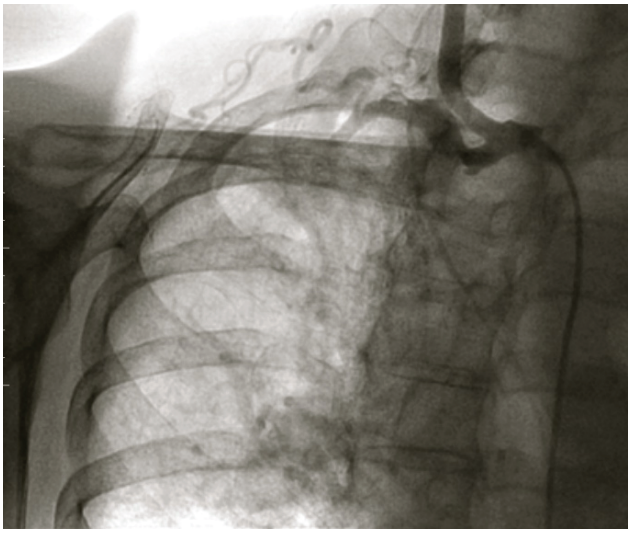

Figure 1. Arteriogram shows occlusion of subclavian artery in middle third.

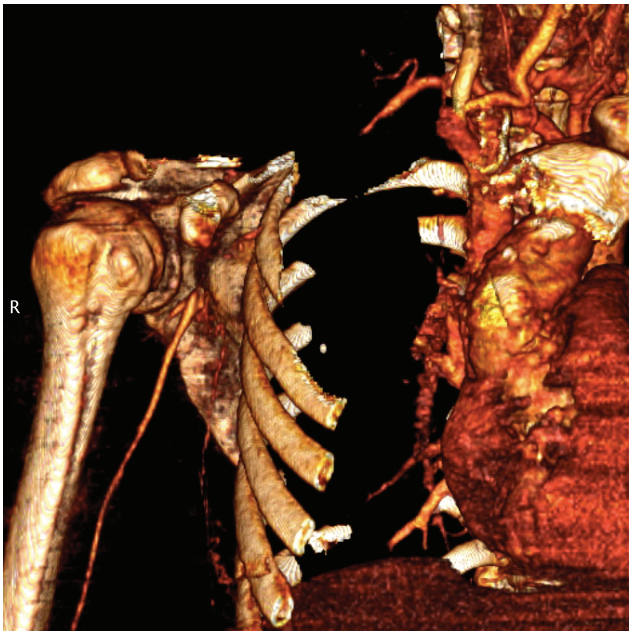

Figure 2. CT angiogram with three-dimensional reconstruction shows occlusion of subclavian artery in middle third and refilling of proximal third of brachial artery. No local anatomic anomalies were found.

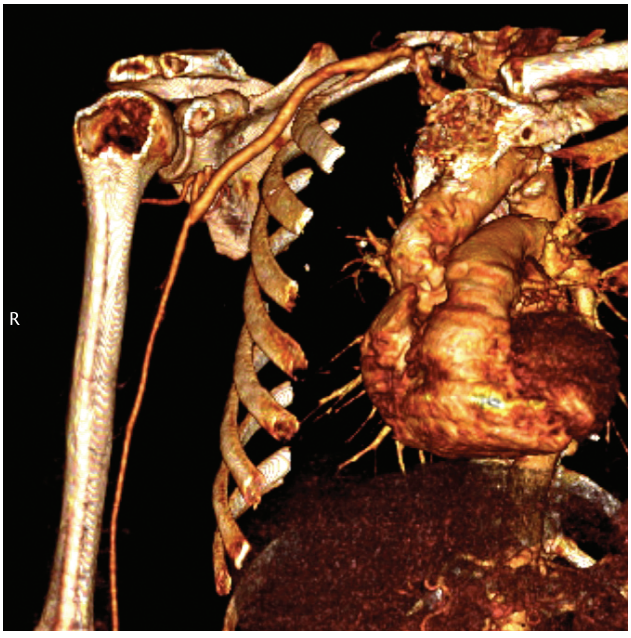

Figure 3. CT angiogram and three-dimensional reconstruction obtained after placement of arterial graft and PTFE prosthesis.

Discussion

Woolbach, in 1909, was the first author to report that vessels exposed to radiotherapy might suffer lesions. After histological evaluation, he described the increase of subendothelial connective tissue, thickening of the middle layer and hyalinization of the internal elastic lamina. The endothelium was described as soft and having vacuolated cells that projected into the vessel lumen[8]. Forty years later, Warren described similar results and reported that the hyalinization of the internal elastic lamina was progressive, even up to four years after irradiation[9]. In the same decade, Sheeha not only confirmed those findings in a series of necropsies, but also showed evidence of foam cells in the intima of those vessels. Those cells had migrated from the blood current and implanted in the site of the lesion induced by radiotherapy[10]. After those reports, numerous authors described similar findings and confirmed the pattern of injury to the vessels of human beings that are exposed to therapeutic doses of radiation[11-13]. Fajardo organized and described the histological changes found in actinic arteritis: proliferation of the subendothelial connective tissue, rupture of the internal elastic lamina, accumulation of fibrinoid substances in the intima and subintimal layers, degeneration of smooth muscles, dense fibrosis in the adventitia, foam cell aggregates on the injured wall and possible obliteration of vasa vasorum[14].

The actual incidence of arterial disease induced by radiotherapy is hard to determine because it varies substantially with anatomic site. Artery lesions of the supra-aortic trunks in their intrathoracic portion have been rarely described and seem to be less common than the involvement of coronary arteries.[15] However, lesions in the cervical segment of carotid arteries have been described more frequently and usually affect the carotid bifurcation[16]. Likewise, the involvement of the subclavian artery after radiotherapy in patients with cancer has already been defined, and some reports about it have already been published[5].

Table 1 sows the results of a thorough review of the literature about this topic[3,5,7,17-20]. We found twelve cases of actinic arteritis of the subclavian artery, particularly after radiotherapy to treat breast cancer. In agreement with our report, the interval between irradiation and onset of symptoms was extremely variable, ranging from 2 to 42 years (mean 14.7 years). Clinical presentations varied from discrete symptoms to the development of limb gangrene. Symptom onset was gradual, as in the case reported here, or sudden, when there was thrombosis or embolization.

The main difference between patients that receive radiotherapy and those with atherosclerosis is that, in the first group, large or small caliber arteries are affected by the irradiated field and, therefore, collateral circulation is compromised, whereas vessels out of the field of irradiation are supposedly normal. Another important difference, seen in the case reported here, is that tissues change after

Table 1. Cases of actinic arteritis of subclavian artery after radiotherapy to treat breast cancer described in the literature.

Authors	Journal	Year	Number of Cases	Treatment	Progression
Hassen-Khodja RH et al.[17]	*Journal of Vascular Surgery Vol 40, Number 2*	2004	2	Carotid-humeral bypass with saphenous vein and carotid-subclavian bypass after carotid artery angioplasty.	Good progression in long term follow-up of both cases.
Lewis J et al.[18]	*Clinical Oncology* 9:122-123	1997	1	Stent angioplasty and warfarin as anticlotting agent.	Good progression, improvement of subclavian steal symptoms.
Piedbois et al.[5]	*Radiotherapy and Oncology;* 17: 133-140	1990	1	Carotid-humeral bypass and saphenous vein graft.	Good progression in long term follow-up.
Hughes WF et al.[19]	Am J Surg. May; 147(5): 698-700	1984	1	Subclavian-brachial bypass using PTFE.	Amputation of second finger (sequela of ischemia). Good progression in the long term.
Mavor GE et al.[3]	Brit. J. Surg. Vol 60, No 12, December	1973	2	Clinical treatment.	Intermittent claudication.
Hashmonai et al.[20]	Cancer 61:2015-2018	1988	2	Subclavian-brachial bypass using PTFE; clinical treatment.	Good progression in both cases; patient treated clinically overcame claudication.
McCallion et al.[7]	Br. J. Surg. Vol 78, September, 1136-1138	1991	3	Carotid-brachial bypass using saphenous graft; carotid-brachial bypass using saphenous graft; subclavian-axillary bypass using PTFE.	Good progression of all cases in long term follow-up.

mastectomy and local radiotherapy, which results in local fibrosis and make access to arteries difficult. As in the case reported here, good results are expected because vessels out of the irradiated area are supposedly normal, regardless of which vessel is used for the graft.

Another possible treatment is balloon percutaneous transluminal angioplasty, which has the advantage of not requiring access in previously irradiated areas. In the few cases reported so far,[2,5,17] subclavian artery stenosis progressed gradually. As in our case, onset takes a long time and, when symptoms appear, there has already been progression into an extensive lesion for which endovascular treatment is no longer effective.

The analysis of the case reported here and the ones in the studies reviewed indicates that the results of revascularization of lesions induced by radiation in the subclavian artery are usually satisfactory. Indications and surgical planning should be carefully made because of the difficulties that may be found during the operation to treat these complex lesions.

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