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# Retroperitoneal Fibrosis as the First Sign of Metastatic Breast Cancer: A Case Report

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## Abstract

Retroperitoneal fibrosis (RPF) is an uncommon condition characterized by fibro-inflammatory tissue in the retroperitoneum that can compress adjacent structures, particularly the ureters. RPF secondary to malignancy has been described in several tumor types, including breast cancer, mostly of lobular histology. We report the case of a 56-year-old woman, a BRCA2 carrier, treated with bilateral mastectomy, axillary dissection, adjuvant chemotherapy, radiotherapy and endocrine therapy for a low-grade invasive carcinoma of no special type (pT1c pN3a, estrogen receptor-positive, human epidermal growth factor receptor 2 (HER2) low). Forty months after surgery, she presented with urinary incontinence, vulvar and right lower limb edema and fatigue. Imaging showed bilateral hydroureteronephrosis and a retroperitoneal soft-tissue mass suggestive of RPF, and she had severe hypercalcemia. The mass progressed rapidly, compressing the inferior vena cava and infiltrating the pelvis. Biopsies of the retroperitoneal mass, inguinal lymph nodes and a skin lesion confirmed metastatic breast carcinoma, with only focal estrogen receptor expression in the retroperitoneal tissue. Bilateral ureteral stents were placed, but her general condition precluded systemic therapy, and she died three months after presentation. This case shows that new-onset RPF in a patient with a history of breast cancer, including non-lobular subtypes, should raise suspicion of metastatic disease and prompt early histological diagnosis, as the prognosis is poor.

**Categories:** General Surgery, Oncology
**Keywords:** cutaneous metastasis, estrogen receptor discordance, invasive carcinoma of no special type, metastatic breast cancer, retroperitoneal fibrosis, ureteral obstruction

## Introduction

Retroperitoneal fibrosis (RPF) is a rare disorder characterized by fibro-inflammatory tissue that typically surrounds the abdominal aorta and iliac arteries and extends into the retroperitoneum, frequently encasing the ureters [1]. Most cases are idiopathic, but RPF may also be secondary to drugs, infection, surgery or malignancy [1]. Malignancy accounts for approximately 8% of cases and has been described in breast, lung, gastrointestinal, genitourinary and thyroid cancers and in carcinoid tumors [2]. In most of these cases, the fibrosis results from a desmoplastic reaction to retroperitoneal metastases [3].

Although retroperitoneal metastasis from breast cancer is uncommon, breast carcinoma is one of the more frequently reported causes of malignant RPF [2]. Most reported cases involve invasive lobular carcinoma, which has a distinct metastatic pattern, with peritoneal and retroperitoneal involvement markedly more frequent than in invasive ductal carcinoma [2,4].

The clinical presentation is insidious and nonspecific, and imaging cannot reliably distinguish benign from malignant RPF. Histological confirmation is therefore essential, particularly in patients with a history of cancer [3,5].

We report a case of RPF caused by metastatic low-grade invasive carcinoma of no special type in a BRCA2 carrier, diagnosed 40 months after surgery and adjuvant treatment, with concurrent pelvic, inguinal lymph node and cutaneous dissemination and a fatal course within three months of presentation. This case highlights that new-onset RPF in a patient with a history of breast cancer, regardless of histological subtype, should prompt early tissue diagnosis.

## Case Presentation

A 56-year-old woman, fully independent in her daily activities, with a history of hypertension and dyslipidemia controlled with medication, was diagnosed with left breast cancer at 52 years of age, after detecting a nodule herself. She had a family history of breast cancer (mother and brother). She was postmenopausal at diagnosis. Ultrasound and mammography showed an ill-defined 2.5 cm nodular lesion in the upper outer quadrant of the left breast, with axillary lymphadenopathy. Core needle biopsy revealed invasive carcinoma NST, Nottingham grade 1 [6], estrogen receptor-positive (80%), progesterone receptor-positive (10%) and human epidermal growth factor receptor 2 (HER2) low (immunohistochemistry 2+, not amplified on silver in situ hybridization), with a Ki-67 index of approximately 5%. Biopsy of an axillary

lymph node showed only reactive changes. Germline genetic testing identified a pathogenic BRCA2 variant.

After multidisciplinary team discussion, she underwent bilateral mastectomy with left sentinel lymph node biopsy and risk-reducing bilateral salpingo-oophorectomy one month after diagnosis. Intraoperative frozen section showed metastases in all five sentinel nodes, and a left axillary lymph node dissection was performed. Final pathology showed a 1.2 cm invasive carcinoma NST, grade 1, without ductal carcinoma in situ or lymphovascular or perineural invasion, with negative margins. In total, 15 of 18 lymph nodes contained metastatic carcinoma, with extranodal extension (pT1c pN3a). The right breast showed only benign fibrocystic changes, and the ovaries and fallopian tubes were unremarkable.

Adjuvant treatment consisted of four cycles of dose-dense doxorubicin and cyclophosphamide followed by 12 weekly doses of paclitaxel, completed without complications five months after surgery, then adjuvant radiotherapy, completed eight months after surgery, and letrozole. Chest, abdominal and pelvic computed tomography (CT) after chemotherapy showed no evidence of disease. The follow-up consisted of six-monthly clinical review with blood tests and yearly sonography, all without abnormal findings.

Forty months after surgery, while still on letrozole, she was referred by her primary care physician to our emergency department with a two-week history of urinary incontinence without dysuria, vulvar and right lower limb edema that had developed over the previous days, and progressive fatigue over the previous month. She was hemodynamically stable and afebrile. Examination showed suprapubic and vulvar edema without erythema and with mild tenderness, and pitting edema of the right lower limb from the proximal thigh to the foot. Femoral and popliteal pulses were palpable bilaterally.

Laboratory tests showed anemia, elevated serum creatinine, hypokalemia and an elevated C-reactive protein (Table *1*). The Doppler ultrasound of the right lower limb showed no signs of deep vein thrombosis, but showed inguinal lymphadenopathy. Renal and pelvic ultrasound showed bilateral hydroureteronephrosis, more pronounced on the right, without an identifiable obstructing lesion. The bladder was poorly distended, with circumferential wall thickening. Increased echogenicity of the pelvic soft tissues and a small amount of free fluid suggested an inflammatory or infiltrative process, and CT was performed.

| Parameter | First Presentation | Readmission | Reference Range |
|---|---|---|---|
| Hemoglobin (g/dL) | 10.0 | 9.7 | 11.5-16.0 |
| Leukocytes (×10⁹/L) | 5.55 | 6.21 | 4.0-10.00 |
| Creatinine (mg/dL) | 1.30 | 1.53 | 0.5-1.10 |
| Potassium (mmol/L) | 3.1 | - | 3.5-5.1 |
| C-reactive protein (mg/dL) | 1.82 | - | <0.51 |
| Total calcium (mg/dL) | 15.7 | 11.8 | 8.8-10.8 |
| Albumin (g/dL) | 3.6 | - | 3.5-5.0 |
| Parathyroid hormone (pg/mL) | 17.0 | - | 15-65 |
| CA 15-3 (U/mL) | 40.8 | - | <31.3 |
| CEA (ng/mL) | 2.2 | - | <5 |

**TABLE 1: Laboratory results at first presentation and at readmission**

CA 15-3: cancer antigen 15-3; CEA: carcinoembryonic antigen; -: not measured.

Abdominal and pelvic CT showed normally positioned kidneys with moderate bilateral pelvicalyceal dilatation. A heterogeneous solid soft-tissue component in the retroperitoneal fat encased the ureters and the abdominal vessels, with prominent vascular structures, raising the possibility of retroperitoneal fibrosis. Bladder wall thickening was also noted. There was no ascites. Multiple simple hepatic cysts were present, the largest measuring approximately 3.1 cm. The portal vein was patent, and the remaining upper abdominal organs were unremarkable (Figure *1*).

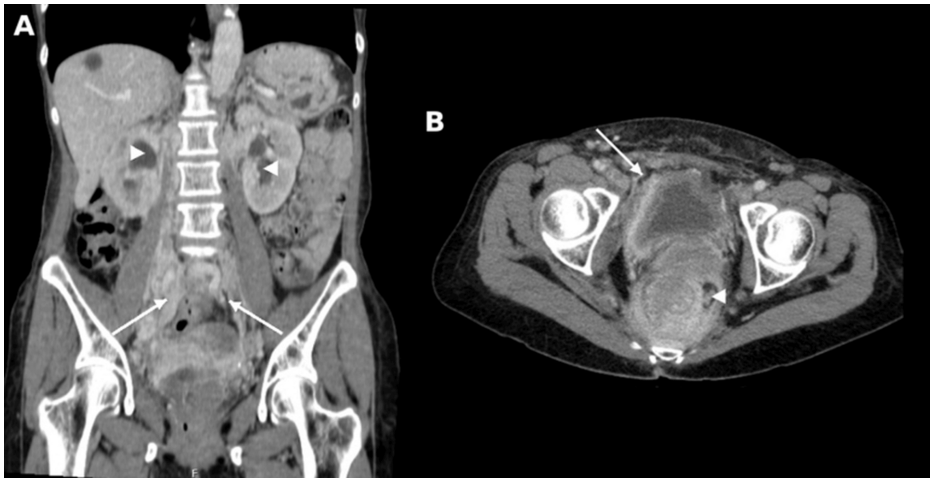



**FIGURE 1: Abdominal and pelvic computed tomography at presentation.**

(A) Contrast-enhanced coronal reconstruction showing a soft-tissue mantle surrounding the iliac vessels (arrows) and bilateral hydronephrosis, more pronounced on the right (arrowheads). A simple hepatic cyst is also visible. (B) Axial image of the pelvis showing circumferential bladder wall thickening (arrow) and a thickened rectal wall (arrowhead).

She was admitted to the internal medicine ward. Further work-up revealed severe hypercalcemia with parathyroid hormone within the normal range. Cancer antigen 15-3 (CA 15-3) was elevated, and carcinoembryonic antigen was normal (Table *1*). Renal function and calcium levels improved with intravenous hydration and pamidronate. After a discussion with urology and general surgery, a bone scan and outpatient cystoscopy were planned. Bone scintigraphy, compared with a study performed three years earlier, showed new faint uptake at the left sacroiliac joint and the right acetabular region, possibly degenerative, and a nonspecific focus in the posterolateral right sixth rib. Ultrasound of the right inguinal region showed heterogeneity and edema of the subcutaneous tissue, a small amount of fluid in the inguinal canal and nonspecific lymph nodes, the largest measuring 19x14 mm with a heterogeneous, thickened cortex. She was discharged with outpatient urology and general surgery follow-up.

At the urology appointment, cystoscopy was normal and urinary cytology was negative for high-grade urothelial carcinoma. Placement of long-term ureteral stents was proposed.

Eight days after discharge, before her general surgery appointment, she returned to the emergency department with worsening pain and edema of the right lower limb and further deterioration of renal function (Table *1*). Pelvic ultrasonography showed a vascularized retroperitoneal soft-tissue mass compressing the inferior vena cava, causing venous congestion and subcutaneous edema of the pelvis and lower limbs, more pronounced on the right. There was no deep vein thrombosis of the right lower limb. The mass caused bilateral hydronephrosis, worse on the right, and extended into the pelvis, involving the bladder, which had thickened walls, and the uterus, and occupying the mesorectal fat and presacral space. The rectal wall was thickened. Right inguinal lymph nodes were enlarged, the largest measuring 20x16 mm.

She was admitted under General Surgery for 14 days. After discussion at the breast cancer multidisciplinary tumor board, excisional biopsy of the right inguinal lymph nodes and CT-guided biopsy of the presacral component of the mass were performed (Figures *2*, *3*). During excision of two inguinal lymph nodes, suspicious skin lesions were noted in the right inguinal region, and one was excised. Because of progressive renal dysfunction and worsening bilateral ureterohydronephrosis, bilateral double-J ureteral stents were placed during the same admission, with progressive improvement of renal function and of the limb edema. She was discharged with her symptoms controlled.

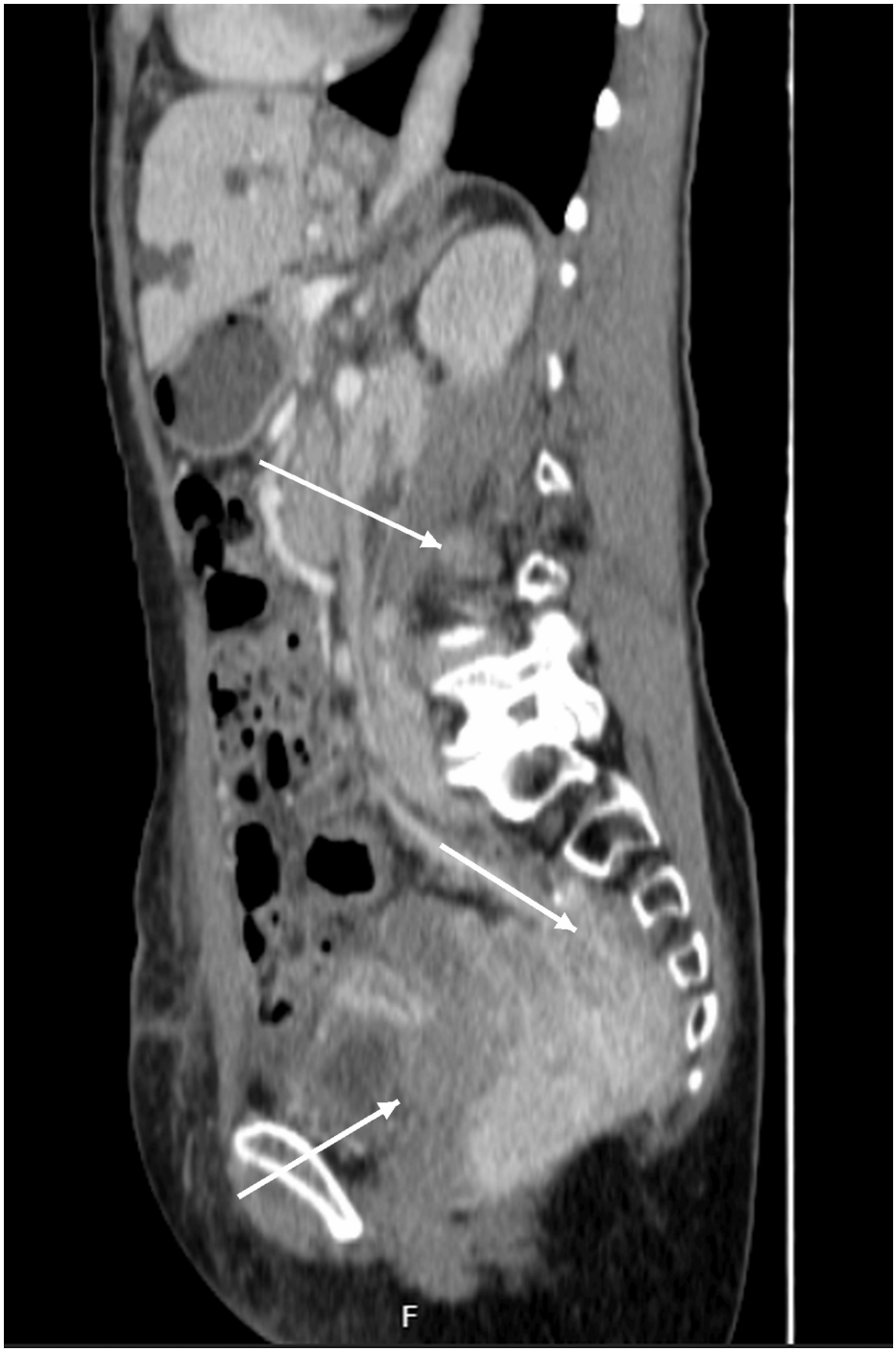



**FIGURE 2: Follow-up computed tomography, on the day of the biopsy, three weeks after presentation.**

Sagittal reconstruction showing infiltrative soft tissue anterior to the lumbar spine (upper arrow), extending into the presacral space (middle arrow) and the pelvis, involving the bladder and uterus (lower arrow).

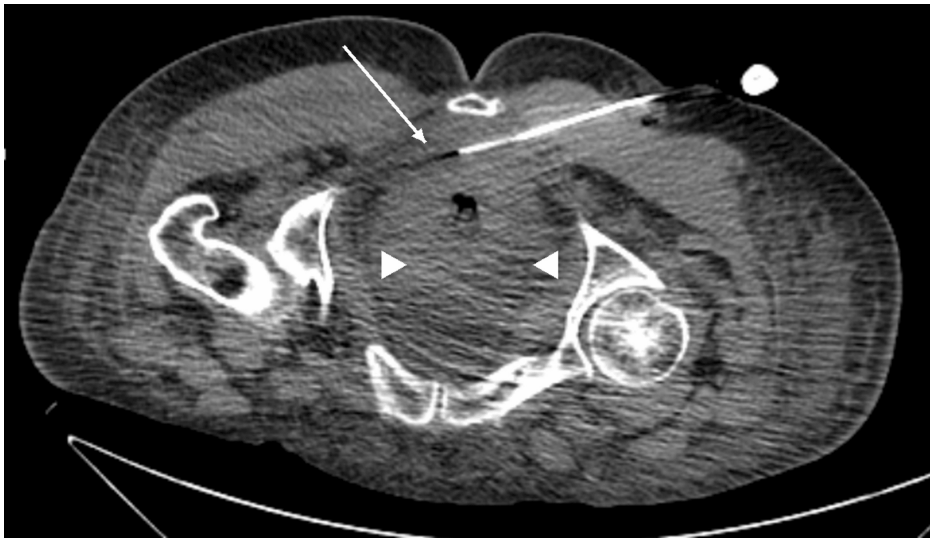


**FIGURE 3: Biopsy.**

Computed tomography-guided biopsy of the presacral component of the mass (arrowhead), performed with the patient in the prone position. The arrow indicates de needletip.

Histology of the skin lesion showed dermal infiltration by carcinoma. The two inguinal lymph nodes were extensively replaced by metastatic carcinoma. The retroperitoneal cores consisted of fibrous tissue with crush artifact, containing neoplastic cells with nuclear hyperchromasia arranged in single files or as isolated cells. All three specimens expressed cytokeratin AE1/AE3, GATA3 and estrogen receptor (diffuse cytokeratin and GATA3 with focal estrogen receptor expression in the retroperitoneal biopsy), consistent with metastatic breast carcinoma.

Given the rapid deterioration of her general condition, systemic anticancer therapy was not deemed appropriate following discussion at the multidisciplinary tumor board meeting, and management focused on symptom control.

The patient was subsequently readmitted with fever and general deterioration and was diagnosed with pyelonephritis. During this admission, she was also followed by the palliative care team. The patient died three months after her first presentation to the emergency department.

## Discussion

This case describes RPF caused by metastatic breast carcinoma 40 months after the diagnosis and treatment of a low-grade invasive carcinoma of no special type (NST). The initial imaging suggested RPF, and the hypothesis of a benign process, idiopathic or treatment-related, delayed histological confirmation. By the time tissue was obtained, during the second admission, the disease had already extended to the pelvis, the inguinal lymph nodes and the skin.

In most published cases of breast cancer presenting as RPF, the primary tumor is an invasive lobular carcinoma, consistent with the known tendency of this subtype to spread to the peritoneum and retroperitoneum [2,4,7]. In some of these cases, RPF was the first manifestation of breast cancer [2,7]. Our patient differs in two respects: the primary tumor was an invasive carcinoma NST, grade 1, with a Ki-67 index of approximately 5%, and she had no evidence of disease during more than three years of follow-up.

The retroperitoneal biopsy showed neoplastic cells arranged in single files or as isolated cells, a growth pattern classically associated with lobular carcinoma [8]. Because E-cadherin immunostaining was not performed, a lobular component in the metastasis could not be confirmed or excluded. In either case, this report shows that a diffusely infiltrative, fibrosis-inducing pattern of spread is not restricted to tumors diagnosed as lobular carcinoma.

The receptor profile also differed between the primary tumor and the metastasis: estrogen receptor (ER) expression was 80% in the primary tumor but only focal in the retroperitoneal biopsy. Such discordance is well documented. In a meta-analysis of 48 studies, the pooled discordance rates between primary tumors and metastases were 20% for ER, 33% for progesterone receptor (PR) and 8% for HER2 [9]. Because receptor status guides systemic therapy, this variability is a further reason to obtain tissue from suspected metastases whenever feasible.

Several features of this presentation should raise suspicion of malignancy. In a patient with a history of breast cancer, new-onset RPF should prompt early tissue diagnosis [3]. The urinary incontinence, diffuse bladder wall thickening and bilateral hydronephrosis were consistent with metastatic involvement of the urinary tract, which may present with urinary incontinence [10] or ureteral obstruction [11]. A normal cystoscopy and negative urinary cytology do not exclude extrinsic infiltration, as this case illustrates. The right lower limb and vulvar edema, later explained by compression of the inferior vena cava, was another sign of a growing retroperitoneal mass.

Management in this setting is largely palliative. Ureteral obstruction is a common complication of malignant RPF, and a meta-analysis of malignant ureteral obstruction favored ureteral stents over percutaneous nephrostomy whenever stenting is feasible [12]. In our patient, renal function improved after bilateral double-J stent placement. Severe hypercalcemia, another marker of advanced disease, was treated with pamidronate, in line with current recommendations [13,14]. Hypercalcemia of malignancy results mainly from tumor secretion of parathyroid hormone-related peptide (PTHrP), which increases bone resorption and renal calcium reabsorption, or from local osteolysis caused by bone metastases; reduced renal calcium clearance, as in acute kidney injury, may further aggravate it [13]. In our patient, PTH was appropriately low-normal and bone scintigraphy showed no definite metastases, which suggests a humoral, PTHrP-mediated mechanism, possibly aggravated by renal dysfunction. However, as PTHrP was not measured, this could not be confirmed. The cutaneous metastases also indicated advanced disease: cutaneous metastases account for only about 2% of skin malignancies but nearly 70% of those occurring in women originate from breast cancer, and they are usually associated with a poor prognosis [15].

Malignant RPF carries a poor prognosis [3]. In our patient, her general condition at the time of diagnosis precluded systemic therapy, and she died three months after presentation. Despite the favorable histological features of the primary tumor, the extensive nodal involvement at diagnosis (15 of 18 lymph nodes, pN3a) placed her in the group at highest risk of distant recurrence [16]. Adjuvant olaparib and abemaciclib, now options for high-risk patients, were not available at the time of her initial treatment.

This report has limitations. E-cadherin, PR and HER2 were not assessed in the metastatic tissue, and parathyroid hormone-related peptide was not measured.

## Conclusions

Retroperitoneal fibrosis may be the presenting sign of metastatic breast cancer, even years after treatment and in patients with low-grade carcinoma of no special type rather than lobular carcinoma. In any patient with a history of breast cancer, new-onset RPF should be considered malignant until proven otherwise, and early biopsy is essential: it establishes the diagnosis and provides tissue to reassess receptor status, which may differ from that of the primary tumor. Delayed recognition can allow rapid local and distant progression and limit treatment options.

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

**Concept and design:** Inês Arnaud, Conceição Monteiro, Ana Gonçalves

**Acquisition, analysis, or interpretation of data:** Inês Arnaud, Cláudia Lima, Fábio Correia Viveiros, Ana Gonçalves

**Drafting of the manuscript:** Inês Arnaud, Cláudia Lima, Fábio Correia Viveiros, Ana Gonçalves

**Critical review of the manuscript for important intellectual content:** Conceição Monteiro

**Supervision:** Conceição Monteiro

### Disclosures

**Human subjects:** Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **AI use statement:** The authors used Claude (Anthropic, San Francisco, CA) as follows: language polishing, translation in Introduction, Case Presentation, Discussion. Claude was used only to help translate certain phrases and to identify any writing/grammar mistakes on the article itself. All of its structure and the references mentioned was written and researched by the authors. The authors confirm that they have reviewed and verified all AI-assisted content and take full responsibility for the work. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have

no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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