

Breast Cancer Relapse in a BRCA2-Mutated Patient with Moyamoya Disease Treated with Mastectomy Under Hypnosis Sedation: A Case Report

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Abstract

Moyamoya Disease (MMD) and breast cancer due to a BRCA2 germline mutation are both rare diseases, and there are no data in the literature to assess the cumulative incidence of these two complex conditions. We present here the case of a 62-year-old woman with a history of MMD who developed a recurrence of invasive non-special type breast carcinoma in the right breast. The patient was diagnosed with a BRCA2 germline mutation in 2018 and an MMD in 2023.

The cancer extension assessment was negative. The patient refused a surgical procedure under general anesthesia out of fear of complications. She therefore underwent a simple right mastectomy under hypno-sedation with an excellent postoperative evolution. Given the tumor's prognostic factors, she was treated with an aromatase inhibitor and is currently in complete remission.

Keywords: Moyamoya disease • Invasive breast cancer • BRCA2 mutations • Mastectomy • Hypnosis sedation

Introduction

Moyamoya Disease (MMD) is a rare, progressive intracranial arteriopathy characterized by occlusion of the distal portions of the internal carotid arteries and/or the proximal portions of the middle cerebral arteries. This

occlusion stimulates the formation of a network of fragile collateral vessels, visible on angiography as a hazy image, from which the disease derives its name ("moyamoya" meaning "puff of smoke" in Japanese) [1].

MMD presents with ischemic or hemorrhagic stroke. Current guidelines recommend (when possible) surgical revascularization for patients with a history of ischemic strokes to improve cerebral hemodynamics, reduce the risk of future strokes, and enhance neurocognitive outcomes and activities of daily living [1]. Anesthetic management in patients with MMD is challenging due to the potential risk of stroke [2,3].

Germline mutations in the BRCA1 or BRCA2 genes affect homologous recombination repair, notably increasing the risk for breast and ovarian cancer. Mutated patients are advised to follow preventive strategies to decrease the incidence of these cancers. Typically, this involves chemopreventive treatments (essentially for the breast) and risk reduction surgeries: mastectomies associated with breast reconstructions and adnexectomies preceded or not by salpingectomies for the ovaries [4].

Case Presentation

Patient information

A 62-year-old Caucasian female presented to our breast clinic with a diagnosis of recurrent right-sided breast cancer. Her oncological history includes the diagnosis of a Non-Special Type (NST) carcinoma of the right breast at age 38, treated with lumpectomy and axillary lymph node dissection, followed by chemotherapy, radiotherapy, and endocrine therapy.

The patient has a family history of breast cancer, with her sister diagnosed at age 40 and both her mother and aunt diagnosed after age 60. However, no family history of ovarian cancer was reported. In 2018, the patient was diagnosed with a BRCA2 germline mutation. Despite this, she opted not to undergo prophylactic surgery and chose regular annual monitoring.

At age 61, the patient was diagnosed with Moyamoya disease following an ischemic stroke. She also experienced two Transient Ischemic Attacks (TIAs) post-diagnosis. The residual effects of the stroke include hyperacusis, attention deficits, and verbal function impairment. She was placed on acetylsalicylic acid, and no surgical intervention was performed for her MMD because revascularization surgery was deemed too dangerous and unfeasible (Figure 1).

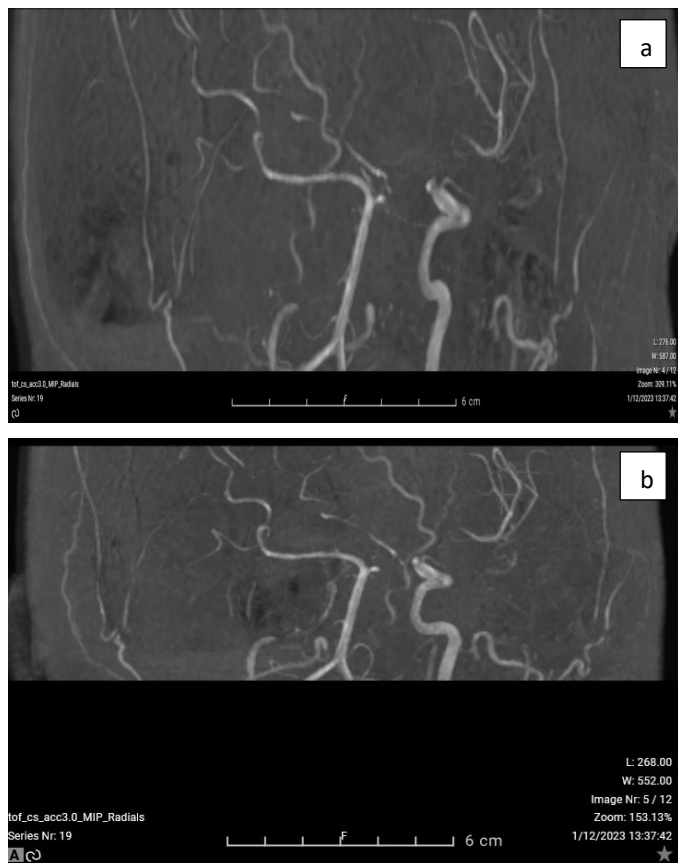


Figure 1a). This cerebral arteriography shows stenosis or subocclusion of the left posterior cerebral artery, and intracranial stenosis of the right internal carotid artery. **1b)** It also shows occlusion of the right middle and anterior cerebral arteries, and stenosis of the left middle cerebral artery with collateral circulation.

Clinical findings and diagnostic evaluation

Her obstetric history includes gravida 3 para 3, and she is postmenopausal without hormone replacement therapy. She also underwent a total hysterectomy (without bilateral oophorectomy) for leiomyomas. The particular concern was a laparoscopic cholecystectomy performed in 2020, prior to the MMD diagnosis, during which the patient experienced postoperative complications. She remained unresponsive for 8 hours in the intensive care unit following the procedure, though the hospitalization report did not provide details on the incident (Figure 2).

Nevertheless, a hemorrhagic stroke can be suspected retrospectively.

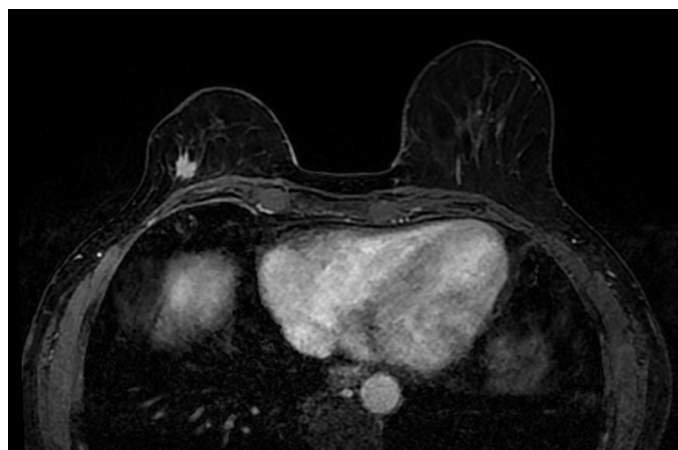


Figure 2. This cerebral arteriography shows stenosis or subocclusion of the left posterior cerebral artery, and intracranial stenosis of the right internal carotid artery. It also shows occlusion of the right middle and anterior cerebral arteries, and stenosis of the left middle cerebral artery with collateral circulation.

Therapeutic strategy

Following discussions with the neurology department, the multidisciplinary team recommended a simple right mastectomy, as the patient already underwent a complete axillary dissection plus radiotherapy for her initial breast cancer diagnosis. The standard of care for this patient would typically involve a bilateral mastectomy with right axillary lymph node exploration. Bilateral oophorectomy is also recommended for BRCA2 mutation carriers. However, given the patient's condition and the risks associated with general anaesthesia, a simple right mastectomy without breast reconstruction was deemed appropriate. The patient was highly motivated not to undergo general anaesthesia. After discussion with the anaesthetist, we proposed the procedure under hypno-sedation and local anaesthesia. PEC (interpectoral block) 1 and serratus block with levobupivacaine 2.5 mg/ml was also performed.

The peri-incisional skin was injected with local anaesthetic (1% lidocaine). The patient also received intravenous remifentanyl (0.05 µg/kg/min) during all the procedure and midazolam (0.5 mg) to be more comfortable. Small doses of 5 mg of propofol was administered twice during the more uncomfortable part of the dissection.

The mastectomy was uneventful from both the surgical and anaesthetic perspectives except for a surge of hypertension reaching 180/100 mmHg at the more uncomfortable part of the dissection.

The patient arrived in the operating room with a blood pressure of 170/90 and a mild hypertension at 150/90 remained one day post-operatively and was not medicated.

The patient quickly regained her usual blood pressure of between 140 and 130/90 mmHg. She did not require any post-operative pain medication and quickly felt very comfortable.

She was discharged two days postoperatively without complications and reported no issues during her follow-up visit 10 days later (Figures 3-6).

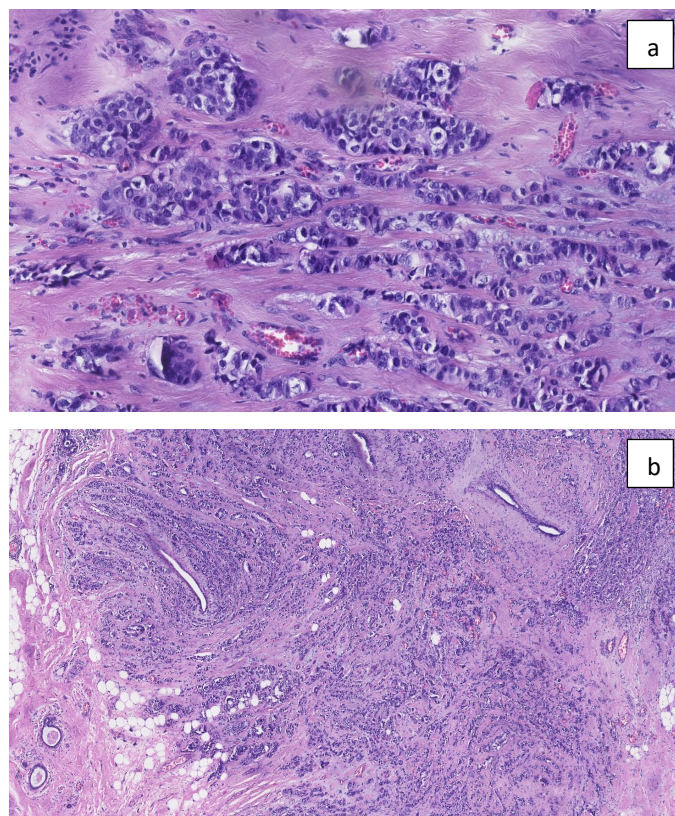


Figure. 3a): Invasive non-special type breast carcinoma (haematoxylin eosin), **3b)** The resection specimen contained a nodule measuring 12 mm in its largest diameter, with a whitish appearance and star-like contours, located at the junction of the external quadrants.

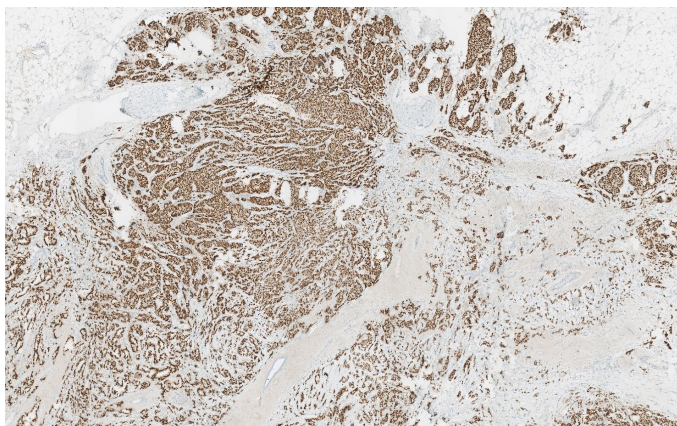


Figure 4. Estrogen Receptor (ER) positive staining

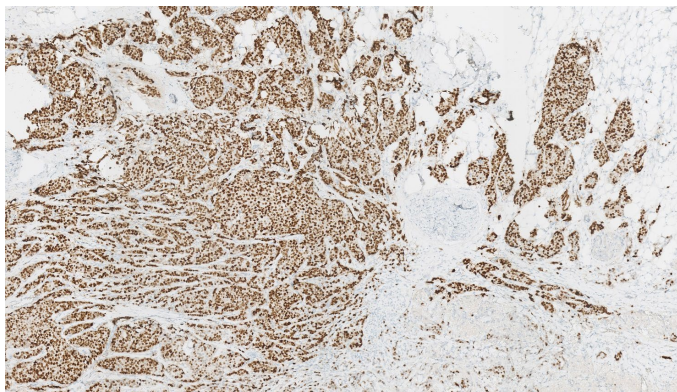


Figure 5. Progesterone Receptor (PR) positive staining

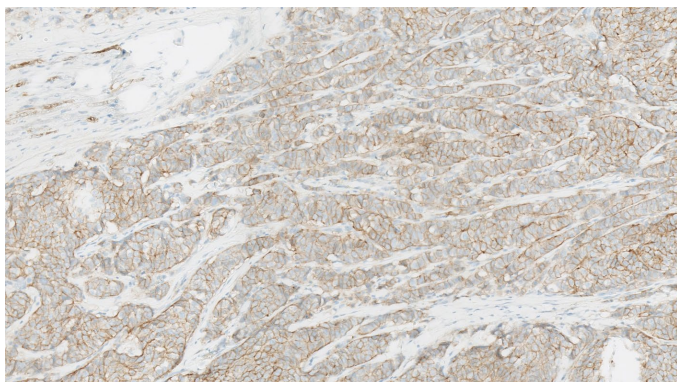


Figure 6. HER2 2⁺ staining, Immunohistochemical analysis shows a luminal phenotype, with positive estrogen and progesterone receptors (Allred score 8 for both), a Ki-67 index of 40%, and a negative HER2 status (score 2⁺, dual-probe SISH non-amplified).

Histologically, invasive ductal carcinoma of No Specific Type (NST), grade III, is observed. It is predominantly composed of trabecular structures, with very limited glandular differentiation. The tumor cells exhibit significant atypia, with 9 mitoses counted per 10 High-Power Fields (HPF).

Discussion

The anaesthesiology team in charge of a surgical intervention on a patient suffering from Moyamoya disease faces multiple challenges, as general anaesthesia and surgery can generate a series of conditions increasing the risk of stroke. Hypotension in particular can alter cerebral perfusion. Hypercapnia can lead to cerebral vasodilatation and to a steal phenomenon, since MMD's fragile vessels are already maximally dilated. This is especially seen in laparoscopy where the insufflated CO₂ is resorbed by the peritoneum. Some reports describe the discovery of MMD in this case, which reinforces our opinion that the patient suffered from a hemorrhagic stroke during her cholecystectomy.

Pain and the stress reaction it induces can trigger activation of the sympathetic nervous system, cause hypertension and hyperventilation, both of which can alter cerebral hemodynamics.

In this patient, the goals are to maintain normocapnia and normal blood pressure during the intraoperative and postoperative periods [2,3,5].

Mastectomy under hypnosis sedation and local anaesthesia provided by cutaneous, PEC 1 and serratus block has already been described as a viable and profitable technique in carefully selected patients, as our 2019 study showed [6].

The intended benefit of this choice was to reduce the amount of drugs given and thus limit the potential side effects on the patient's hemodynamics. However, concerns were raised regarding a possible perioperative stroke, as the patient is in hypnosis trance and thus might not be able to tell if something is happening.

Additionally, while hypnosis sedation generally poses fewer respiratory risks compared to general anaesthesia, hypnosis sedation involves the use of light sedatives (such as benzodiazepines or low dose opioids), representing a potential for mild respiratory inhibition. Contrary to general anaesthesia, there is no monitoring of PCO₂, but respiratory frequency is monitored allowing an efficient intervention by the anesthetist in case of acute complication. Unlike general anaesthesia, where medications can be used proactively to control the blood pressure, hypno-sedation relies more on the hypnotic effect and light sedation. This may not always be sufficient to prevent hypertensive spikes. An overdose of local anaesthetics can cause serious effects on the central nervous system first and cardiovascular system secondarily. It is crucial to calculate the maximum allowed dose based on the patient's weight and to respect the dosage limits to be distributed between PEC and local injection. Postoperative care should aim at maintaining stable parameters including blood pressure, oxygen saturation, normocapnia, preventing shivering, nausea and vomiting. Performing surgical cerebral revascularization before breast cancer treatment could have been an alternative to the approach we chose. This procedure can be direct, indirect or combining both approaches. In adult patients, a direct or combined approach was proven more effective compared to an indirect approach. It can provide immediate blood flow improvement but is harder than indirect revascularization that takes several months to improve cerebral blood flow. The procedure's benefits are bigger the younger the patient is [7].

After discussion with the neurosurgery department, the patient's cerebral vascular web was deemed ineligible for direct revascularization. Indirect revascularization could have been an alternative (with letrozole as neoadjuvant therapy for 1 year-2 years), but the expected result of the intervention and the delay needed before operating the breast tipped the balance against an MMD surgery.

Risk of ovarian cancer in BRCA2 mutated patient at age 80 is estimated to be around 17%, and 69% for breast cancer. Differences in expression of this mutation in both breast and ovarian cancer are observed between families, suggesting a polygenic influence. The more breast and ovarian cancer cases there are in a family, the bigger the risk [8].

In addition to her BRCA2 mutation status, other risk factors for contralateral breast cancer in our patient include the number of breast cancer cases in her family (3 relatives) and the young age of onset of her first cancer (17.2%) if diagnosed before 41 years old [9].

However, the surgical decision was to perform a unilateral mastectomy with close senological monitoring of the contralateral breast and adjuvant endocrine therapy. Indeed, for a bilateral mastectomy, hypnosis sedation would be insufficient, and under general anaesthesia, the duration of the anaesthesia and the complexity of the intervention would increase the risk of disrupting cerebral vascularization.

Bilateral oophorectomy was discussed because the patient is a BRCA2 germline mutation carrier, but was not recommended by our multidisciplinary team for several reasons. There is no case of ovarian

cancer in the family and a bilateral salpingectomy had already been performed, which is suspected to decrease the risk even further, even if studies are still ongoing on this subject [10].

The operative risk is considered especially high since the procedure would be done *via* laparoscopy, as previously discussed.

Additionally, patients are usually put in Trendelenburg position that would increase intra-cranial pressure. Anaesthesia is deeper with a higher risk of hemodynamic instability.

All these parameters increase the risk of stroke. In addition, the patient has already been operated by laparotomy with risk of pelvis adhesions that can lead to a more complicated and long procedure. Although there is no strict screening method for ovarian cancer, regular clinical follow-up is recommended.

Conclusion

Moyamoya disease presents unique challenges in the surgical management of breast cancer, particularly in BRCA2 mutation carriers. This case demonstrates the importance of individualized care and describes for the first time in the literature the potential role of hypno-sedation as an alternative option to general anaesthesia in highly selected patients.

The additional key to success of this approach is a patient who is collaborating and motivated to undergo such a procedure, which greatly depends on her personality and coping capabilities as it requires her active participation during the procedure.

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