



# Atrial Septal Aneurysm and Persistence of the Oval Foramen in a Young Patient with Breast Cancer: Risks, Uncertainties and Therapeutic Opportunities

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## Abstract

Cryptogenetic stroke is not a rare entity but represents about 30-40% of ischemic strokes and the pathogenetic mechanism at the basis is the passage of microemboli through the patent foramen ovale. The probability of having a second cerebral ischemic event increases if the patency of the oval foramen is associated with the presence of an aneurysmal interatrial septum. We took care of a patient who was then diagnosed with breast cancer and potentially cardiotoxic chemotherapy started. During routine cardiological checks, we noticed the co-presence of two cardiac anomalies potentially the source of important complications such as embolism and stroke. At that time, it was necessary to take care of the patient also from the cardiological point of view, since a tumor already represents a condition of hypercoagulability that can potentially be the cause of thrombosis and embolism, in addition to the discovery of a possible way of passage for emboli metastatic. Faced with a first decision concerning a modification of the oncological therapy already underway with an anticoagulant therapy, a subsequent re-evaluation convinced us to subject the patient to an intervention to close the defect via device.

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**Keywords:** Cryptogenic stroke; Atrial septal aneurysm; Patent foramen ovale; Breast cancer.

## Key messages

In some cases the diagnosis of patency of the oval foramen is an occasional finding in concomitant with a basal echocardiographic study of the heart performed for another reason, in this case the correct application of the guidelines of the Italian Society of Cardiology (SIC)/ Italian Society of Echocardiography (SIEC) on the follow-up of the cancer patient in therapy with cardiotoxic drugs. The indications for the treatment of these cardiac conditions are quite left to the decision of the doctors on the

individual case (SPRED and other guidelines). In particular, in the medical literature there are very few cases described in cancer patients, in the form of case reports. We believe that, since the tumor is a source of coagulability but also of different types of emboli, including metastatic ones, resorting to the use of devices to close heart defects, even during chemotherapy, as long as you have a good Karnosky and other indices favorable prognostics and frailties, is currently a suitable choice to be made.

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## Introduction

There are still controversies regarding the optimal therapy for the prevention of recurrent stroke/ Transient Ischemic Attack (TIA)/cryptogenic stroke in patients with Atrial Septal Aneurysm (ASA), in isolated form or with association with a Patent Foramen Ovale (PFO) [1]. Even fewer data are available on cancer patients [2]. Although the cardiac malformation conditions listed are frequent in the general population, there are not many testimonies in the medical-scientific literature of cases of aneurysm of the interatrial septum and persistence of the oval foramen in subjects suffering from breast cancer and more generally from cancer. We take a cue from a case that came to our observation to self-audit and launch some take home message for thought if possible.

## Case history

A 48-year-old housewife, ex-smoker, was taken care of for a hypoechoic nodular formation with spiculated margins, with a major axis of 12 mm, identified on radiography performed for screening. A subsequent Fine Needle Biopsy (FNAB) categorized the lesion as BI-RADS 5 (BI-RADS is a scheme for putting the findings from mammogram screening for breast cancer diagnosis into a small number of well-defined categories. Category 5 is equivalent to injury at highly suspicious of malignancy). Eventually diagnosis by eco-assisted core biopsy of right-sided "no special type" breast cancer subjected to upper right quadrantectomy and ipsilateral lymphadenectomy. On histological examination, there was a moderate differentiation, vascular emboli present, perineural infiltration. The stage of the tumor was then determined with a staging sec. Elston-Ellis pT1-G2; N0; Mx. Immunohistochemical profile: ER (Estrogen Receptors) 90%, PgR (Progesterone Receptors) 80%. Then, we aimed to highlight any association of the proliferation index (Ki67) in breast infiltrative duct carcinoma with the tumor grade, tumor size and nodal status in addition to hormone receptor status: Ki67 was 5%; HER2 score 3+. The patient was started on therapy with cyclophosphamide 960 mg, epirubicin 144 mg, dexamethasone 12 mg, pantoprazole 20 mg, ondansetron 8 mg, folic acid 5 mg, paracetamol 1 g, fosaprepitant dimeglumine 150 mg, pegfilgrastim 6 mg. At the check of fair general conditions (mild amnestic dyspnea), good vital signs and blood chemistry tests, normal EKG tracing (Figure 1).

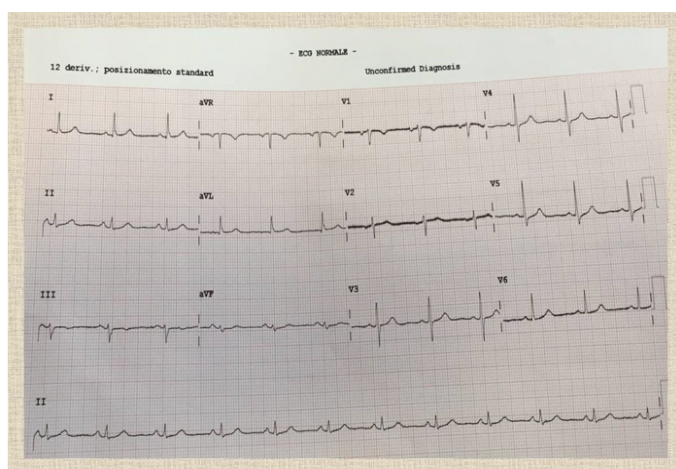


Figure 1: EKG.

The transthoracic echocardiogram showed "normal atrial dimensions (atrial diameter 3.2 cm-right atrial area: 16.2 cm<sup>2</sup>) and left and right ventricular, normokinesis and good ejection fraction (EF > 50%), mitro-tricuspid and pulmonary insufficiency. PAPs approx. 50 mm Hg. Normal vena cava of normal size (1.7 cm), collapsible with the breath. Atrial septal aneurysm was also found with significant ASA patency, septal defect and left-right shunt (Figure 2).

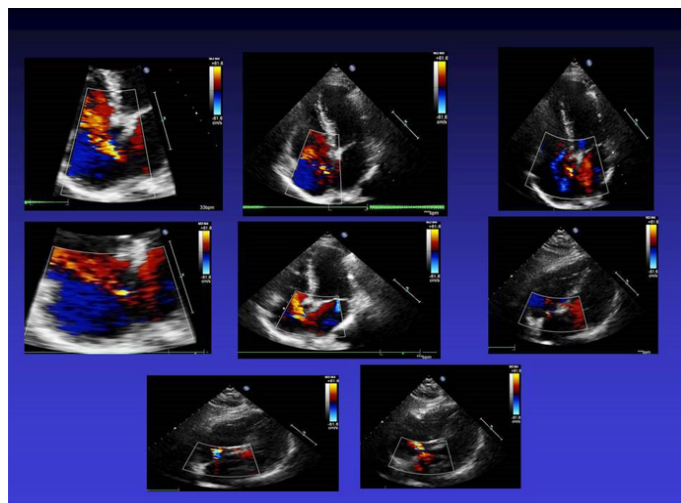


Figure 2: Echocardiographic picture of the patient seen in transthoracic echocardiography. The explanations in the text.

After reassessment of the clinical case, we decided to send the patient to perform the microbubble test for a better definition of the case and the decision of a possible interventional or pharmacological therapy (anticoagulant), the latter preferred at the beginning to then change decision and opt for the use of a device to close the defect.

## Discussion

The interrelationship between stroke and cancer is complex. In fact, they can occur independently in a given patient or cancer can lead directly or indirectly to a stroke through various and heterogeneous mechanisms, including hypercoagulability, non-bacterial endocarditis and adverse events of treatments [3-5]. In this already complex mosaic, the presence of a congenital heart disease can be inserted, which, also through the mechanisms mentioned, can generate repercussions on the intracardiac hemodynamics potentially the source of cerebral emboli. The atrial septal aneurysm is a thinning of the atrial septal wall, sometimes associated with PFO, which tends to move between the atria in systole. It is a cardiac anomaly, diagnosed with echocardiography and the presence of which is often described in literature as associated with stroke (SPARC study) [6-8]. Although the literature has investigated the topic, there are doubts both about the pathogenesis of stroke from potentially emboligenic sources related to this condition. A large-scale meta-analysis by Overall e coll. [9], already for 20 years has confirmed that both SIA and PFO aneurysms are significantly associated with stroke in young patients (age <55 years). Therapeutic choices include only medical therapy (antiplatelet or anticoagulant) or interventional therapy (closure with percutaneous device or open surgical repair). The latest editions of the SPREAD (Stroke Prevention and Educational Awareness Diffusion) guidelines (summary 16,98) recommend in young patients with persistence of the foramen ovale to evaluate the best treatment on a case by case basis, considering the risk of complications or the limitation of daily life that involves long-term drug treatment [10]. In

the decision-making of this case we tried to stick to the conclusions of the study by Cerrato P et al [11], despite the low case studies studied (86 pieces) and without none of these patients being affected by oncological pathology. The first decision to resort only to anticoagulant therapy stemmed from the desire to preserve the patient from possible arrhythmic complications, present and described in the Literature [12,13]. However, we also analyzed the most recent medical literature. The results of three studies suggested that in patients with cryptogenic stroke, the foramen ovale closure might be beneficial in reducing the risk of recurrent vascular events when compared to medical treatment and the benefit of the closure was greater in patients with a substantial shunt [14]. the recurrence of cerebral thromboembolic events also appeared, in the long term, to be reduced with this type of treatment, compared to medical therapy [15]. The most recent guidelines seem to encourage this attitude [16]. Although a big step forward that will benefit many patients has been taken with recent trials, many questions remain unanswered. Therefore, numerous further studies on larger cases are needed to determine the optimal treatment of patients, with particular reference to the selection of subcohorts of patients also affected by neoplasms in order not only to confirm whether the atrial septal aneurysm (isolated or not) is a direct cause of cerebral ischemia or a contributing cause or an additional risk factor for cryptogenic stroke in these patients, but also what is the optimal therapy in the cancer patient [17,18].

#### Declaration

**Contributors:** Magro VM was the primary researchers and wrote the manuscript. Magro VM provided research and editing assistance to the manuscript. Magro VM provided research and editing assistance to the manuscript. Magro VM contributed to overall article design, data collection as well as revising and approving the manuscript.

**Editorial guidelines:** the authors of this article confirm that the contributions of the paper are unpublished, simultaneously not submitted to other journals and that the content conforms to the rules of research ethics.

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**Ethical guidelines:** The authors confirm that the ethical guidelines must be observed and the work has been conducted in accordance with the Declaration of Helsinki (1964).

**Informed consent form of the patient:** not necessary. There are no data or photographs that may identify the patient.

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