CASE REPORT

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Long disease-free survival following total sternal resection and reconstruction of the sternum with acrylic cement for unique massive sternal metastasis after operated breast cancer

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Abstract

Unique sternal metastasis is an uncommon finding in the follow-up of operated breast cancer. We present a case of massive sternal metastasis occurred few years after radical resection of a right mammary cancer, that we solved by total sternal resection and reconstruction of sternum with acrylic cement and Vicryl mesh. The patient is disease-free five years after the operation.

Keywords: breast cancer, sternal metastasis, sternal reconstruction.

Introduction

It is generally agreed since early surgery that breast cancer could migrate along nodes near internal mammary artery. Aggressive mastectomy including ribs and sternum was proposed by Margottini, but later reviews failed to show better outcomes [1]. Holden performed the first sternectomy for sarcoma [2, 3].

Sternal metastasis is not uncommon [3]. Due to particularities in sternal blood sternum lacks communication to the paravertebral venous plexus flow [4]. In contrast with vertebral lesions, some sternal lesions have been observed to remain solitary with time. A singular sternal metastasis can be treated surgically. Magnetic resonance imaging (MRI) studies confirm the role of internal mammary artery in disease proliferation [5].

There is an ongoing debate on the influence of sternum on the thoracic stability, some attributing the name of a fourth column to the sternum [6]. Same author agree that the role of sternum is poorly researched. A study by Watkins *et al.* [7] regarding the biodynamics of the rib cage found that a sternal fracture accounted for up to 40% instability, although the study was performed in an elderly population with no osteodensitometry based screening. Piggott point was that today sternal lesions are not included in the scoring systems, and more research is need for such an approach. The final recommendation is to use a sound clinical judgment, carefully considering the risk benefit ratio [6].

Cakmak found sternal tumors to be rare (5%) in the context of chest wall tumors [8]. According to Piggott *et al.*, the incidence of sternal metastasis is unknown. A study cited by the author found a 15.1% incidence of sternal metastases from 415 necropsies [6].

According to Downey *et al.*, the local recurrence after breast cancer first excision is between 4% to 20%. No details of sternal involvement are given. Even if chest wall involvement is generally associated with poor prognosis, a single solitary lesion has median survival of 5.6 years and a 10-year survival of 30% [9].

Sternal involvement or an isolated sternal metastasis is relatively uncommon after breast cancer. Langstein *et al.* found the total chest wall involvement after breast cancer was 1.65% in 1694 patients [10]. In the Noguchi *et al* study, the incidence was 1.5% of all relapses and 5% of total bone relapses [4]. Chockalingam *et al.* reported incidences that varied from 1.9% to 5.2% [11].

According to Preti *et al.*, any solitary sternal tumor is probably of malign nature [12]. Sheikhy *et al.* found sternal benign tumors to be extremely rare [13]. Cakmak points up to 80% malignancy in sternal tumors [8].

According to Cakmak, a chest radiograph is the first

choice exam, followed by thoracic computed tomography (CT) scan. MRI and positron-emission tomography (PET)–CT maybe indicated for better delimitation of local involvement. Due to high probability of malignancy, pre-operatory biopsy is generally not indicated [8]. Despite that, the Soysal *et al.* study employed a form of biopsy (fine needle in general) for all patients in preoperative stage [14]. According to Piggott *et al.*, any lytic lesion, even without identifiable fracture, could pose a risk and should be closely monitored if surgery is not indicated. Of course, associated spinal lesions are what complicate things, but in this case report, spine was not affected [6].

Singletary review points out that it may be an economical and health benefit for routine screening breast cancer patients by chest radiography, following primary tumor excision [15].

Noguchi *et al.* study identified all nine cases of primary tumor of sternal metastasis as primary ductal breast carcinoma. Axilary lymph nodes involvement was demonstrated in seven patients and parasternal involvement in two. Three out of five cases screened were estrogen positive. Upon secondary resection, parasternal lymph involvement was documented in three patients and mediastinal in one [4].

Novel ^{99m}Tc-3P-RGD2 peptide imaging approach by Shao *et al.* [16] showed great potential for detection of osteolytic bone metastasis due to high expression level of $\alpha_v\beta_3$ integrin on osteoclast and most tumor cells.

Emerging techniques of intraoperatory pathological confirmation of malignancy like the confocal microscopy [17] could be used in the assessment of the resection limits during sternal resections.

Usually, the oncological prescription is either chemo or radiotherapy, or hormonal therapy in selected cases, surgical intervention being an elective approach [6].

Freeman *et al.* point out that for most bone metastasis, bisphosphonates and radiotherapy remain the golden standard. Surgery was indicated for fractures and neurological issues, such as compressions. However, a point of exception was made towards the solitary bone metastasis, where oncological resection may be indicated [18].

Singletary review recommends routine surgery for sternal involvement in breast cancer, as it has been shown to increase median survival [15].

For palliative purposes, there are alternatives to surgery as radiofrequency thermal ablation, reviewed by Masala *et al.* [19] with good results on the pain and disability scale, and minimal complications. Obviously, no claim of radical treatment can be achieved with this approach.

Kuranishi *et al.* report good results with a modern technique of autologous formalin-fixed tumor vaccine after resection therapy [3].

According to Incarbone *et al.* [20], the most indicate resection is 2–4 cm from the affected or irradiated area. Bongiolatti *et al.* [21] recommend less than 3 cm free margins resection. Soysal *et al.* [14] point towards a 5 cm free margin.

According to Sanna *et al.* [22], the reconstruction techniques best option was methyl methacrylate for many years. Modern, titanium is favored due to good material properties, great tolerability and MRI compatibility. Apart from commonly use meshes, additional techniques were proposed. Ceramic prosthesis has numerous advantages, but they are costly. Allografts have an undeniable biological advantage, promoting good bone recovery. Recent techniques like three-dimensional (3D) printing and computer-aided simulation may be used to tailor the graft to perfection, increasing the chances of success. A case report of such approach was documented by Lipińska *et al.* [23]. Allografts studies generally report good results. For musculocutaneous flap, *pectoralis major* remains the foremost candidate, followed by *rectus abdominis* in either vertically or transverse technique.

On the emerging front, Torregrossa *et al.* [24] point towards the value of vascularized allograft transplantation, partially supported by the laboratory experiments on rat.

Aim

Considering that secondary sternal tumors are quite rare and the available reconstruction techniques and indications vary between studies and even between patients of the same study, current case presentation is aiming for a shared experience to be useful for all practitioners in thoracic cancer treatment.

Case presentation

We present the case of a 24-year-old woman, M.C., with a radical surgery for a right breast cancer two years before her current presentation (initial presentation at the end of 2012). Correct postoperatory oncological treatment (chemo- and radiotherapy) followed a right mastectomy.

Ethical clearance was obtained and the patient provided informed consent for the use of all relevant medical data and imaging, in accordance with current national and international legislation.

A PET-CT requested by the plastic surgeon before a planned mammary prosthesis implant (demanded by the patient) revealed a unique, giant sternal metastasis and possible small local recurrence area (Figure 1).

The anamnesis and clinical examination excluded any clinical symptoms but revealed the small local recurrence area (Figure 2). The patient accepted the radical surgical treatment (complete sternal resection and reconstruction) proposed by our team due to the oligometastatic status.

We performed a battery of laboratory tests, including a complete blood count, erythrocyte sedimentation rate, C-reactive protein, glucose level, blood lipid profile, liver function tests, creatinine, urea, coagulation times, serum ionogram, total serum proteins and urinalysis. No significant abnormalities were revealed by these tests.

Therefore, we performed under general anesthesia a complete resection of the small recurrence area and total sternal resection of the sternum. Due to initially no free margins on intraoperatory histological examination of the resected specimen, we had to perform three sequential cuts of the sternum, involving ultimately even the two heads of the clavicles, until we obtained a R0 resection – microscopic margins negative for tumor invasion (Figure 3).

Following resection, a sternal reconstruction was performed using acrylic cement (surgical bone cement, Groupe Lépine SA) and two layers of Vicryl meshes (Figure 4). No pleural or subcutaneous drainage was used.

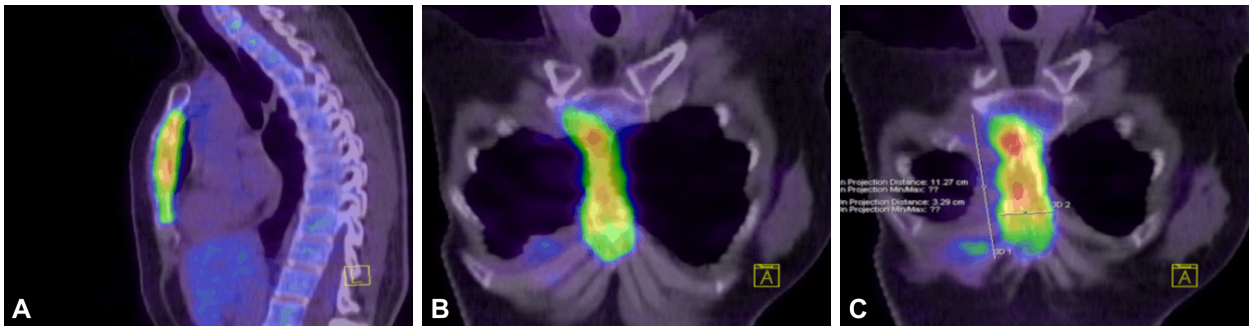

Figure 1 – *(A–C) PET-CT scan demonstrating unique, giant metastasis of the sternum and small local recurrence area after right mastectomy. PET-CT: Positron-emission tomography–computed tomography.*

Figure 2 – *The small local recurrence area after right mastectomy.*

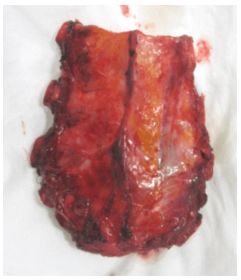

Figure 3 – *Sequential sternal resections: the resected specimen.*

Figure 4 – *(A and B) Sternal reconstruction using acrylic cement and two layers of Vicryl meshes.*

The post-operatory evolution was favorable, with a small right pleural effusion observed few days after and solved by two thoracocenteses without further recurrence. We discharged the patient on postoperatory day four with a satisfactory aesthetic result appreciated by the patient, without pain nor paradoxal movement of the neo-sternum.

The excised pieces were immediately fixed in 10% neutral formalin solution and sent to the Department of Pathology for histopathological diagnosis. The biological material was embedded in paraffin and cut to 4 µm by microtome, then stained with Hematoxylin–Eosin (HE) and Goldner–Szekely (GS) light green trichrome. For the immunohistochemical study, we used the following antibodies: anti-Ki67 (monoclonal mouse anti-human Ki67, clone MIB-1, 1:50 dilution, Dako); anti-cytokeratin (CK) 7 (monoclonal mouse anti-human CK7, clone OV-TL 12/30, 1:50 dilution, Dako); anti-CK20 (monoclonal mouse anti-human CK20, clone Ks20.8, 1:25 dilution, Dako); anti-c-erbB2 (polyclonal rabbit anti-human c-erbB2 onco-protein, 1:500 dilution, Dako); anti-vimentin (monoclonal mouse anti-vimentin, clone V9, 1:50 dilution, Dako); anti-cluster of differentiation (CD) 34 (monoclonal mouse anti-human CD34 Class II, clone QBEnd 10, 1:100 dilution, Dako).

The histopathological study of the sternum tumor showed the existence of a cellular epithelial tumor structure organized in islets or lobules separated by fine connective septa (Figure 5). Tumor cells showed varied sizes and shapes, basophilic cytoplasm, large, hypochromic and nucleolate nucleus, with the nucleus/cytoplasm ratio in favor of the nucleus (Figure 6).

The tumor replaced the sternal red bone marrow at this level and destroyed most of the bone structure; thus, we identified rare, partially lysed, bone trabeculae (Figure 7).

The use of the anti-Ki67 antibody showed a relatively low tumor proliferation index (Figure 8) which, in conjunction with the macroscopic tumor size, posed a question on the age of the metastasis and the efficiency of oncological treatment applied. The tumor cells were weakly positive for the anti-CK7 antibody (Figure 9) and negative for the anti-CK20 antibody (Figure 10). In addition, tumor cells were positive for c-erbB2 (Figure 11) and negative for vimentin (Figure 12).

The use of the anti-CD34 antibody enabled us to find a relatively abundant blood supply of the tumor stroma, formed mainly of a capillary network organized around the islands of tumor cells (Figure 13).

Microscopic examination revealed the presence of local recurrence of tumor cells, either isolated or grouped into islands or cords, infiltrating the dermal connective tissue, adipose tissue of the hypodermis or the remaining muscle fibers after mastectomy (Figures 14–16).

The patient is disease free and doing well five years after the total sternal resection and reconstruction.

Discussions

There is no consensus regarding the optimal treatment for patients with breast cancer and isolated sternal involvement. Though classified as *American Joint Committee on Cancer* (AJCC) stage IV, this group of patients may have prolonged distant disease-free survival [11].

According to Sheikhy *et al.* [13], chest flail and ventilatory restriction are the most pressing issues to address with reconstruction, although cosmetic aspect should never come last. On a case of rare aneurysmal cyst, reconstruction with cryogenized allograft showed good results.

Cakmak [8] reports a 1.1% rate of severe problems upon chest reconstructions (paradoxical movement and respiratory failure) after sternal resection.

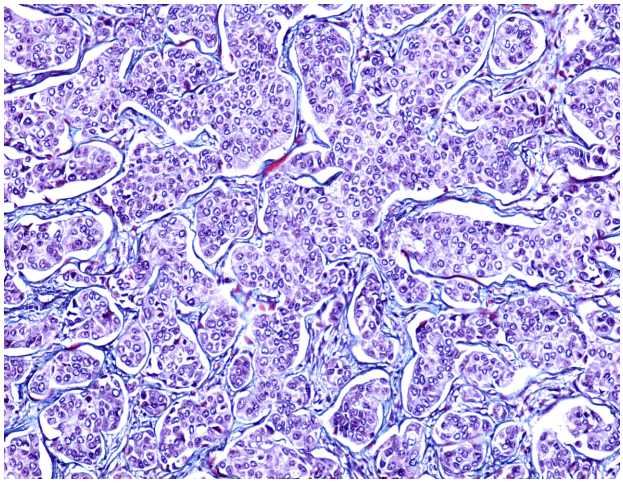

Figure 5 – ***Overall microscopic image of the sternum tumor; the tumor cells organized in the lobules are delimited by fine connective septa (GS trichrome staining, ×100).***

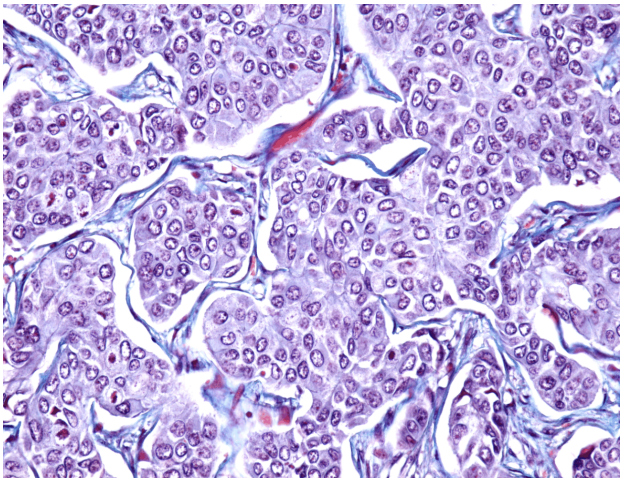

Figure 6 – ***Tumor cells organized in lobules, with basophilic cytoplasm, large nucleus, hypochromic and having prominent nucleoli (GS trichrome staining, ×200).***

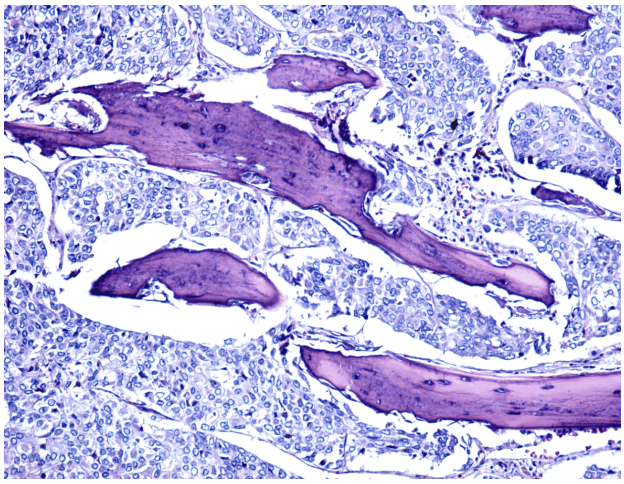

Figure 7 – ***Sternal bone trabeculae (spongy bone debris), deformed, absent endostasis, partially lysed by tumor metastasis (HE staining, ×100).***

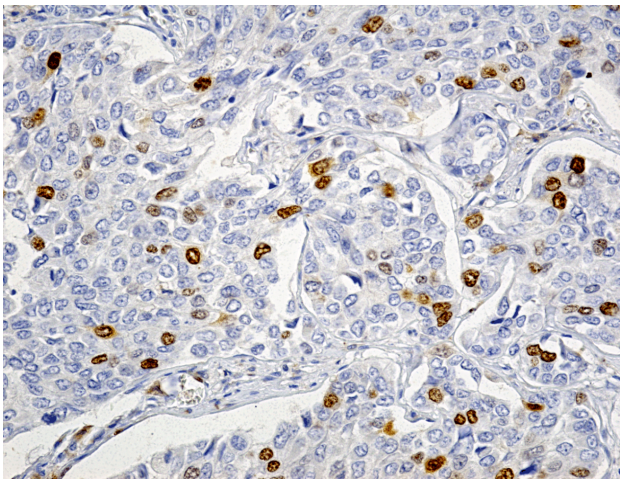

Figure 8 – ***Tumor cell islets with a relatively low proliferation index (Anti-Ki67 antibody immunostaining, ×200).***

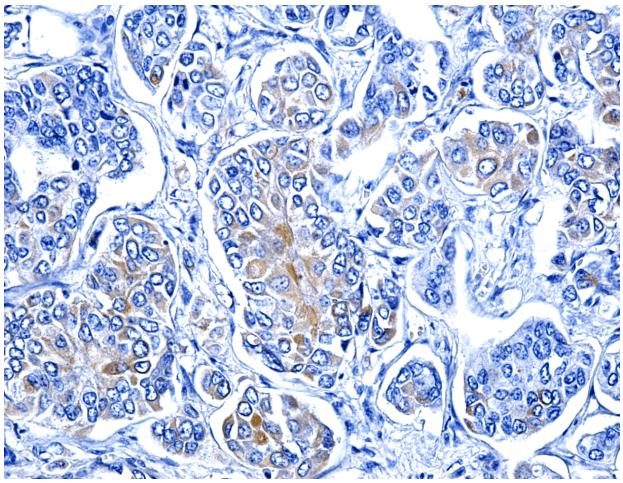

Figure 9 – ***Positive tumor cells to the anti-CK7 antibody (Anti-CK7 antibody immunostaining, ×200).***

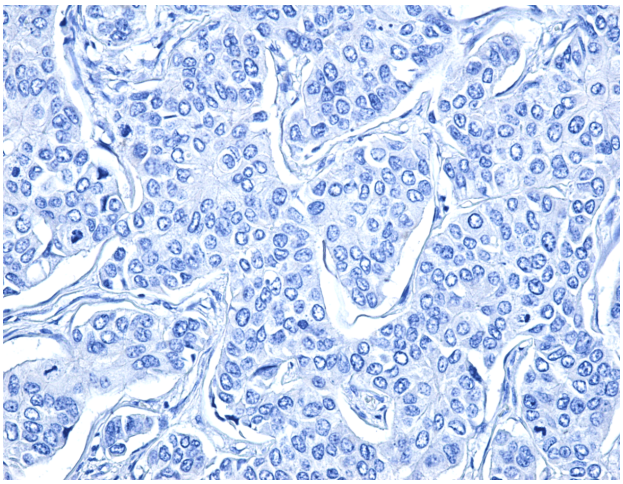

Figure 10 – ***Tumor cells without anti-CK20 antibody reaction (Anti-CK20 antibody immunostaining, ×200).***

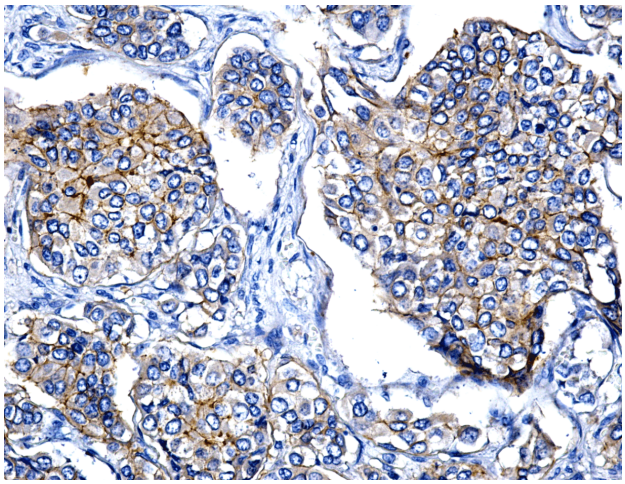

Figure 11 – ***Positive tumor cells to the anti-c-erbB2 antibody (Anti-c-erbB2 antibody immunostaining, ×200).***

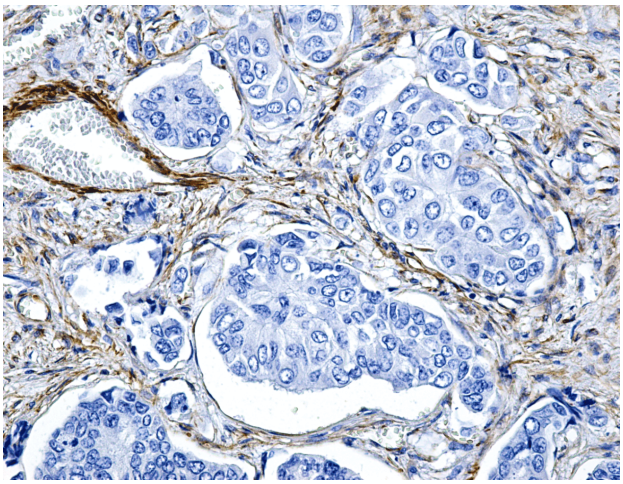

Figure 12 – ***Immunostaining with vimentin revealed the negative reaction of tumor cells, but the stromal cell positivity (Anti-vimentin antibody immunostaining, ×200).***

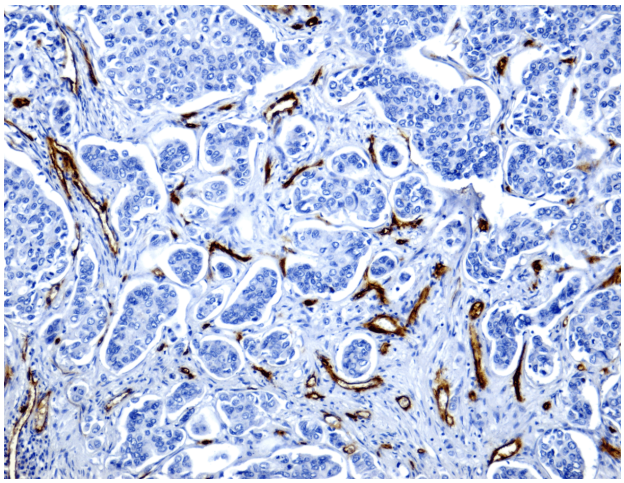

Figure 13 – ***Capillary network well developed around the islets of tumor cells (Anti-CD34 antibody immunostaining, ×100).***

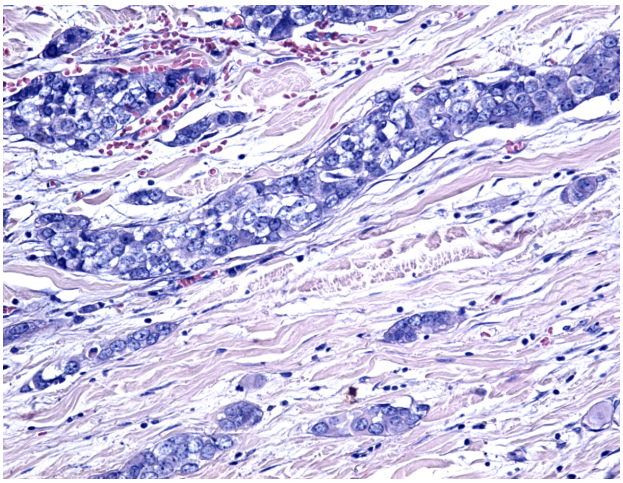

Figure 14 – ***Isolated cells, islets and tumor cell lines, disseminated diffuse into dermal connective tissue (HE staining, ×200).***

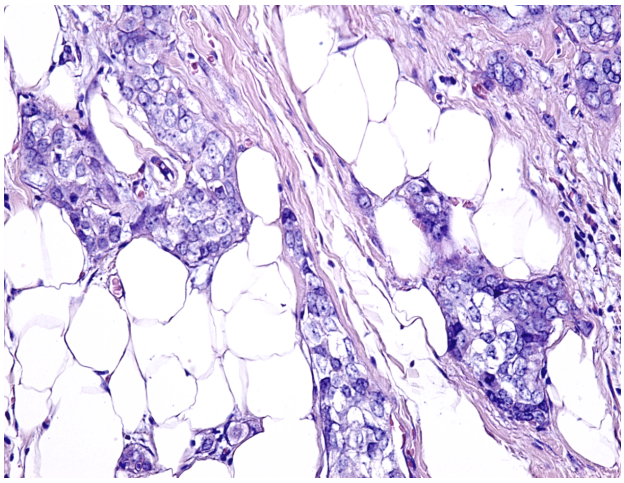

Figure 15 – ***Tumor invasion in hypodermis fat (HE staining, ×200).***

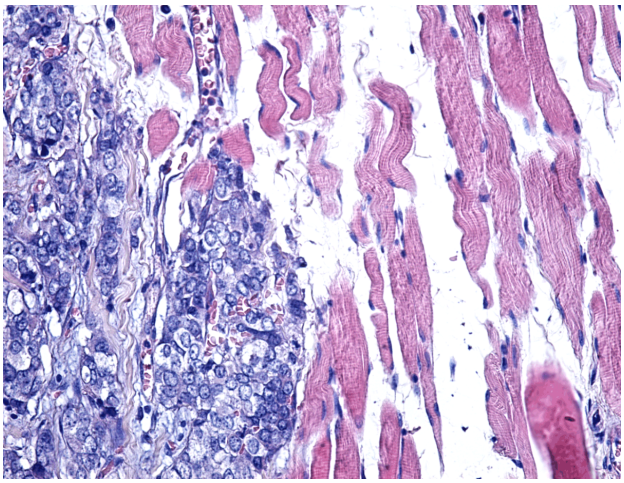

Figure 16 – ***Invasive tumor metastasis in the muscular tissue in the chest wall (HE staining, ×200).***

According to Lipińska *et al.* [23], negative predictive factors are patient's age greater than 60 years old, size of the chest defect and simultaneous lung resection procedure.

Good prognosis factors, identified by Bongiolatti *et al.* [21], are histological low grading, good margins of resection, young age and no adjuvant treatment.

There is good data on general reconstruction techniques and their outcome but few are dedicated to breast cancer secondary sternal involvement. A review of general data is first necessary.

A study by Deschamps *et al.* [25] employed chest wall resection for 197 patients, 65 of indication being secondary wall chest involvement. From the total, sternal resections were involved in 46 patients. The extent of sternal and rib resection was deemed to have no effect on outcome. 67.5% of reconstructions were made with polytetrafluoroethylene and 32.5% with polypropylene. Approximately 60% of soft tissue reconstruction was by transposed muscle. Although the rate of complications was high (46.2%), severe complications (infection, seromas) were under 10% and 70.9% of the patients experienced full recovery (from surgical, not oncological point of view). Most authors agreed that prosthetics are generally not necessary in partial sternal resection.

Chockalingam *et al.* [11], on a series of eight patients with isolated sternal recurrence after breast cancer, found six cases with no other evidence of whole body spreading in 10 years. On this group, only four patients received surgery. There are no data on how surgery influenced survival, but the whole point of the study was to consider sternal involvement a regional extension and not a stage IV disease. Langstein *et al.* [10], addressing chest wall involvement after breast resection, support the theory of locoregional involvement. Total chest wall involvement after breast cancer was 0.64% on 1694 patients.

Bongiolatti *et al.* [21], following 36 patients after sternal tumor resection (seven of which had breast cancer), performed total resection in six cases and extended resection in seven cases. Reconstruction was made by a rigid system (STRATOS) and muscular flap in 11 cases, with polytetrafluoroethylene patch in six cases and by musculocutaneous patch alone in 19 cases. Complications rate was 19%. Disease-free survival at five years was 61%. Incomplete resection (including not enough free margins) was marred by relapses.

According to Lipińska *et al.* [23], the most often observed complications associated chest wall reconstruction are respiratory disorders, chronic pain, chest flail, local pleural thickening, necrosis of used pedicle muscle lobes, mediastinitis and implant instability of the chest. Secondary fracture has also been reported.

The Soysal *et al.* [14] study found a 26.7% morbidity after sternal resection, and local recurrence in six patients (four amongst breast cancer, three in stage IV disease). Overall five-year survival after sternal resection of recurrent breast cancer was 33%.

Mansour *et al.* [26] performed sternal resection on 56 patients out of 200 chest wall tumor group. Most cases were sternectomy (16 patients) or hemisternectomy (18 cases). Most reconstructions were by flaps. No separate data on sternectomy complications are given.

Syazni *et al.* [27] have used titanium mesh and acrylic plate reconstruction for thyroid carcinoma sternal involvement, with rather disappointing results, mostly due to onsite infection of implant. Implant was eventually removed and repair was made with musculocutaneous flap.

Incarbone *et al.* [20], on a series of 52 patients with primary or secondary sternal tumors, found that 19 were either metastases or local recurrences of breast cancer. Most patients benefited from a subtotal sternal resection and the preferred repair technique was the myocutaneous flap. The five-year survival cited by this study in breast cancer recurrences ranges from 34% to 63%. Based on lower risk of metastasis of single sternal lesion due to blood flow particularities, the authors advocate that resection surgery maybe indicated for breast cancer recurrences as part of the multimodal therapy, which is thought to be the golden standard.

Chapelier *et al.* [28] performed a study on 38 cases of primary chest tumor, reported eight total, seven subtotal and 23 partial sternal resections. Most reconstruction employed a polypropylene patch. Four septic complications and seven local recurrences were reported. The reference study in the field was done by Lequaglie *et al.* [29]. The sternotomies were total in eight cases, subtotal in 32, and partial resections in other 48. Prosthetics covered by musculocutaneous flaps were used in majority of reconstructions. Five-year survival was 41.8%, one of the highest in literature. Broad sternal resections should be recommended with curative purposes, especially since today we have adequate prosthetic techniques and materials.

A study by Noguchi *et al.* [4] was focused on sternal resection after breast cancer metastasis. Nine cases were found, eight with partial and one with total sternal resection. Acrylic plate was used in three cases and myocutaneous flap in six cases. All nine cases received chemotherapy or chemoendocrinotherapy. The median survival was 30 months. Involvement of a mediastinal or parasternal structure was a marker of poor prognosis. Moreover, radical resection of lymph nodes appeared not to influence survival. Three of the cases survived more than six years. None of the cases received radiotherapy post-resection. Authors conclude that, despite the seemingly good results, a randomized trial against radiotherapy only treatment is necessary. Noguchi *et al.* study cited data points in good evolution of sole sternal secondary involvement, with survival up to four years, even with conservative treatment.

Kim & Chlebowski [30] reported a case of a 59-year-old female with hormone receptor positive human epidermal growth factor receptor 2 (HER2)-negative breast tumor. Discussing the significance of sternal involvement, recommend that such lesion should be regarded as loco-regional extension rather than a manifestation of whole body metastasis, hence a much better prognosis. Following own experience, Kim & Chlebowski recommend use of Fulvestrant for all patients with sternal involvement due to hormone receptor positive breast cancer, even with surgical correct resections.

Demondion *et al.* [31] experience with custom tailored titanium mesh was favorable, with full surgical recovery at six months follow-up. No further oncological data are given.

Abdel Rahman *et al.* [32] series report a 17.3% complication rate, with either musculocutaneous flap or methyl methacrylate with Prolene mesh. Perioperative mortality was 1.02%.

The Soysal *et al.* [14] study found 26.7% morbidity after sternal resection, and local recurrence in six patients (four amongst breast cancer, three in stage IV disease). Overall five-year survival after sternal resection of recurrent breast cancer was 33%.

Girotti *et al.* [33] advocates a rib-like technique, an advanced reconstruction method. On 101 cases (30 with breast cancer recurrence) reports good post-operatory results, but no influence on long-term survival for aggressive cancer. Chan *et al.* [34], reporting on 13 cases, found a non-significant trend towards better median survival in surgical treated cases *vs.* conservative ones.

Unlike the pulmonary metastases, which are usually multiples [35, 36], the unique sternal metastasis after breast cancer can be radically resected with a good quality of life following the operation due to the various armamentarium of sternal reconstruction [37, 38]. According to Scarnecchia *et al.* [39], good preoperatory planning and choice of reconstruction method are keys to a good outcome. Not all cases like this are successes. Lee *et al.* [40] present a case of lymphatic extension following a procedure not unlike the one presented with current case. The possibility of pre-existing lung conditions may further influence the quality of life of such oncological patients that undergo major reconstruction of the thorax. Chronic lung diseases cause major distress, especially to elder patients, which reflects in lower chest compliance [41, 42]; reconstructive surgery may further decrease respiratory volumes due to morphological changes leading to restrictive dysfunctions that superpose pre-existing conditions.

Considering the above data, in our case the surgical indication and surgical execution were correct and good five-year survival was proved. Part of this case success is no doubt due to the radical approach on resection. Careful planning of preoperatory and operatory stages are the key to success.

Conclusions

The total resection of the sternum is feasible in selected cases of oligometastatic breast cancer involving only the sternum. The acrylic cement (covered by two Vicryl meshes) represents a good option for sternal reconstruction. No paradoxical movement and no displacement should occur if a rigorous fixation of the neo-sternum to the anterior parts of the ribs is performed.

Conflict of interests

The authors declare that they have no conflict of interests.

Authors' contribution

Alin Dragoş Demetrian and Mihai Olteanu contributed equally to the paper and share first authorship.

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