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CASE REPORT

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A rare case of immune thrombocytopenia secondary to breast cancer

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Key Clinical Message

Immune Thrombocytopenic Purpura (ITP) is in rare cases secondary to solid tumors, particularly breast cancer. In these cases, the clinical course of the ITP may follow the clinical course of the primary tumor, and remission of the ITP may be induced by treatment of the primary tumor.

KEYWORDS

autoimmunity, breast cancer, purpura, thrombocytopenia

1 | INTRODUCTION

Immune Thrombocytopenic Purpura (ITP) occurs in 2-4/100000 adults and results in thrombocytopenia with variable bleeding symptoms.[1] An association of ITP with lymphoproliferative disorders is well known and comprises up to 30% of cases of secondary ITP.[2] Paraneoplastic secondary ITP in solid tumors is less well known but has been described,[3] including in breast cancer patients.[4] A correlation between the clinical courses of ITP and of solid tumor was infrequently observed.

We describe the case of a patient presenting with ITP shortly after diagnosis of a localized breast cancer, who achieved complete remission of ITP after curative surgery of breast cancer despite rapid weaning of oral steroid therapy.

2 | CASE PRESENTATION

A 63-year-old woman was referred to the emergency room by her oncologist for severe thrombocytopenia (platelet count 2 x 10^9/L), without signs of active bleeding. Past medical history was relevant for ductal invasive right breast cancer diagnosed 14 years earlier, which had been treated by tumorectomy, radiotherapy, and tamoxifen. Comorbid conditions were non insulin-dependant type 2 diabetes, heterozygous mutation for factor V Leiden, and a chronic stable isolated elevation of gamma-GT liver enzyme of unclear significance.

Eighteen days prior to hospital admission, a routine mammography showed a peripheral opacity of the superior external quadrant of the left breast (Figure 1). Biopsy showed an invasive ductal carcinoma, estrogen-receptor 27% positive, progesterone-receptor negative, HER-2 positive (Figure 2). Bone scintigraphy, abdominal ultrasound, and chest X-ray did not show any metastases. A total-body ^{18}F-FDG PET-CT (Figures 3, 4) showed a hypermetabolic mass of the left breast, with multiple hypermetabolic lymphadenopathies in the axillar, internal mammary, intercostal, and para-vertebral regions. In addition, multiple other hypermetabolic lymphadenopathies were seen in supra- and infra-diaphragmatic regions, as well as retro-peritoneal lymphadenopathy, and splenomegaly with 2 hypermetabolic nodules. A puncture of a left para-aortic lymphadenopathy was planned.

A routine blood test unexpectedly showed an isolated severe thrombocytopenia, with platelet count of 28 x 10^9/L. It is noteworthy that all previous blood counts were normal (last month before admission). The next day, the platelet count had decreased to 2 x 10^9/L, and the patient was referred to the hospital and admitted for observation and treatment.

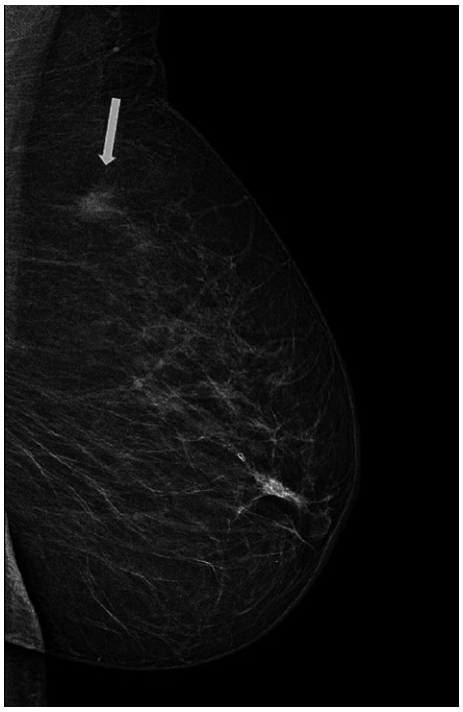

FIGURE 1 Mammography with suspect opacity of the superior external quadrant of the left breast

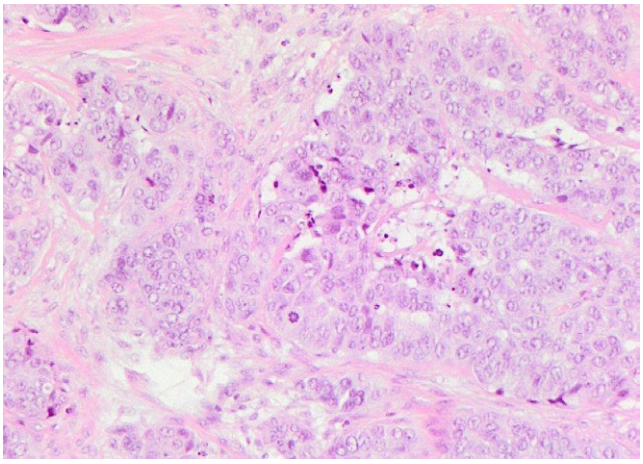

FIGURE 2 Breast biopsy (HE coloration): invasive ductal carcinoma

3 | INVESTIGATIONS

Complete blood count showed severe thrombocytopenia, and a moderate normocytic normochrome nonregenerative anemia (hemoglobin 110 g/L). Clotting tests were normal. Renal and hepatic functions were normal, except for the known and stable elevation of gamma-GT enzymes.

Protein electrophoresis, immunoglobulin dosage, light chain dosage, CD4+/CD8+ cell count, and immunofixation were normal. Serology for HIV, hepatitis B, C, EBV, and CMV were negative. Antinuclear antibodies were slightly and non-specifically elevated (1/180), without anti-ds DNA antibiodies.

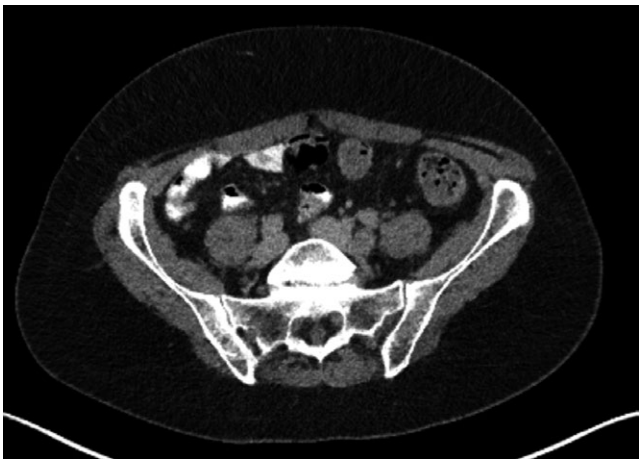

FIGURE 3 CT with infra-diaphragmatic lymphadenopathy

Peripheral blood flow cytometry did not show any B or T lymphocyte monoclonal population.

A bone marrow biopsy with cytology and flow cytometry was obtained and did not show any evidence of a lympho- nor myelo-proliferative disorder, nor of an infiltration of the bone marrow by the breast cancer (Figure 5).

A biopsy of a left latero-aortic lymphadenopathy was obtained under CT-scan after increase in the platelet count and showed normal follicular architecture without signs of malignancy (Figure 6).

4 | DIFFERENTIAL DIAGNOSIS

ITP being an exclusion diagnosis, we had to rule out other causes of isolated thrombocytopenia. Based on the medical history, we had no evidence for drug-related or para-infectious thrombocytopenia.

Central causes of thrombocytopenia, such as hematological malignancies, or infiltration of the bone marrow by the breast cancer, were ruled out by the normal bone marrow biopsy.

Thanks to the laboratory diagnostic work-up, we were able to exclude other causes of secondary ITP, such as autoimmune or viral causes.

Based on the result of the PET-CT with multiple lymphadenopathy, we initially suspected a lymphoma with secondary ITP. However, the normal biopsy of the left latero-aortic lymphadenopathy did not support this diagnosis.

After exclusion of all other causes, we reached the diagnosis of primary ITP or secondary ITP related to concomitant breast cancer.

5 | TREATMENT

Our patient received on the day of hospital admission and the following day a treatment of intravenous immunoglobulin

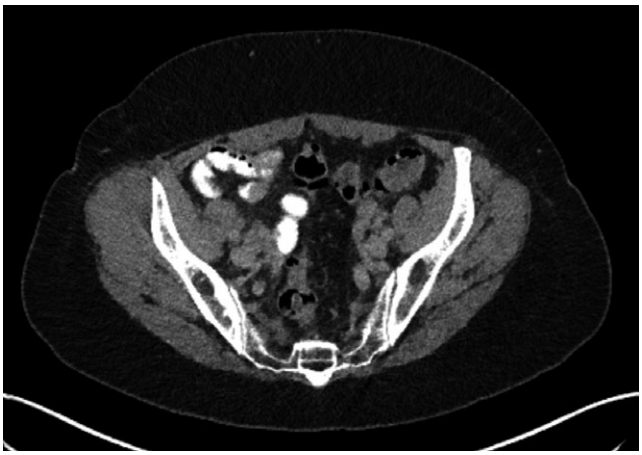

FIGURE 4 CT with infra-diaphragamatic and retroperitoneal lymphadenopathy

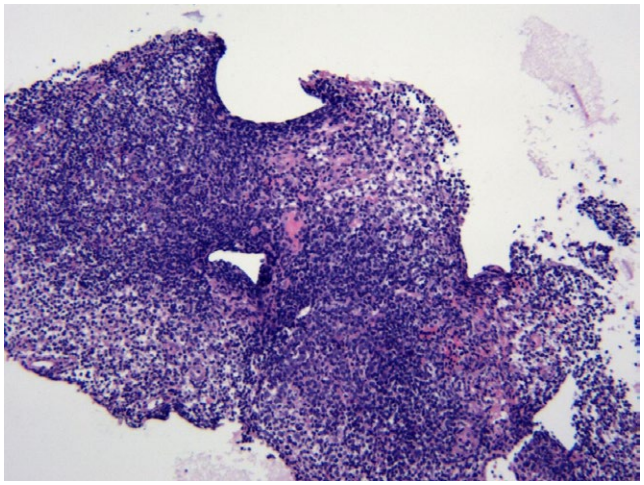

FIGURE 6 Biopsy of left latero-aortic lymphadenopathy (HE coloration)

(IVIG) with a dosage of 1 g/kg/d. Oral steroids were not started until after the biopsy of the lymphadenopathy (4 days after admission) so as not to tamper with the result of the biopsy.

6 | OUTCOME AND FOLLOW-UP

After the 2-day IVIG treatment, platelet count rapidly increased (Figure 7). After starting oral steroids, platelet count continued to increase and attained a value of 135 x 10^9/L 7 days after admission. The patient was then discharged.

During hospitalization, the patient also developed neutropenia without agranulocytosis, which resolved completely after the start of oral steroid treatment. Central causes were ruled out by normal bone marrow biopsy, as discussed above. We suspected a peripheral autoimmune paraneoplastic neutropenia. The moderate anemia stayed stable, without any signs of hemolysis, and was attributed to anemia of chronic disease.

Approximately one month after discharge from hospital, platelet count remained stable around 120 x 10^9/L. The initial plan of a neoadjuvant chemotherapy followed by surgery was then reversed to surgery followed by adjuvant chemotherapy. We expected a raise of the platelet count after removal of the tumor, allowing to deliver the chemotherapy in an easier way.

Our patient underwent tumorectomy of the left exterior quadrant of the left breast. An invasive ductal carcinoma pT1c SnN0 G3 Her2+ tumor was removed. Three sentinel lymph nodes were negative. A new ^{18}F-FDG PET-CT revealed the disappearance of all the metabolic lymph nodes initially observed. We explain this disappearance by a remission of the autoimmune phenomenon causing ITP. The patient then started adjuvant chemotherapy with Epirubicin, Cyclophosphamide, Paclitaxel, and Trastuzumab one month

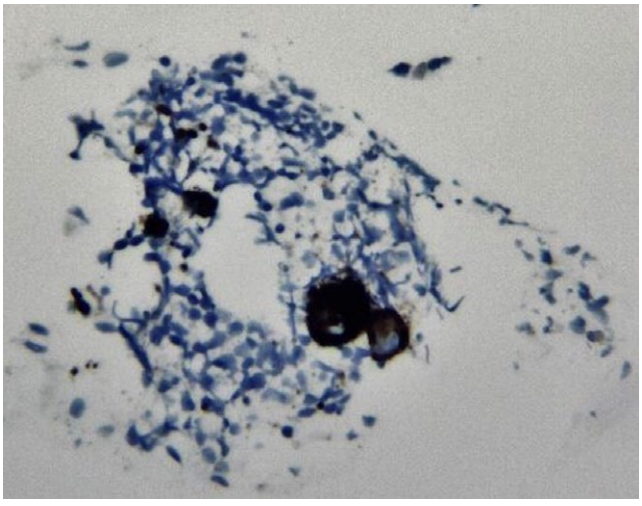

FIGURE 5 Bone marrow biopsy: CD 61 staining (showing stained megacaryocytes)

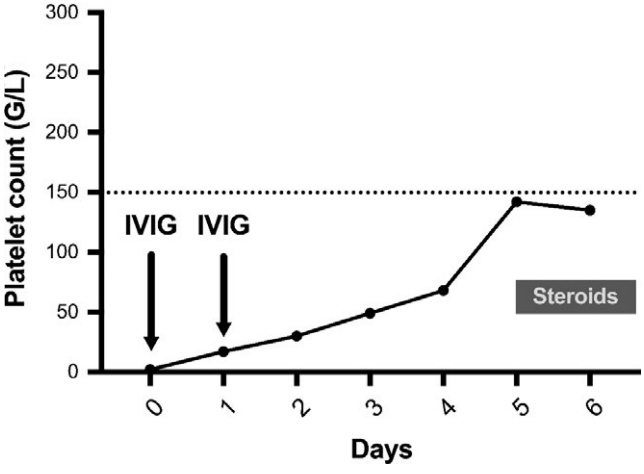

FIGURE 7 Platelet count (G/l) during hospital stay under treatment (IVIG day 0 and day 1, oral steroids 1 mg/kg/d since day 5). The dotted line represents the lower limit of the normal range

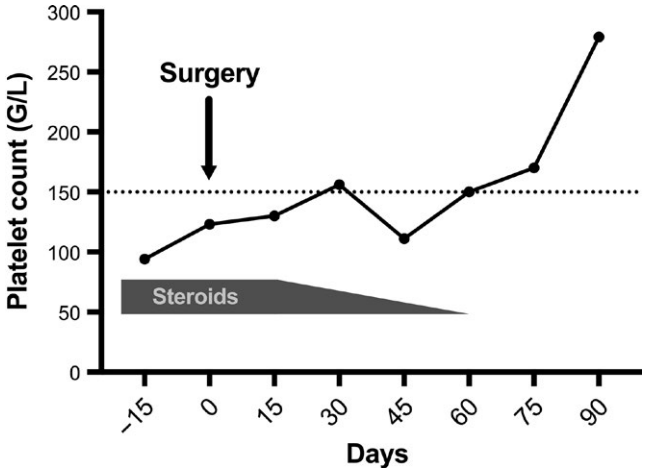

FIGURE 8 Platelet count (G/l) during follow-up and progressive weaning of oral steroids. Day 0: surgery. The dotted line represents the lower limit of the normal range

after the surgery. She has now received 4 cycles of Epirubicin/Cyclophosphamide, and 12 weeks of Paclitaxel/Trastuzumab are planned in total.

Oral steroids were weaned after one month of full dosage (1 mg/kg/d), over the course of 3 months. Platelet count remained within the normal range during this time period, and up to 3 months after total cessation of oral steroids, which is the duration of our follow-up for the time being (Figure 8).

7 | DISCUSSION

Approximately 80% of ITP are primary, due to autoreactive antiplatelet antibodies.[1] The remaining cases are secondary, to autoimmune diseases, HIV infection, *Helicobacter pylori*-colonization, lymphoid neoplasms and occasionally solid tumors.[1,5]

ITP associated with solid tumors has rarely been reported. Most common solid tumors associated with ITP are lung and breast cancer.[3] A 2012 study reviewing 68 published cases of ITP associated with solid tumors regardless of temporal relationship found that 35 (53%) patients in the study had an occurrence of ITP concurrent to the cancer diagnosis, of which only 2 patients achieved complete remission of ITP after cancer treatment (1 after cancer surgery alone, 1 after chemotherapy alone).[3] Of a published French series of 10 women with breast cancer and ITP, only three patients had a concurrent diagnosis of both diseases, and only one patient had a platelet count related to the clinical course of the breast cancer.[4]

There is therefore currently little evidence to support surgical resection of the solid tumor as a means to improve the paraneoplastic ITP.

Our patient is an example of ITP secondary to a solid tumor, with clinical course concomitant to the course of the breast cancer. Indeed, ITP occurred shortly after the diagnosis of breast cancer, responded well to IVIG and oral steroid therapy, but even better to surgery and adjuvant chemotherapy. ITP stayed in remission with normal platelet count after treatment of the breast cancer (surgical tumorectomy and chemotherapy) despite weaning of oral steroids. Indeed, weaning of steroids was done quicker than recommended for primary ITP.

This case supports the relationship between the breast cancer and the immune disease. We believe that removing the tumor led to remission of the ITP. Indeed, once the antigenic source triggering the immune reaction was removed, ITP disappeared. It also suggests the disease was truly localized at diagnosis. It is also plausible that chemotherapy played a role in inducing remission of ITP, as the chemotherapy included Cyclophosphamide, a potent immunosuppressor that may have helped wean oral steroids rapidly.

This case highlights the importance of treatment of the primary tumor in order to improve the clinical course of ITP. It also helped to conduct chemotherapy for breast cancer normally, as the platelet count returned to normal and was not a drawback to starting chemotherapy anymore. We suggest standard treatment of ITP, concomitant with treatment of the solid tumor if possible. We believe that further research should be conducted in this direction.

Furthermore, current guidelines do not recommend to screen for solid tumors when confronted with an ITP without a clear cause. We believe that further studies should be made to explore efficiency of such screening.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

SH: drafted the manuscript; AH: critically revised the manuscript; FS: critically revised the manuscript and provided help with the figures; YC: critically revised the manuscript.

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REFERENCES

1. Lambert MP, Gernsheimer TB. Clinical Updates in Adult Immune Thrombocytopenia (ITP). *Blood J*. 2018; http://www.bloodjournal.org/content/bloodjournal/early/2017/04/17/blood-2017-03-754119.full.pdf
2. Visco C, Rodeghiero F. Immune thrombocytopenia in lymphoproliferative disorders. *Hematol Oncol Clin N Am*. 2009;23:1261-1274.

3. Krauth MT, Puthenparambil J, Lechner K. Paraneoplastic autoimmune thrombocytopenia in solid tumors. *Crit Rev Oncol Hematol*. 2012;81:75-81.
4. Peffault de Latour R, Des Guetz G, Laurence V, et al. Breast Cancer Associated with Idiopathic Thrombocytopenic Purpura : A single center series of 10 cases. *Am J Clin Oncol*. 2004;27(4):333-336.
5. Kistanguri G, McCrae KR. Immune Thrombocytopenia. *Hematol Oncol Clin North Am*. 2013;27(3):495-520.

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