Palmar fasciitis and polyarthritis associated with secondary ovarian carcinoma. Case report

Ch. K. Giannakopoulos, G.K. Kyriakidou, G.E. Toufexi

Department of Gynecology, Laiko General Hospital, Athens (Greece)

Summary

Palmar fasciitis and a polyarthritis syndrome (PFPAS) is an uncommon paraneoplastic syndrome often associated with occult neoplasms, including ovarian and pancreatic carcinomas. A 67-year-old patient with presenting symptoms of PFPAS is reported. Twelve months after onset of the symptoms an ovarian and pancreatic adenocarcinoma was diagnosed synchronously. The spread pattern and other features of the neoplasm indicate that it was a primary pancreatic cancer with ovarian metastasis. Surgical excision of tumor and adjuvant chemotherapy caused remission of symptoms. A literature review of PFPAS and secondary ovarian neoplasms with a pancreatic primary tumor is discussed.

Key words: Palmar fasciitis; Paraneoplastic syndrome; Secondary ovarian carcinoma; Pancreatic carcinoma.

Introduction

Palmar fasciitis and polyarthritis (PFPAS) is a rare paraneoplastic syndrome associated with ovarian and a variety of non-ovarian malignancies including chronic lymphocytic leukemia, pancreatic adenocarcinoma, squamous cell carcinoma of the lung, chondrosarcoma and Hodgkin's disease [1].

It presents with progressive flexion contractures of both hands, inflammatory fasciitis, fibrosis and inflammatory polyarthritis. The diagnosis of an underlying neoplasm is often overlooked initially [2].

Metastatic tumors to the ovary from a primary pancreatic cancer are also rare and particularly difficult to distinguish from primary ovarian carcinomas [3, 4].

A patient with PFPAS in whom the underlying carcinoma was a pancreatic and ovarian tumor discovered synchronously is reported. Based on clinical and pathologic features, we concluded that probably the primary tumor was pancreatic carcinoma.

In the literature no other report of pancreatic adenocarcinoma with ovarian metastasis presenting as PFPAS was found, so a review of PFPAS and secondary ovarian tumors is reported.

Case Report

A 67-year-old woman presented with a 12-month history of progressive swelling, bilateral digital stiffness and pain, palmar thickening and erythema, proximal interphalangeal (PIP) joint and metacarpophalageal (MCP) joint contractures. She also developed polyartharlgia and nodules. Anti-inflammatory treatment with non-steroids and after that with prednisone did not improve symptoms.

Laboratory testing revealed a normal complete blood count and routine chemistry results. Antinuclear antibody, extractable nuclear antigen antibodies and rheumatoid factor testing were normal. Cancer antigens 15, 3 and 19,9 were normal but CA125 was increased to 470 U/ml and to 520 U/ml a week later (normal 0-350 U/ml).

Bone radiography showed PIP deformities and generative changes of the shoulders, hips and knees. A nodule and skin biopsy from the right hand revealed granulomatosis with leukocyte infiltration.

A computed tomography abdomen scan showed no pathology, but four days later magnetic resonance imaging of the abdomen revealed a tumor in the left adnexa of 3.5 cm in diameter.

The patient underwent exploratory laparotomy mainly because of the increased levels of Ca125. During laparotomy a solid tumor of the left ovary was found with omentum metastases and also a solid enlargement of the pancreas. There was no ascetic fluid. A hysterectomy with bilateral salpingo-oophorectomy was performed and also omentectomy, appendectomy and peritoneal biopsies; another biopsy from the surface of the pancreas was taken.

Microscopic examination revealed poorly differentiated ductal adenocarcinoma in the left ovary with capsule infiltration but not rupture. The same carcinoma was infiltrating the right salpinx and omentum. The right ovary, left salpinx, appendix, peritoneal biopsies and pancreatic sample were disease-free. Immunohistochemical staining with the pattern of CK 7, 18 and 19 were positive but CK 20 was negative.

Adjuvant chemotherapy with paraplatin and endoxan was started.

Symptoms improved progressively including pain and finger motion. Digital contractures resolved and the patient had no sign of recurrence one year after laparotomy.

Discussion

PFPAS is a paraneoplastic syndrome which presents with progressive symptoms, especially polyarthritis and flexion contractures of both hands. Other paraneoplastic myoskeletal syndromes are dermatomyositis, carcinomatous polyarthritis and hypertrophic pulmonary osteoarthopathy. The differential diagnosis of PFPAS includes rheumatoid arthritis, Dupuytren's contracture,

Revised manuscript accepted for publication January 19, 2005

scleroderma, eosinophilic fasciitis and reflex sympathetic dystrophy [5].

The patients are 25-75 years old, with an average age of 60 years. Rheumatoid factor and antinuclear antibodies (ANAs) are usually negative. Treatment with steroids or nonsteroidal anti-inflammatory drugs has little effect on symptoms [2, 6].

Usually the underlying malignancy is an ovarian carcinoma and 14 such cases have been reported since 1982, when Medsger *et al.* reported the first cases of this syndrome [2, 7, 8]. It is also known that other tumors, including pancreatic adenocarcinomas, are associated with PFPAS. Naschitz *et al.* have reported a 23% incidence of not initially diagnosed malignancies in patients with undiagnosed rheumatoid disorders [9]. Patients with PFPAS develop myoskeletal symptoms before the diagnosis of the underlying carcinoma.

Secondary ovarian carcinomas from a primary pancreatic tumor have not been associated with PFPAS up to now, and are considered to be very rare. The incidence of these tumors is difficult to determine due to many reasons. Firstly, it is known that the most frequent secondary ovarian carcinomas are Krukenberg tumors, which have a primary gastric site. The World Health Organization reports that the following features should be present when making a diagnosis of Krukenberg tumor: 1) presence of stromal involvement 2) presence of mucine-producing neoplastic signet-ring cells and 3) ovarian stromal sarcomatoid proliferation. In recent years the term "Krukenberg tumor" has been more loosely applied to describe a metastatic carcinoma to the ovary and in many cases, secondary ovarian carcinomas from a primary pancreatic tumor are included in Krukenberg tumors, though they represent only a small proportion of gastric tumors. In other reports, pancreatic primary tumors are reported separately [10, 11]. Furthermore, very often it is difficult to distinguish clinically or histopathologically secondary ovarian carcinomas from primary ones, and often these tumors are found at autopsy. It is reported that 3,5-6% of pancreatic carcinomas give ovarian metastases, when autopsy findings are included. In these cases, the ovarian metastases were incidental findings. In agreement with this is the fact that very often pancreatic and ovarian carcinomas are diagnosed synchronously during laparotomy [12].

Concerning the case we report, it is interesting to note the type of malignancy. Histopathology revealed a solid and partially ductal adenocarcinoma in the left ovary, right salpinx and omentum, while the pancreatic tissue sample was disease free. In spite of the absence of malignancy in the pancreatic biopsy, we concluded that probably the pancreas was the primary site. Mainly the significant intraabdominal spread of tumor indicated this. It would be unusual to find spread to the opposite salpinx, omentum and pancreas, which was palpated as solid and enlarged, giving the clinical impression of malignancy from an early ovarian neoplasm. The size of the whole ovary measured 4 x 3.7 x 2 cm, the capsule was unruptured and no ascetic fluid was present. It is known that Stage I ovarian carcinomas are bilateral in less than 10%. Furthermore, the ductal type of the tumor and immunohistochemical stain were in favor of a pancreatic carcinoma.

It was believed that pancreatic carcinomas spread by direct invasion or transserosal, but since these tumors often have contralateral metastases to the ovarian stroma or both to the ovarian stroma and surface, it is accepted that the metastatic route is hematogenous or lymphovascular [10].

The cause of PFPAS is unknown. Since it mainly affects women, as all paraneoplastic syndromes, it is probable that the female hormonal status may predispose to this, as happens in most autoimmune diseases. It is also possible that neuronal factors produced by the neoplasm or fibroblast proliferative factors may play a role. Finally, PFPAS may have an immunologic cause owing to the presence of immunoglobulin (IgG and IgM) and complement (C3) deposits on affected tissue [8, 13].

Chemotherapy improves myoskeletal symptoms in some cases, including the one we report, but it is unclear whether this is a result of tumor necrosis, immunomodulation or an anti-inflammatory effect [1].

The majority of patients with PFPAS syndrome present with hand or polyarthritis symptoms before the diagnosis of the underlying malignancy, which is diagnosed with a mean delay of 8,6 months [2]. Concerning the case we report, the delay was longer, since the underlying malignancy gave no symptoms and also was too small to be easily detected by imaging techniques.

The reason that the symptoms do not respond to anti-inflammatory or steroid therapy is unclear but in many cases there is a remission after surgery and chemotherapy [14].

The prognosis of the syndrome is poor and most patients die without improvement of symptoms at an average of 19 months. Survival has somewhat improved in later reports compared with older ones.

Since PFPAS is often associated with an occult carcinoma, a thorough work-up including gynecological examination and imaging techniques for women presenting with a sudden onset of unexplained hand pain, inflammatory polyarthritis, fasciitis and digital contractures may allow an earlier diagnosis and treatment. Moreover, the possibility of metastasis should be considered whenever evaluating ovarian cancers with unusual features and spread. The pancreas is an important source of metastatic tumors that stimulates primary ovarian carcinomas.

References

[1] Pfinsgraff J., Buckingham R.B., Killian P.J., Keister S.R. *et al.*: "Palmar fasciitis and arthritis with malignant neoplasms: a paraneoplastic syndrome". *Semin. Arthritis Rheum.,* 1986, *16,* 118.

[2] Martorell E.A., Murray P.M., Peterson J.J., Menke D.M. *et al.*: "Palmar fasciitis and arthritis syndrome associated with metastatic ovarian carcinoma: A report of four cases". *J. Hand Surg.,* 2004, *29,* 654.

[3] Ulbright T.M., Roth L.M., Stehman F.B.: "Secondary ovarian neoplasia". *Cancer*, 1984, *53,* 1164.

[4] Mazur M.T., Hsueh S., Gersell D.J.: "Metastases to the female genital tract: analysis of 325 cases". *Cancer*, 1984, *53,* 1978.
[5] Champion G.D., Saxon J.A., Kossard S.: "The syndrome of palmar fibromatosis (fasciitis) and polyarthritis". *J. Rheumatol.,* 1987, *14,* 1196.
[6] Memarzaden S., Berek J.S.: "Advances in the management of epithelial ovarian cancer". *J. Reprod. Med.*, 2001, *46,* 621.
[7] Medsger T.A., Dixon J.A., Garwood V.F.: "Palmar fasciitis and polyarthritis associated with ovarian carcinoma". *Ann. Intern. Med.,* 1982, *96,* 424.
[8] Vinker S., Dgani R., Lifschitz-Mercer B., Sthoeger Z.M. *et al.:* "Palmar fasciitis and polyarthritis associated with ovarian carcinoma in a young patient: A case report and review of the literature". *Clin. Rheumatol.,* 1996, *15,* 495.
[9] Naschitz J.E., Yesburun D., Rosner I.: "Rheumatic manifestations of occult cancer". *Cancer,* 1995, *75,* 2954.
[10] Moore R.G., Chung M., Granay C.O., Gajewski W. *et al.*: "Incidence of metastasis to the ovaries from nongenital tract primary tumors". *Gynecol. Oncol.*, 2004, *93,* 87.
[11] Young R.H., Scully R.E.: "Metastatic tumors in the ovary: a problem-oriented approach and review of the recent literature". *Semin. Diagn. Pathol.*, 1991, *8,* 250.
[12] Young R.H., Hart W.R.: "Metastases from carcinomas of the pancreas simulating primary mucinous tumors of the ovary: a report of seven cases". *Am. J. Surg. Pathol.*, 1989, *13*, 748.
[13] Farhey Y., Luggen M.: "Seropositive symmetric polyarthritis in a patien with poorly differentiated lung carcinoma: carcinomatous polyarthritis, hypertrophic osteoarthropathy, or rheumatoid arthritis?". *Arthritis. Care Res.*, 1998, *11,* 146.
[14] Leslie B.M.: "Palmar fasciitis and polyarthritis associated with a malignant neoplasm: a paraneoplastic syndrome". *Orthopedics,* 1992, *15,* 1436.

Address reprint requests to:
Ch. K. GIANNAKOPOULOS, M.D., Ph.D.
LAIKO General Hospital
Agiou Thoma 17, Goudi
11527 Athens (Greece)