Pancreatic Hamartoma and SAPHO Syndrome: a Case Report

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Abstract

We report the first case of an association of pancreatic hamartoma with SAPHO syndrome mimicking disseminated bone metastases. A 46 year old male with intermittent back pain for 10 years, relieved by NSAIDs and desquamation erythematous palmo-plantar eruption one year before, presented with symptoms of duodenal stenosis, a cystic tumor at the head of the pancreas and osteoformative (hyperostosis) and osteodestructive (osteitis) lesions of the clavicle, mandible, lumbar spine. The bone lesions resembled bone metastases, but an inflammatory infiltrate and fibrosis were found on the excisional biopsy of left clavicle, compatible with the SAPHO syndrome. The pancreatic tumor grew rapidly and showed a histological aspect of malignancy at laparoscopy. A cephalic duodenopancreatectomy was performed, but the histological findings established the diagnosis of pancreatic hamartoma. Several months later, the bone Tc99m scintigraphy was normal.

Keywords


Case report

A 46-year-old male patient was admitted to the Medical Clinic IV in June 2006 for: epigastric pain, acid regurgitation starting a week before, accompanied by 14 kg weight loss over the past 14 months against a background of appetite loss, asthenia and fatigue. The patient also complained of intermittent pains in the lumbar spine, for approximately 10 years, which were relieved by NSAIDs, and for several weeks he had had pains at the level of the left clavicle and mandible.

The personal history of the patient included the appearance of a desquamative erythematous palmo-plantar eruption one year before, which remitted spontaneously.

The family history was insignificant for the current pathology. The patient was a chronic drinker and smoker (40 cigarettes/day for 10 years).

The clinical examination evidenced: general altered state, emaciation, a tumor palpable at the level of the left clavicle, 5-6 cm in size, of hard consistency, immobile and painful, tumefaction in the left mandibular angle ~ 2 cm in size, painful on palpation, left mobile laterocervical lymph node 0.5 cm in size, pain at the percussion of the lumbosacral spinous apophyses, pain on palpation in the right upper abdominal quadrant.

Biological tests on admission showed an inflammatory syndrome: increased ESR, leukocytosis, thrombocytosis, hyperfibrinogenemia, increased alpha1 and alpha 2 globulins, high serum IgG levels. Renal, and liver function tests were within normal limits, serum and urinary calcium and phosphorus within normal limits, normal alkaline phosphatase, negative rheumatoid factor, ASLO titer < 200 U.

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Upper digestive endoscopy was performed, which detected esophageal hyperemia, antropyloric mucosal hyperemia, and an infiltrative process in the duodenal bulb and D2. Biopsies were taken, which found inflammatory infiltration with eosinophils and polymorphonuclears.

Echoendoscopy showed the head of the pancreas of normal appearance with the duct of Wirsung 2 mm in diameter, a thickened up to 12 mm duodenal wall at the apex of the bulb, several round hypoechoic adenopathies 8 mm in size and the common bile duct without suspect images inside. The established diagnosis was stenosing duodenitis (Fig. 1).

Abdominal CT showed the liver without nodular images, a homogeneous spleen, and a cyst 0.6 cm in size in the body
of the pancreas. Increased volume of the head of the pancreas (Fig. 2), with a 0.9 cm cyst. In the peripancreatic region, in the head of the pancreas, and around the pancreatic duct, a dense weakly iodophilic muff-shaped mass was visualized. In D2 and the lower jejunum, the wall was significantly infiltrated. Lumbo-aortic and interaortic caval adenopathies were also described.

The thorax CT evidenced areas of osteolysis and sclerosis in the middle third of the left clavicle up to the sternal extremity level. The radiograph of the lumbosacral spine showed a homogeneous bone compression of the L4 vertebra by anterior osteophytosis in the middle dorsal and lower lumbar region (Fig. 2). As a first bone scintigraphy suggested bone metastases, the patient was referred to the Oncology Institute Cluj, where an excisional biopsy of the left clavicle was performed, revealing a spongy bone with marked fibrosis of medullary spaces. A second Tc99m bone scintigraphy detected a pathological hyperfixation at the level of the L3 and L4 vertebrae, left hemi-mandible, left clavicle over the whole length, with the involvement of the left sternocostal joint, hyperfixation in the right sternoclavicular joint, sternal manubrium, left chondro-costal joints VI and VII and in the right iliac bone.

Based on clinical data (inflammatory osteoarticular symptomatology relieved by NSAIDs), the biological inflammatory syndrome, lytic and osteocompressive lesions detected by imaging, scintigraphic changes, clavicular biopsy, and the history of palmoplantar skin lesions, the diagnosis of SAPHO syndrome was established.

After one month, the patient presented a general good state, remission of epigastric pain, improvement of bone pain, disappearance of mandibular tumefaction and minimal tumefaction of the left clavicle. Biological tests detected an increased ESR, serum fibrinogen, PCR, with the rest of biological values normal. The tumor markers CEA and CA 19-9 were negative.

The patient was transferred to Surgical Clinic IV for diagnostic laparoscopy with intraoperative duodenal, hepatic, and (peripancreatic) lymph node biopsy. The histopathological examination of the duodenal biopic sample evidenced medium sized cells with a high nucleocytoplasmic ratio, moderate nuclear pleomorphism (an aspect which might indicate malignancy). A clinical and biological reassessment was decided after 4 weeks, but the patient came back only 9 months later, complaining of upper abdominal pain and vomiting, as well as of intermittent pain in the lumbar spine that was relieved by NSAIDs. Abdominal ultrasound showed a nodular tumor 80/65 mm in size in the head of the pancreas, invading the duodenal wall, also confirmed by echoendoscopy and abdominal CT scan, which excluded secondary hepatic metastases.

Cephalic duodenopancreatectomy was performed in June 2007. The histopathological examination established the diagnosis of pancreatic hamartoma (Figs. 3, 4).

Discussion

In 1987, a group of French rheumatologists established the SAPHO acronym for a clinico-radiological entity.
combining bone and joint symptoms with skin lesions [1]. Its history started much earlier, in 1961, when Windom et al reported on the association between acne conglobata and inflammatory polyarthritides. In 1967 Sasaki et al described the association between palmoplantar pustulosis and clavicular hyperostosis. Until 1987 there were more than 50 terms referring to the clinical picture of SAPHO such as pustulotic arthropo- 
stesitis [2] and the acquired hyperostosis syndrome, known to German radiologists [3]. In 1986, Schilling et al described two clinical entities frequent to the syndrome: spondylarthritis hyperostotica 
pustulo-psoriatica (SHPP) and chronic recurrent multifocal 
osteomyelitis (CRMO).

Due to its clinical heterogenicity the diagnosis is difficult to establish, therefore in 1994 Kahn et al established the three diagnostic criteria specific to the SAPHO syndrome [4], one of them being sufficient to establish the diagnosis: multifocal 
osteitis with or without skin manifestations; sterile acute or 
chronic joint inflammation associated with either pustules or 
psoriasis of palms and soles; and sterile osteitis in the 
presence of one of the skin lesions mentioned below.

The prevalence is difficult to establish, and many 
cases remain undetected because of non-recognition of the 
syndrome. It has been described especially in Japan, 
Western Europe, particularly in Scandinavian countries, 
but all ethnic groups can be affected. This is a disease of the young adult, 
the mean age at the time of diagnosis being 38 years, but it 
can also be found in children, where it manifests as aseptic 
CRMO. Sex distribution seems to be equal.

The etiology of the syndrome is not completely 
understood. A recent hypothesis suggests that it might be 
caused by an immunological response to an infectious 
agent that triggers an inflammatory reaction in bone or 
joint tissue, taking advantage of a type of “paresis” of 
the immune system, which is favored by a predisposing 
genetic background. The infectious agent incriminated by 
some authors is Propionibacterium Acnes, a common skin 
saprophyte isolated from some open bone biopsies in one 
study [5], which might explain the therapeutic effect of 
antibiotics; but this gram-negative bacterium grows under 
an aerobic condition and can be difficult to culture [6].

On the other hand, the elements supporting the 
connection between SAPHO syndrome and seronegative 
spondyloarthropathies should not be neglected; association 
with psoriasis, involvement of the spine, of the sacroiliacs, 
association with inflammatory bowel disease (Crohn’s 
disease, ulcerative colitis), presence of the HLA B27 
antigen.

Osteoarticular disorder may be clinically acute or 
chronic, having the appearance of inflammatory osteitis.

The main site of the inflammatory process is the 
anterior thoracic wall, with the inflammation of the sternum 
and sternocostoclavicular joint. If thoracic involvement 
facilitates diagnosis, the involvement of the spine, of long 
bones in adults, especially the tibia and the femur, of cranial 
bones raise differential diagnosis problems with a tumor or 
infected lesion. Sterile osteitis of the mandible represents 
10% of bone lesions. This should be taken into consideration, 
because tooth ablation or long duration antimicrobial therapy 
have no results [6]. Peripheral joints are equally affected, 
sometimes having a pseudoseptic appearance.

Skin involvement is not a requirement for making the 
diagnosis. It is most frequently preceded by 1 to 20 years 
ostearticular involvement in both children and adults. 
Palmoplantar pustulosis, conglobate acne, acne fulminans, 
s suppurrative hydrenitis or different types of psoriasis may 
occur. Our patient also reported a history of palmoplantar 
skin disease, most probably psoriatic.

There are no biological stigmata specific for the 
syndrome, only an increase in inflammatory parameters 
(ESR, PCR), in immunoglobulin levels or in the complement 
fractions C3, C4.

The radiological aspect is frequently suggestive: 
hypertrophy and compression or even osteolysis. CT shows 
lytic lesions surrounded by sclerotic areas, changes also 
found in our patient.

Bone scintigraphy with Tc 99m shows hyperfixation and 
is extremely useful for the detection of osteoproliferative 
(hyperostosis) and osteodestructive lesions (osteitis), left 
undetected by imaging. In our patient, the bone lesions 
were first interpreted as metastases, but histopathological 
examination and the second scintigraphy refuted this 
diagnosis. Histopathological examination supported the 
diagnosis of the disorder by early lesions, in which 
 polymorphonuclear cells were dominant, later the 
inflammatory infiltrate mainly consisted of monocytes and 
fibroblasts, and bone remodeling and bone marrow fibrosis 
occur[7].

Patients diagnosed with SAPHO syndrome require 
long-term monitoring in order to prevent complications: 
retroperitoneal fibrosis, mediastinal fibrosis, compressive 
venous thrombosis, intercostal neuralgia.

The literature reports no case of association of this 
syndrome with pancreatic hamartoma or other digestive 
disease, except for enterocolopathies (Crohn’s disease, 
ulcerative colitis).

The long-term prognosis is favorable, the evolution of 
the disease being characterized by prolonged remissions 
followed by relapses.

The treatment of the disease is symptomatic. It consists of 
NSAIDs or sulfasalazine [6]. The dosage is adapted to each 
individual case, taking the side effects into consideration. 
Corticoids are prescribed quite rarely and are indicated 
for emergency cases in limited time periods. Some trials 
have studied the effect of immunomodulatory treatment 
represented by anti TNF-alpha [8]. TNF-alpha inhibitors 
such as Infliximab or Etanercept have been successfully 
used due to the high TNF-alpha concentrations found 
during bone biopsy [9]. In some cases, methotrexate has 
been used. Antibiotics have not proved to be useful, except 
for azithromycin, which has both an anti-inflammatory and 
immunomodulatory effect [10]. Some authors recommend 
long-term treatment with azithromycin (or clarithromycin) as
first line treatment in CRMO, especially when the presence of *Propionibacterium Acnes* is confirmed [9].

At the same time, the usefulness of a hormone treatment for this disease was discovered. Calcitonin has both an osteotrophic and anti-inflammatory effect. Over the past years, due to a number of cases resistant to this treatment, calcitonin has been replaced by bisphosphonates (pamidronate, zoledronic acid), which have an anti-osteoclastic, antiinflammatory action, with the suppression of IL6, IL1 or TNF-alpha. All pharmacological options require careful interdisciplinary monitoring, as well as the participation of a rheumatologist and dermatologist in decision.

In conclusion, we presented the first case of an association of pancreatic hamartoma with SAPHO syndrome mimicking disseminated bone metastases.

References