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 alpha 1 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, antrypyloric 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 nucleo-cytoplasmic 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 polyarthritis. 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 arthro-osteitis [2] and the acquired hyperostosis syndrome, known to German radiologists [3].

In 1986, Schilling et al described two clinical entities frequent to the syndrome: spondylarthritides 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 anaerobic conditions and can be difficult to culture [6].

On the other hand, the elements supporting the connection between SAPHO syndrome and seronegative spondylarthropathies should not be neglected: association with psoriasis, involvement of the spine, of the sacroiliac, 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 infectious 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 osteoarticular involvement in both children and adults. Palmoplantar pustulosis, conglobate acne, acne fulminans, suppurative 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 occurred [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 osteotropic 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, anti-inflammatory 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