CASE REPORT: NECROTIZING FASCIITIS OF ODONTOGENIC ORIGIN IN A SUBJECT AFFECTED BY UNCOMPENSATED TYPE 2 DIABETES MELLITUS

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[Caso clinico: fascite necrotizzante di origine odontogena in soggetto affetto da diabete mellito tipo 2 scompensato]

SUMMARY

Necrotizing Fasciitis (NF) is a highly aggressive infectious process that affects soft tissues, with a high risk of rapid progression through superficial and deep levels of fascia, to the muscle layers. Some forms originate from odontogenous centres with the possibility of rapid evolution into forms of mediastinitis with high mortality rates. Systemic conditions that compromise the immune system of an organism can very easily induce the fatal development of these infectious processes.

Prognosis is dependant upon the isolation of the germs that may be responsible in order to start a timely and specific therapeutic treatment; if the isolation is not supported by enough laboratory data to identify the range of action of the pathogens responsible, a wide ranging antibiotic treatment, and possibly surgical drains or treatment in a hyperbaric chamber, should be started. The clinical case that we shall describe is typical and rather complex.

Key words: Necrotizing fasciitis, infections, complications

RIASSUNTO

La fascite necrotizzante (FN) è un processo infettivo altamente aggressivo, coinvolgente i tessuti molli, con elevato rischio di progressione rapida attraverso i piani fasciali superficiali e profondi, fino agli strati muscolari.

Alcune forme hanno origine da focolai odontogeni con possibilità di rapida evoluzione in forme di mediastinite ad elevata mortalità. Condizioni sistemiche tali da compromettere l'attività immunitaria di un organismo, possono più facilmente predisporre all'evoluzione fatale di questi processi infettivi.

La prognosi è legata all'isolamento degli eventuali germi responsabili al fine di iniziare un trattamento terapeutico specifico e tempestivo; qualora l'isolamento non fosse supportato da dati di laboratorio sufficienti per individuare lo spettro d'azione dei patogeni responsabili, va intrapresa una terapia antibiotica ad ampio spettro e l'eventuale apposizione di drenaggi chirurgici o trattamento in camera iperbarica.

Il caso clinico che descriveremo risulta alquanto complesso ed emblematico.

***Parole chiave**: Fascite necrotizzante, infezioni, complicanze*

Introduction

Necrotizing fasciitis (FN), known since antiquity, was described by Hippocrates in the Vth Century B.C as a complication of erysipelas[1, 2].

It is a highly aggressive infectious process of the soft tissue, characterised by the involvement surface and deep fascial structures; it can spread rapidly to the skin, subcutaneous tissue, muscular tissue and other adjacent soft tissue structures[3, 4].

It is characterised by skin necrosis, suppurating fasciitis and thrombosis of the small subcutaneous vessels, with a high risk of spreading rapidly across the muscular fasciae. The areas involved are mainly the neck, thorax, perineum, abdomen and groin[5].

Cervical necrotizing fasciitis originates more frequently from odontogenic sources like dental abscesses, gingivitis and pulpitis[6].

Descendent mediastinitis is a possible complication of oropharyngeal and neck infections, which reach the mediastinum through the cervical planes[3].

It has a high mortality rate, if not detected early and suitably treated. This disease is usually caused by polymicrobial infections.

Even if it is historically associated with Group A beta-haemolytic Streptococcus, necrotizing fasciitis can be linked to a variety of bacteria including Staphylococcus Aureus, Pseudomonas spp., and other gram negative coliforms as well as anaerobic ones.

Systemic conditions, like disease of the small vessels frequent in diabetic subjects and those with kidney deficiencies, cirrhosis of the lever and above all weakening of the immune system, predispose to this type of tissue infection[2, 7].

As opposed to complicated infections, which are generally cured after antibiotic therapy, lancing and draining, FN treatment generally requires full surgical removal of the necrotic tissue and further treatment in a hyperbaric chamber[8].

Clinical case

A 74-year-old woman with a history of arterial hypertension and diabetes mellitus for about two years, the latter not treated with medication.

She has a history of type 2 diabetes mellitus and mixed dyslipidemia. Nothing of significance in the remote pathological case history.

She came to us for observation with an abscessed lesion to the right cheek (Photos A and B) by the lower right arch, covered in purulent matter which had appeared ten days previously and been treated with third generation cephalosporin; after 4 days this lesion fistulated painlessly to the skin with the associated symptoms of high temperature (Max temp. 37.5°C).

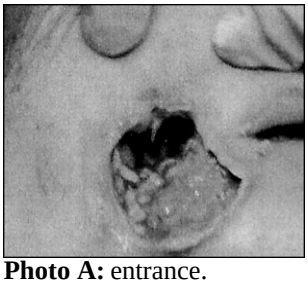

Photo A: entrance.

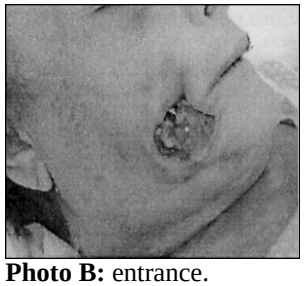

Photo B: entrance.

On entry to the department the patient was in average clinical conditions, breathing normally, temperature of 37.5°C, dry dehydrated skin and mucous membrane, objective examination of various organs and systems within the normal range.

Of note was the presence of reduced tactile and pain sensitivity mainly in the lower limbs, more on the right than the left.

The cutaneous lesion was fistulated on the outside (Photo C), at the right genal space with necrotic matter and perilesional oedema; at the homolateral laterocervical level and the base of the neck, the skin was translucent and red, without showing crepitus or appreciable masses on palpation.

Chemical analysis of the blood showed electrolytic alteration, hyperglycemia, an increase in glycosylated haemoglobin, glycosuria, an increase in the phlogosis indices, anaemia, a slight neutrophil leucocytosis and mixed dyslipidemia (Tab. 1).

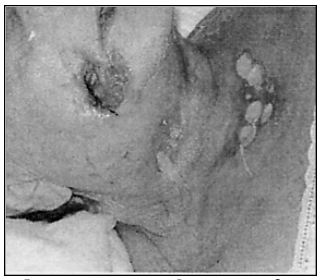

Photo C: 48 hours after recovery.

Haemoculture series, serologies for Leishmania, Brucella, EBV, CMV, toxoplasma and Manteaux tests were also carried out with negative results.

We continued with CVC poisoning and drug treatment with calcium gluconate infusion, potassium chloride and hydrating therapy, total parenteral nutrition balanced from a calorific point of view (1400 Kcal), insulin and broad-spectrum antibiotic therapy (Table 2): Metronidazole (500 mg i.v. x4/day), Cefotaxime (2 g i.v. x4/ day), Gentamicin (80 mg i.m.x2/day).

The lesion was treated daily with collagenasis+chloramphenolic, and wads of sodium riphampicin and iodine-povidone 2%.

Two days after recovery slight symptoms of pain arose in the neck, due to the spontaneous draining of the abscess matter in the right laterocervical seat, and in base of the neck, no smell. The pain regressed spontaneously after a few hours.

A microbiological swab was taken for aerobic, anaerobic and mycetic bacteria; the culture dish showed colonies of Candida Tropicalis and Candida Albicans, Staphylococcus Epidermidis and Staphylococcus Capitis with a low microbe count for the isolated colonies.

She underwent a first neck-thorax CT with mdc, which showed the presence of "multiple liquid collections with small air bubbles, a voluminous collection in the retropharyngeal space extending to the retrotracheal mediastinum, right posterior paraoesophageal, with an extension to the pulmonary trunk. Bilateral pleuric effusion with consensual compression atelectasis" (Fig. 1).

On the fourth day the clinical picture was unchanged, so metronidazole was replaced with amphotericin B (1.5 mg per Kg x 2 day) and a steroid was added (desametasone 4 mg/day).

Lenght of stay in hospital	1	5	10	18	25	30	80	6 months	1 year
Signs/ Symptoms	Fever (38.5 °C)		Fever (38.5 °C)		Fever (39 °C)	Fever (38 °C)	No Fever	No Fever	No Fever
White blood cells (cells/mcL)	12530		16440	8800	7800	7000	5400	5450	6280
Neutrophils (%)	82.5		79.3	59.2	56.3	54.2	53.3	56.5	59.2
Lymphocytes (%)	11.9		15.7	27.2	28.6	29.2	36.9	36.7	33.3
Red blood cells (cells/mcL)	4320000		3400000	2960000	2600000	2260000	3700000	4470000	4420000
Hb (g/dl)	11		9.8	8.6	7.7	6.6	11.6	12.8	12.5
Ferritin Hb (ng/dl)	655		566	437			178.5	165	106
Fibrinogen C (mg/dl)	534		339	310	325		288	300	380
HbA1c (%)	9							7.5	6.5
Glycemia (mg/dl)	187-234	261-319					98-120		
Tot. cholesterol (mg/dl)	279		221				278	280	202
LDL(mg/dl)	178		145				184	220	126
Triglycerides (mg/dl)	368		333				171	170	91
Tot. protein (g/dl)	5.4		5.8	5.8			7.49	8.11	7.7
Albumin (g/dl)	1.7		2.6	3			4.1	4.2	4
ESR (mm)	62						4.5	22	21
Pcr (mg/dl)	14.37						0.74	0.18	0.12
Na^{+} (mEq/L)	139		136	144	140	142	140	143	142
K^{+} (mEq/L)	3.39		2.48	3.27	3.3	4	4.14	4.38	4.5
Ca^{++} (mg/dl)	7.1		7.52	8.7	8.9	9.4	9.3	9.5	9.3

Table 1: Laboratory Analysis.

Lenght of therapy (days)	Antibiotic	Swab	Microrganism Cultured	Resistance	Sensitivity
1°-3°	Metronidazolo	1st day	Candida Tropicalis	No	Amphotericina B
1°-9°	Cefotaxime		Candida Albicans	No	Amphotericina B
1°-15°	Gentamicina		Staphylococcus Epidermidis	Methicillina-R	Clindamycina Eritromycina Vancomycina Levofloxacina Ampicillina
4°-45°	Amphotericina B		Staphylococcus Capitis	Eritromycina	
10°-15°	Piperacillina				
16°-40°	Vancomicina	15th day			Amikacin Meropenem
16°-40°	Amikacina		Enterobacter Cloacae	No	Clindamycina Levofloxacina Vancomycina
25°-40°	Meropenem		Staphylococcus Capitisspp Ureolyticus	Methicillina-R Piperacilina Gentamycina	
25°-40°	Ciproflaxacina				

Table 2: Treatment administered, culture test with antibiogram.

The glycemic values, hepatic and renal function parameters, serum electrolytes and haemochrome were monitored daily, bringing some small changes in the electrolyte enriched infusion solutions and/or insulin units.

On the tenth day there was continuous-intermittent high temperature (max 38°C), so the anti-

biotic therapy was changed again with piperacillin (2 g ev x 3) and the cefotaximine was interrupted.

Surgical removal was carried out by the thorax surgeon (Photos D and E) (drainage was not recommended either by the radiologist or the thorax surgeon because of the anatomical location of the collections, in that the seat was rich in vessels, nerves and organs) and a culture examination of the tissue taken showed an average number of Enterobacter cloacae, a few colonies of

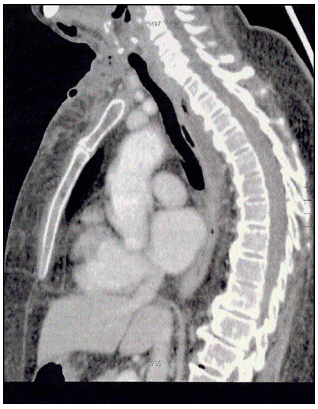

Fig.1: A) Computed tomography (CT): sagittal multiplanar reformation after contrast media administration shows in posterior mediastinum, close to oesophagus, an hypodense fluid collection with air bubble circumscribed by a peripheral enhancement rim, as anaerobic abscess. Other two fluid collections with the same appearance are located in suprahyoid region (submandibular space) and in sternal region.

Staphylococcus Capitis spp. Ureolyticus and a few colonies of mycetes; the antibiogram showed meticillin-resistant strains and colonies resistant to two of the antibiotics administered (gentamicin and piperacillin), which were interrupted and replaced with vancomicin (500 mg x 4 i.v.), amikacin (500 mg i.m. x2/day) and Meropenem (1gx3 i.v.), in addition to the amphotericin B already administered.

The steroid was also reduced in stages. After two days of this therapy the high temperature had disappeared and the white blood cells were back to normal. On the twenty-fifth day, a new outbreak of high temperature (max 39°C) and, because of this, the drug therapy was further modified with the addition of ciprofloxacin (200 mg i.v./day) to the antibiotics which continued to be administered.

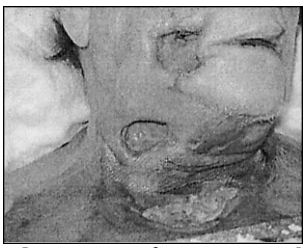

Photo D: after surgical removal.

Photo E: after surgical removal.

On the suspicion there was inflammation of the lower urinary tract (the patient had a permanent vesical catheter), a urine culture test was carried out, which was negative.

In the meantime the CVC was taken out which on examination of the culture resulted negative. On the thirtieth day the symptoms of high temperature disappeared ("foreign body fever?"). On the thirtieth day the high temperature disappeared after the CVC had been removed and an examination of the culture from it was also negative (true foreign body fever picture).

The antibiotic therapy was continued for another two weeks with a notable improvement in the clinical conditions with a progressive reduction by granulation of the lesions and the purulent mediastinal collection, a picture confirmed by the CT scan carried out on the fiftieth day (Fig. 2).

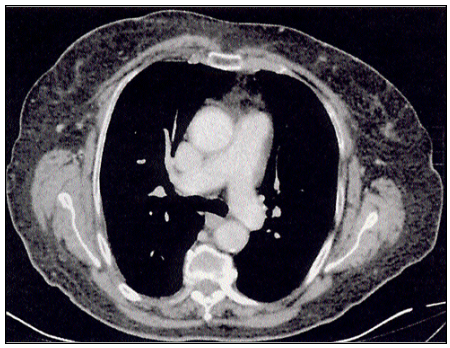

Fig. 2: Axial CT scan after iodinated contrast media i.v. administration performed after conservative treatment 5 months later, shows disappearance of mediastinal fluid collection and "restitution ad integrum" of subcutaneous fat of pectoral and sternal regions.

Also, the biochemical-humoral parameters returned to normal. Five months later, radiological examination confirmed complete recovery and the replacement of the abscess collections with fibrous tissue.

Discussion

In necrotizing fasciitis the pathogens responsible are mainly anaerobic and mycetic; their virulence and the evolution of the infection is determined by the general and local immune system conditions of the host patient, whilst dissemination is promoted by a reduction of the oxygen reserves in the tissues, activating the enzyme systems which aggravate the tissular ischemia.

If left untreated, the infection can spread into the sublingual, submental and parapharyngeal space and from there to the cephalic region at base of the neck, into the mediastinum and the thoracic cavity[11, 12]. In our case spreading also occurred via the retropharyngeal space and from there to the mediastinum.

Once it reaches the mediastinum, one can get pericarditis, pleuric or pericarditic effusion, empyema, pulmonitis, cardiac tamponade, oesophageal haemorrhage, up to septicemia[13, 14]; in fact the mortality rate for NF with mediastinitis varies from 8 to 73% depending on the time of diagnosis, start of treatment and the patient's clinical conditions[15, 16].

In this case report, significant roles were played by diabetes and old age; the patient had also neglected good behavioural practices, the required diet and, of course, correct oral hygiene.

In fact the origin of the process can be attributed to a mouth infection in a subject with uncontrolled diabetes. Patients with necrotizing fasciitis typically show symptoms of intense pain, high temperature, leucocytosis, hypocalcaemia, hypoalbuminemia and anemia. Hypocalcemia is determined by necrosis of fat in that the ionised calcium is seized in the liponecrosis areas where through the action lipases of bacterial origin it is bound to the fatty acids; anaemia derives from a combination of intravascular haemolysis caused by bacterial toxins and, in the advanced stages of the disease, from bone marrow depression following prolonged sepsis.

It is important to note that, despite the tissue devastation and concomitant compression of the abscess collections on the nearby organs and above all on the vessels and nerves, the patient only once felt moderate symptoms of pain, when the spontaneous fistulization of the abscesses occurred; this is a picture of clear diabetic neuropathy, which was also detected at a peripheral level by the objective examination of tactile and pain sensitivity.

Imaging is fundamental for clearing the spread of the infection and the structures involved, for the evaluation of a correct therapeutic approach, monitoring and the evolution of the clinical picture.

The principal treatment provides for a combination between surgical removal, the use of i.v. antibiotics and oxygenation of the damaged tissues with a hyperbaric chamber[17, 18, 20].

Antibiotic therapy must be started promptly, using broad spectrum drugs whilst awaiting the results from the cultures; it will subsequently be modulated in the wake of the antibiogram and then changed periodically to reduce the incidence of resistant germs appearing.

In our case a broad spectrum empirical therapy was modulated from the outset, considering the clinical, radiological and microbiological picture; reduction in the spread of the lesions was more evident when amphotericin B was added to the various antibiotics suggesting participation of mycotic agents in the etiopathogenis of the clinical picture.

Maisel and Karlen[19] have suggested how the association between cephalosporin and clindamycin or metronidazole promotes a good initial antibiotic coverage; other authors suggest the use of penicillin G, metronidazole and gentamicin and, for those with reduced immune system, the association between piperacillin and imipenem.

Recent studies show how the use of cortisone, e.g. desametasone i.v., through its anti-inflammatory effect, reduces the oedema and the tissue inflammation promoting decompression, protecting the air ways and determining greater penetration of the antibiotic into the damaged tissues[21, 22].

In the literature, cases of NF with mediastinitis are promptly treated with a surgical approach differing according the spread of the infection to the various mediastinal structures (Guidelines, Endo et al.); mortality in this case varies from 16 to 23%[23].

In our case we opted for a mainly drug approach given the age of the patient, the none too favourable general clinical conditions and the outcome of x-ray picture showing how the seat of the abscess collections ("fluid collection posterior to the oesophagus and the trachea with contact above the azygos vein") was such as not to permit a safe surgical percutaneous approach.

Therapy by hyperbaric oxygen is highly recommended to accelerate the reduction of the infection process and thus healing and can be used as support or added treatment[24]. Some authors maintain that its use, added to surgical removal, improves survival through its capacity to increase the oxygen tension in the tissues and the oxygen deficient infected zones. Conversely, some authors have not observed any benefits in terms of survival rate increases (Lille et al. 1996; Hasham et al. 2006). In our case the patient refused the hyperbaric chamber because of added anxiety and a history of claustrophobia.

The prognosis for severe forms of NF is considerably conditioned by the patient's immune and general clinical status. In an immune deficient subjects saprophytic germs also become virulent, thus promoting the rapid progression of the disease.

In our case it was not possible to isolate one or more germs responsible; one took into account the evolution of the clinical picture and the response to the medical therapy administered.

The rapid curing of the infection picture was obtained through a prompt broad spectrum antibio-

tic drug therapy also supported by steroid therapy and controlling, at the same time, the diabetes.

Surgical removal, daily irrigation of the lesions with anti-bacterial saline solution and swabbing with antibiotic wads played an important role and also promoted tissue granulation and healing as a spin-off (Photo f).

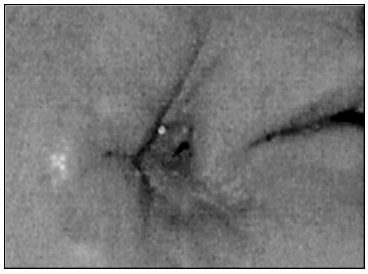

Photo F: 3 months later.

Conclusions

Necrotizing fasciitis is a highly aggressive infectious pathology, whose prognosis is heavily conditioned by the promptness of the antibiotic drug treatment, the opportunity to intervene surgically with any added drainage and/or exploit oxygen therapy in a hyperbaric chamber.

This case shows how in, devastating complicated forms, immediate polychemotherapeutic treatment in the absence of one or more virulent responsible germs can be an excellent aid, if taken in time, for checking the infectious pathology and limiting its damage.

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