International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 06, Issue 10, October 2021,
https://doi.org/10.23958/ijirms/vol06-i10/1226

Case report

A Rare Case of Necrotizing Fasciitis as Side Effect of Methimazole Administration for Basedow Disease

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Received 09 September 2021; Accepted 28 September 2021; Published 08 October 2021

Abstract

A rare case of agranulocytosis due to Methimazole administration for Basedow disease is presented.
After 30 days since the therapy beginning a 45 year old female patient has developed a necrotizing fasciitis on both legs, with muscle bellies and Achille's tendon exposure.
Immediate surgical debridement was necessary to save her life and control the progression of infection.
Several plastic surgery procedures were performed to accomplish wounds healing (vacuum-assisted closure therapy, dermal substitute, free flap, skin graft), and after 75 days the patient was discharged.
An intensive rehabilitation program permitted a complete functional recovery.
After 12 months a reshaping procedure was performed to improve right leg and ankle contour.
The close cooperation between endocrinologist and surgeon revealed to be essential to perform a safe surgery and to permit the return to the job and daily activities.

Keywords: ***Basedow, Flap, Methimazole, Necrotizing fasciitis, Thyroid***

Case report

A 45-years-old female referred to the Emergency Room of our hospital complaining, during the last five days, high temperature (T > 40° C), myasthenia, sore throat and diarrhoea, spontaneously treated with Amoxicillin-Clavulanic acid twice a day.

The patient had no history of chronic disease, infection, recent trauma or surgery, she underwent to laparoscopic myomectomy because of uterine fibroids years ago.

Three months before admission, the patient had been diagnosed with Basedow Disease (BD) and started standard medical treatment with Methimazole and Propanolol as adjuvant therapy for correlated tachycardia.

Patient initial assessment revealed a temperature of 38 C°, heart rate 120 bpm and blood pressure of 90/60 mmHg.
Clinical examination showed lower limbs edema, a 1 cm skin ulceration surrounded by erythema on left leg and erythematous papules on left leg, no pain or crepitus were induced by palpation.

Laboratory tests revealed a WBC count of 0,13 10^9/L with severe agranulocytosis, mild anemia (110 g/L), thrombocytopenia (62 10^9/L) and an overall increase of inflammatory indices (CRP 232,2 mg/L; ESR 40 mm/h; PCT 18,5 ug/L).

Thyroid function showed a mild hypothyroid.

Lower limbs CT scans revealed diffuse lower limbs edema, a bilateral subfascial effusion and fascial contrast enhancement.

Because of rapidly worsening of general conditions and septic shock development, she was taken to operating room for urgent soft tissue debridement and both legs fasciotomy distally to knee level for suspected necrotizing fasciitis (NF).

The post-operative recovery required intensive care unit admission, large spectrum antibiotics therapy with Clindamicin, Daptomycin, Meropenem and granulocyte-colony stimulating factor (G-CSF) administration.

Hyperbaric oxygenation therapy (HBOT) was indicated to reduce soft tissues necrotization, and a daily change of dressing was planned.

During the period from 1st to 8th postoperative day the granulocyte level has progressively recovered together with an overall reduction of inflammatory parameters (**Tab 1**).

Table: 1 Granulocytes count variations during hospitalization

Event / procedure	Granulocytes (10^9/L)
Hospitalization	0.05
Fasciotomy (1st day)	0.08
G-CSF therapy (2nd day)	19.18
Debridement and VAC (12nd day)	8.29
VAC dressing change (18th day)	4.74
VAC dressing change (23rd day)	3.15
VAC dressing change (30th day)	3.37
VAC dressing change (35th day)	4.14
VAC dressing change (41st day)	4.31
VAC dressing change (46th day)	5.75
Latissimus dorsi free flap (51st day)	8.19
Total thyroidectomy (70th day)	4.21
Discharge (75th day)	4.77

The soft tissue and pus cultures yielded a Pseudomonas aeruginosa growth, with susceptibility to Meropenem and Ciprofloxacin, so adequate therapy was set up.

On the left leg, a full-thickness loss of skin and subcutaneous envelope about 25 per 10 cm was localized on medial gastrocnemius muscle surface, so Acti V.A.C.® device of KCI® (Kinetic Concepts – Texas – USA) was applied with negative pressure function.

On the right side instead, much more extensive soft tissue coverage was missing, and Achilles' tendon, ankle joint and gastrocnemius muscle belly resulted exposed.

V.A.C. Ulta™ device of KCI® (Kinetic Concepts - Texas - USA) was applied, alternating irrigation with saline solution to negative pressure function to obtain a deeper cleaning of wound bed and quicker cells growth stimulation.

Patient exhibited negative Pseudomonas aeruginosa swab in 40th postoperative day.

A two-step reconstruction surgery was planned: an Integra Dermal Regeneration Template (IDRT - Life Sciences, Plainsboro, NJ) was grafted on the left side, while microsurgical latissimus dorsi musculocutaneous flap transplantation was performed on the right leg.

Then, in 70th day, meshed half-thickness skin grafts were applied to complete total soft tissue replacement.

Because of relapse of BD and symptomatic tachycardia on the 70th day after hospitalization, total thyroidectomy was performed.

The postoperative was uneventful, and patient was discharged 75 days after initial admission with scheduled rehab program.

After 30 days of intense rehabilitation, patient has reached a full recovery of gait and at 60th day after discharge patient presented complete and stable healing of all wounds (**Fig 1**).

Due to the persistent bulking of the latissimus dorsi flap transplanted to the right leg a reshaping procedure was performed after 12 months.

Fig 1: The right leg: at presentation after decompressive fasciotomy (above left), after several debridements and negative pressure therapy (above right), the flap anastomosed to the right leg vessels (below right), complete wound healing at the 2-months follow up (below left).

Discussion

Agranulocytosis is a rare, unpredictable and potentially deadly side effect of anti-thyroid drugs (ATD) such as Methimazole and Propylthiouracil [1].

Agranulocytosis is supposed to be caused by idiopathic immune response to Methimazole.

The incidence of agranulocytosis induced by anti-thyroid drugs is estimated to be around 0.2-0.5% of patients diagnosed with Graves' disease [2].

Treatment of agranulocytosis includes immediate discontinuance of ATD, hospitalization, use of G-CSF to reduce the duration of agranulocytosis and broad-spectrum antibiotics intravenous administration.

Most common complications following agranulocytosis are bacterial infections and, in case of sepsis development, mortality rate reaches 21.5%.

A routine blood cell count 30 days after the first administration of Methimazole can reveal a drop of granulocytes,

so a follow up is usually scheduled to check patient general conditions and blood cell level.

In this clinical case no blood cell count has been scheduled by endocrinologist, so the granulocytes have been likely decreasing for 90 days before the first hospital access.

NF is a life-threating infection that may arise spontaneously or after a minimum injury.

Its early stage is characterized by few symptoms like stiffness, hyperemia and mild pain, thus it is not alarming, causing late diagnosis, granulocytes count and inflammatory parameters can be only partially altered, the LINREC score [3] is useful to best assess the risk of NF.

The diagnostic has to be completed with CT scan, that can reveal suprafascial effusion, and/or subcutaneous emphysema.

CT scan is also of main importance for the surgeon, who needs to know the exact extension of infection process through anatomic compartments, in order to avoid subtotal debridement [4].

Urgent fasciotomy and aggressive surgical debridement are mandatory, oxygen exposure of deeper soft tissues may alone be effective to counteract anaerobic bacterial growth.

Wounds have to be left open until complete sterilization is achieved, so pain management is crucial during hospitalization.

Vacuum-assisted closure system device (V.A.C. therapy) has proven to be quite effective in maintaining dry the wound bed and promoting healing through angiogenesis stimulation [5].

All reconstructive procedures, such as skin grafts, acellular dermal matrix application, and free flaps can promote an intense inflammatory response, therefore a close cooperation between endocrinologist and surgeon is essential to perform a safe surgery.

The consultants have to work together to first save the patient's life, and then to permit the return to the job and daily activities.

Author contributions

Brambullo Tito, research design, drafting of the paper and spelling revision
De Lazzari Alberto, data collection and analysis
Azzena Gian Paolo, data collection and analysis
Masciopinto Giuseppe, data collection and analysis
Vindigni Vincenzo, intellectual content revision

All authors agree to be accountable for all aspects of the work.

Conflicts of interest

All authors have disclosed no conflicts of interest.

Funding/support

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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