Interesting Cases:

Title

Authors and Affiliation

Keywords (3-5)

Case Description (50 to 150 words)

Questions (4 questions about essential aspects of the case)

Discussion (4 paragraphs, each one corresponding to the question asked limited to 500 words)

Summary (one paragraph limited to 50 words)

References (limited to 8)

Below are examples of Interesting case submissions

Example - 1

Interesting Case Series

Levamisole-Induced Vasculitis

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Keywords: levamisole, drug-induced vasculitis, Drug abuse, drug complications, gangrene

DESCRIPTION

T.O. was a 39-year-old woman with a history of intravenous drug abuse, hepatitis C, and hypothyroidism who presented with eschar of her face, lower extremity, and right hand (Figs 1*a* and 1*b*). She indicated that skin lesions began shortly after smoking crack cocaine. Physical examination revealed dry necrotic tissue over the dorsum of her right hand and right ring and small fingers, with the absence of sensation to touch over these regions. Laboratory findings were significant for leukopenia, microcytic anemia, neutropenia, elevated erythrocyte sedimentation rate, positive lupus anticoagulant, positive ANA, and positive p-ANCA. Punch biopsy of her skin demonstrated leukocytoclastic vasculitis with associated intravascular fibrin thrombi, consistent with the diagnosis of levamisole-induced vasculitis (LIV).

Figure 1

Figure 2

QUESTIONS

1. What is levamisole?
2. What is LIV and what are its clinical findings?
3. What is the mechanism of LIV and what laboratory abnormalities are seen?
4. How can LIV be treated?

DISCUSSION

Levamisole is a synthetic imidazathiazole antihelminthic agent once used medically for its immunomodulatory effects; its use in the medical setting was curtailed in 1999 due to associated LIV, agranulocytosis, thrombocytopenia, and arthritis.[1] Other associated effects include multifocal leukoencephalopathy as well as type I and III hypersensitivity reactions.[2] Although its medical use has been discontinued, it is estimated that 1.5% of the US population uses cocaine regularly and that up to 70% of street cocaine is contaminated with levamisole, making it a significant public health issue.[3] It is thought that levamisole acts as a cocaine diluent and may also heighten the euphoric effects of cocaine.[4] The mechanism by which it potentiates the effects of cocaine is due to inhibition of monoamine oxidase and catechol-*O*-methyl transferase, increasing synaptic transmission of norepinephrine and augmenting the sympathomimetic effects of cocaine.[2] Levamisole is partially metabolized into an amphetamine-like compound and inhibits acetylcholinesterase activity, increasing endogenous opioids and dopamine levels in cerebral reward pathways.[2]

Levamisole is associated with 3 clinical syndromes: cocaine-induced midline destructive lesions, cutaneous vasculitis (LIV), and agranulocytosis.[5] Levamisole-induced vasculitis is a cutaneous vasculitis that has been reported with smoked crack cocaine and inhaled cocaine powder. It has a greater frequency in women (male to female ratio 1:3), with a mean age of presentation of 44 years.6 Although other compounds can be added to cocaine, vasculitis has been associated with chronic use of cocaine mixed with stimulants such as levamisole.[1] Patients with LIV develop tender purpuric lesions 1 to 3 days after exposure.[4] These lesions first develop as symmetric erythema, evolve into retiform purpura, bullae, and finally undergo necrosis and eschar formation.[4] Most commonly, lesions develop over the ear, malar eminences, and tip of the nose. Diagnosis of LIV is on its clinical presentation and histopathological findings of leukocytoclastic vasculitis of small vessels containing fibrinoid necrosis of the vessel wall, erythrocyte extravasation, and multiple fibrin thrombi within small vessels in the superficial and deep dermis.[6]

The exact mechanism by which LIV occurs has not been fully determined. However, LIV is associated with the generation of autoantibodies such as p-ANCA, ANA, and lupus anticoagulant. Levamisole acts as a haptan, triggering an immune response and upregulation of antibody formation. Consequently, it is thought that LIV develops due to immune complex deposition (IgM, IgG, IgA, and C3 complexes) and secondary hypercoagulability caused by the immune complexes, leading to tissue thrombosis and skin necrosis.[3] A specific genotype of human leukocyte adhesion

factor, HLA B27, has been indicated as a risk factor for development of LIV.[2] Patients who present with agranulocytosis are often ANA positive. In LIV, p-ANCA is more common than c-ANCA.[2] Anti-PR3, anti-MPO, and anti-HNE distinguish LIV from the other conditions associated with levamisole.[2] Testing for levamisole can be difficult, as its half-life is 5.6 days and it is not part of routine toxicology screening.

Management of LIV is supportive.[4] The most effective treatment of any of the levamisole-induced syndromes is the cessation of cocaine use.[2] In addition, steroids may be beneficial.[2] Other treatments that have been advocated include nonsteroidal anti-inflammatories and colchicine. Surgical debridement of necrotic tissue, amputation, skin grafting, and local wound care are typically necessary for patients with advanced lesions.[6]

Our patient presented with advanced necrotic lesions of her hand, face, and lower extremity. The diagnosis of LIV was supported by reported development of lesions immediately after smoking crack cocaine. Her laboratory values (agranulocytosis, + ANA, + p-ANCA, + c-ANCA, + lupus anticoagulant) and skin biopsy showing leukocytoclastic vasculitis with associated intravascular fibrin thrombi were confirmatory for LIV. She underwent debridement and amputations of 2 fingers (Fig 2) and later skin grafting. She was counseled against future substance abuse and elected to receive outpatient drug rehabilitation.

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Example – 2

Interesting Case Series

Primary cutaneous mucinous carcinoma of the eyelid

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Keywords: eyelid, mucinous carcinoma, sweat gland, adenocarcinoma, malignant

DESCRIPTION

An 89-year-old man presented with a right eyelid lesion of several months' duration. The lesion measured 1×2 cm and involved one-third of the lower eyelid, including the lateral canthus. The tumor initially resembled a basal cell carcinoma; however, after excision pathology revealed lesion to be a primary mucinous carcinoma.

Figure 1 (upper left)

Figure 2 (upper right)

Figure 3 (lower left)

Figure 4-6 (lower right and above)

QUESTIONS

1. What is mucinous carcinoma of the eyelid?
2. How is it diagnosed?
3. How is it treated?
4. What is the prognosis?

DISCUSSION

Primary cutaneous mucinous carcinoma is a rare malignant neoplasm of the skin that originates from sweat glands. These lesions have been reported under several names, including adenocystic, colloid, gelatinous, and mucinous eccrine carcinoma with the latter being a misnomer as current evidence supports origination from apocrine differentiation.[1] The majority of these tumors arise on the face, with 30% on the eyelid and 43% elsewhere on the head and neck. These tumors are characterized by an indolent course of local growth over months to years, usually in older male patients. The pattern of growth is often horizontal onto the tarsal plate, compared to the vertical growth pattern of sebaceous tumors.[2] Grossly, these tumors present as a painless papular or nodular lesion, occasionally with ulceration or crusting.[3] They often resemble a cyst, BCC, chalazion, keratoacanthoma, or nevus.

Because these tumors often cannot be identified clinically due to their close resemblance to other carcinomas, primary mucinous carcinoma of the eyelid is almost always diagnosed histologically. They appear as nests of cuboidal cells suspended in pools of sialomucin. Cytologically, they display a low mitotic count and little nuclear atypia. These features are consistent with the low-grade nature of this lesion. Several classifications of primary mucinous carcinoma exist, most notably the endocrine mucinproducing carcinoma variant. The current literature is mixed regarding the significance of this variant, as it does not seem to have prognostic significance.[4] A variety of immunohistochemical markers are employed to distinguish these tumors from metastases of breast or gastrointestinal malignancies, including CK7, CK20, and p63.[1] These analyses were not performed in our case because the patient did not endorse any symptoms of an underlying malignancy, nor did he have a history of cancer. Figure 4-6 depicts pathology from our case.

Primary mucinous carcinoma of the eyelid is treated with surgical excision. Generous margins of 1.5 to 2.0 cm are preferred to reduce the likelihood of local recurrence.[5] However, this is often impractical on the eyelid due to a limited quantity of nearby skin for reconstruction and the necessity to maintain aesthetics and function. Successful resection has been reported with narrow margins. The use of Mohs or frozen sections may allow for tighter control of margins, preserving neighboring tissue. If a large resection is unavoidable, reconstruction can be achieved with a Mustarde flap or other reconstructions, as appropriate.[6,7] Our patient's older age and poor overall health prompted us to choose a simple local tissue rearrangement over a large reconstructive effort with final pathology showing complete, successful resection with adequate functional and aesthetic outcome.

Primary mucinous carcinomas are low-grade tumors, but can be locally destructive, a concern considering their location and the complexity of reconstruction in this area. Additionally, these lesions have a propensity for local recurrence, with recurrence rates as high as 40%. Burris et al described a case with local recurrences requiring re-excision over the course of 30 years.[8] The ability to metastasize to lymph nodes and distant tissues has been reported, but these cases are exceedingly rare. Primary mucinous carcinoma is sufficiently rare to warrant consideration of investigation for underlying visceral malignancy, namely of the breast and gastrointestinal tract.[9]

Primary cutaneous mucinous carcinoma of the eyelid is a rare neoplasm arising from sweat glands. These tumors often resemble common lesions, thus are often unsuspected until confirmed

by tissue diagnosis. They are characterized by slow growth and local invasion with a high rate of recurrence. The preferred treatment is local excision with wide margins, but the location of these tumors often requires more narrow margins with reconstructive efforts depending on the extent and location of the tumor.

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