An Unresolved Ecchymosis on the Face of an Elderly Man

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CASE SUMMARY

History and physical examination

A 73-year-old man presented with progressive ecchymosis over his periorbital region and face. The lesion started as a small asymptomatic papule over the left infraorbital region since May 2000. It progressed to involve the entire left eyelid and left face, sparing the right side. There was no evidence of preceding trauma or topical medication. He was a retired merchant and his occupational history was unremarkable. There was no history of exposure to radiation. He has diabetes and hypertension.

He first presented to us in July 2000. Initially, the bruises only affected the left side of his face (Figure 1). The left upper eyelid was slightly swollen. One month later, the lesion spread to the right side of the face involving the right upper eyelid. There was periorbital oedema (Figure 2). The lesion was dusky red in colour with a well-demarcated border. It was indurated with a firm consistency. There were no lymphadenopathy and hepatosplenomegaly noted.

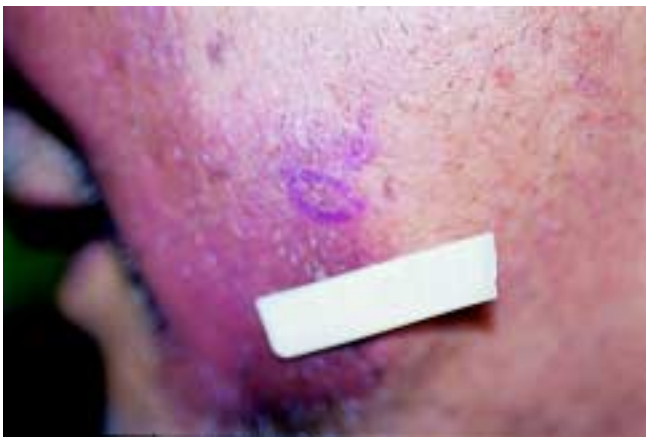

Figure 1: An ecchymosis involving the left side of the face in July 2000

Differential diagnosis

The differential diagnoses are angiosarcoma and primary systemic amyloidosis with possible underlying myelomatosis.

Investigations

The investigations including complete blood picture, prothrombin time (PT) and activated partial thrombin time (APTT) were normal. The erythrocyte sedimentation rate (ESR) was raised at 48 mm/hr. The renal function was impaired with elevated urea and creatinine levels at 14.3 mmol/dL and 241 μmol/l

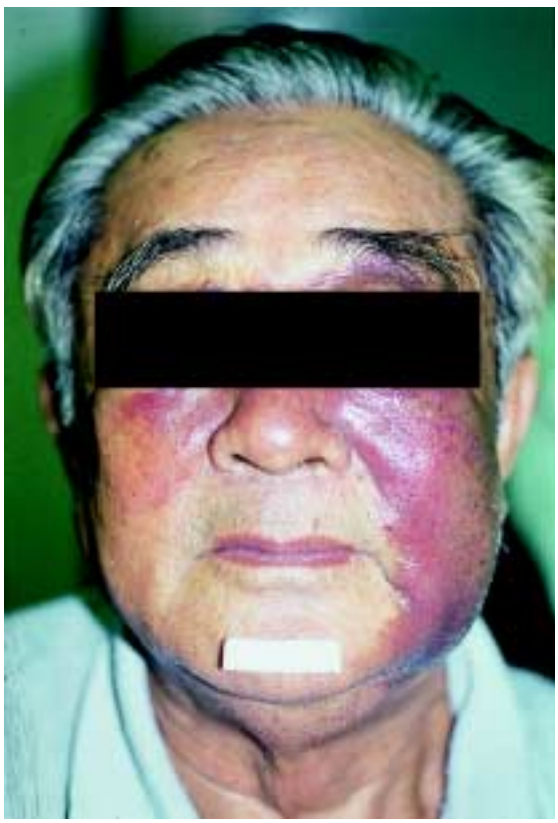

Figure 2: One month later, the facial eruption progressed and spread to the right side of the face. Periorbital edema was noted

respectively. The liver function test showed a raised alkaline phosphatase at 138 U/l and γ-glutamyl transpeptidase (GGT) at 131 U/l. ANF titre was elevated at 1/120. The immunoglobulin pattern (IgG, IgA and IgM) was normal. There was no Bence Jones protein detected in the urine. Chest X-ray was normal.

Four skin biopsies were performed at different stages of the condition. The first biopsy was performed in July 2000 and was reported to be heliodermatitis (solar elastotic syndrome) with no evidence of malignancy. A second biopsy was carried out at the end of August, which was suspicious but inconclusive for angiosarcoma. In view of the inconclusive reports, a third biopsy was done and sent overseas for second opinion. It reported that the lesion consisted of angulated vascular channels lined by a monolayer of hyper-chromatic endothelial cells. There was striking collagen dissection which was highlighted by CD31 immuno-staining in some areas. There were considerable nuclei atypia in one or two foci which showed more solid dissecting pattern. The histology of this atypical vascular proliferation was most consistent with angiosarcoma. Close follow-up and further biopsy were advised to confirm the diagnosis. Finally, a fourth biopsy was done in December which confirmed the diagnosis of angiosarcoma.

Diagnosis

The dermatopathological diagnosis was angiosarcoma.

Management and subsequent course

Once the pathologist reported that the lesion was highly suspicious of angiosarcoma, the patient was referred to the Oncology Unit for management and work-up. Unfortunately, he refused radiotherapy and defaulted follow-up. He consulted dermatologists in the private sector and received repeated courses of intramuscular injections of unknown nature. He claimed that the injections reduce the facial swelling but gave him a hypertensive crisis. He also visited local Chinese herbalists and took several courses of Chinese herbal remedies. The patient was seen again in our clinic in December 2000. The ecchymosis had spread to the other side of the face involving the right eyelid and face. A hard nodule appeared over the inner canthus of the right eye (Figure 3). The fourth biopsy was taken at this site.

REVIEW ON ANGIOSARCOMA

Definition and epidemiology

Angiosarcoma is a rare malignant vascular tumour with a uniformly poor prognosis. Pathologically it comprised of two entities: haemangiosarcoma and lymphangiosarcoma. It only accounts for 2% of all soft tissue sarcomas.[1] It has been estimated that angiosarcoma only represented 0.1% of head and neck malignancies[2] and less than 1% of all cancers.[1] It usually affects the elderly but may occur in young adults especially at risky sites. There is a male preponderance. Factors that have been postulated to increase the risk of developing angiosarcoma are: chronic lymphoedema, post-irradiation, environmental toxins such as thorotrast used in angiography in the past, vinyl chloride used in industry, insecticides in agriculture, anabolic steroids and synthetic oestrogens.[1] The recent speculation about the association between angiosarcoma and human herpes virus type 8 is controversial.

Clinical features

Angiosarcoma may present in three main forms: an enlarging bruise, a blue-black nodule and a non-healing ulcer.[2] Its main site of predilection is head and neck, followed by the upper face. Rare cases have been reported to occur at the maxilla, mandible, pharynx, tongue and larynx.[2] Chronic lymphoedema and places which have been irradiated previously may predispose the occurrence of angiosarcoma. Angiosarcoma may be easily mistaken with cellulitis, ecchymosis secondary to trauma, and haemangioma. Delay in diagnosis is not uncommon.

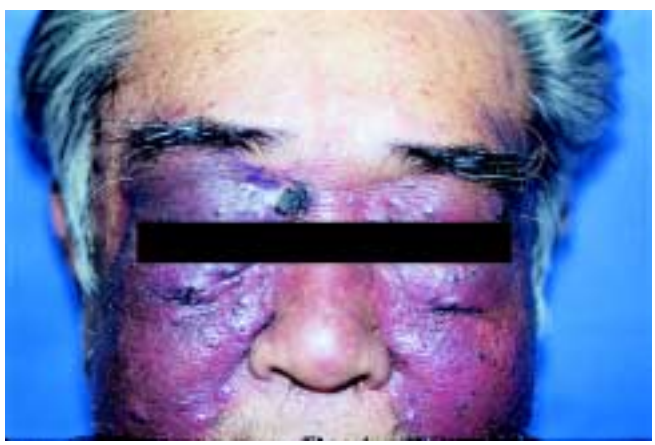

Figure 3: A hard nodule was seen over the inner canthus of the right eye in December 2000

Management

The management of angiosarcoma should be a combined effort involving dermatologist, histopathologist and oncologist. The treatment should be carried out in a specialized centre which has considerable experience in managing patients suffered from this kind of condition. Since angiosarcoma has a high mortality, the treatment plan, prognosis, possible complications and side effects of treatment should be discussed with the patient and their relatives.

Due to the rarity of angiosarcoma, optimal management of angiosarcoma has not been defined. The three treatment modalities are surgery, radiotherapy and chemotherapy. These treatment modalities can be used alone or in combination with one another.

Small resectable lesion had been managed by surgery alone but there is a high rate of local recurrence. For surgery combined with chemotherapy, a series reported by Mark et al showed that only five of 36 (14%) patients remained disease free.[1] Of the remainder, 27 (87%) patients recurred locally and 11 (35.5%) with distant metastasis. In the same study, radiotherapy together with chemotherapy only rendered 1 out of 9 patients (11.1%) disease free.[1] Combination of surgery and radiotherapy improved disease free state by 43% compared with surgery alone (13%).[1]

However, not all reported series could reproduce the same favourable outcome of combining surgery with radiotherapy. Hodgkinson et al from Mayo clinic reported that only two of 13 patients (15.4%) were free of disease after surgery and radiotherapy.[3] In another oncology centre in MD Anderson Cancer Center, Houston, Maddox reported that two of six patients were rendered disease free after surgery and radiotherapy (33.3%).[4] Holden et al noted that five of 13 patients (38.5%) treated with radiotherapy alone were disease free.[5] Nonetheless, combination of surgery and radiotherapy is still the treatment of choice for most of the diagnosed lesion of angiosarcoma.

Recently, a number of systemic chemotherapeutic agents have been used to treat angiosarcoma. They include vinorelbine, doxorubicin, ifosamide, isotretinoin with interferon[1] and paclitaxel.[6] None of these agents were tested with double-blinded, randomized controlled trials. Most of them had only been reported in retrospective case analysis or isolated case reports. This limited their clinical applications.

Systemic paclitaxel (Taxol) had been shown some promising prospect in the treatment of angiosarcoma. Fata et al reviewed their series of nine patients suffered with this disease being treated with paclitaxel over seven years. Three different regimens of paclitaxel were used:[6]

1. Paclitaxel 250 mg/m^2 was administered as a continuous infusion over 24 hours every three weeks. Prophylactic G-CSF was administered at 5 μg/kg.
2. Paclitaxel 175 mg/m^2 was administered as a three-hour infusion every three weeks followed by G-CSF.
3. Paclitaxel 90 mg/m^2 was administered weekly as an one-hour infusion.

Eight patients responded.[6] The duration of response lasted from two to 13 months (median five months). The primary toxicity of paclitaxel was haematological. The drug was well tolerated according to the study and no deaths were attributed to the drug. Unfortunately, these favourable effects of paclitaxel on angiosarcoma were not supported by some other studies.

The outlook of angiosarcoma is still pessimistic. A lot of work still needs to be done to observe the effects of other chemotherapeutic agents that may be useful in treating this condition. As medicine is evidence based nowadays, new agents must have undergone strict double-blinded randomized trials before they are used in human subjects. Hopefully, in the future more evidence based data concerning the treatment of angiosarcoma can be obtained.

Learning points:

Diagnosis of angiosarcoma needs a high index of clinical and histopathological suspicion. Angiosarcoma should be considered when there are chronic unremitting bruises on the head in elderly patients. A collaboration of dermatologist, surgeon, and oncologist is needed in the management of this malignancy.

References

1. Mark R, Poen J, Tran LFY, Juillard G. Angiosarcoma: a report of 67 patients and a review of the literature. Cancer 1996;77: 2400-6.
2. William L, Shaha A, Shah J. Angiosarcoma of the head and neck. Am J Surg 1994;168:451-4.
3. Hodgkinson DJ, Soule EH, Woods JE. Cutaneous angiosarcoma of the head and neck. Cancer 1979;44:1106-13.
4. Maddox JC, Evans HL. Angiosarcoma of skin and soft tissue: a study of 44 cases. Cancer 1981;48:1907-21.
5. Holden CA, Spittle MF, Jones EW. Angiosarcoma of the face and scalp, prognosis and treatment. Cancer 1987;59:1046-57.
6. Fata F, O'Reilly E, Lison D, et al. Paclitaxel in the treatment of patients with angiosarcoma of the scalp or face. Cancer 1999; 86:2034-7.

Answers to Dermato-venereological Quiz on page 191

Answer (Question 1)

1. Proximal subungual onychomycosis (PSO). This is caused by rapid fungal invasion of the stratum corneum of the proximal nail fold and subsequently the nail plate.

2. *Trichophyton rubrum* is the commonest cause. *T. megninii, T. schoenleinii, T. tonsurans and T. mentagrophytes* are also known to cause PSO.

3. Distal and lateral subungual onychomycosis (DLSO). Before the availability of highly active antiretroviral therapy (HAART), PSO was considered to be the most common form of onychomycosis in patients with acquired immunodeficiency syndrome (AIDS). However, recent studies have shown that DLSO accounted for about 90% of all cases of onychomycosis in HIV-infected persons. This could be due to the slowing of HIV disease progression by HAART. The patient in the photograph had already developed AIDS and had a lowest CD4 count of 16/μL.

Answer (Question 2)

1. Epidemic HIV-associated Kaposi's sarcoma (KS). This is almost exclusively found in homosexual and bisexual men and occasionally in the female partners of the latter. KS is an AIDS-defining condition and HIV disease is usually advanced by the time KS develops. However, as in this case, KS can be a presenting symptom of HIV infection. The CD4 count was only 34/μL at the time of presentation.

2. Solid cords and fascicles of spindle cells are arranged between jagged vascular channels which contain trapped erythrocytes. These spindle-celled vascular processes dissect the collagen bundles of the entire dermis. Occasionally, mitotic figures can be seen. A lymphocytic inflammatory infiltration is usually present.

3. Highly active antiretroviral therapy (HAART) should be started for patients who are not already on this. HAART does not only prolong survival but it can also result in complete remission of KS even without KS specific treatment in some cases. KS specific treatments include excision, cryotherapy, laser therapy, radiotherapy, topical and systemic chemotherapy.