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DERMA TODAY

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Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "Derma Today" which contains latest and interesting news in the field of Dermatology.

This issue contains:

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Looking forward to your valuable feedback.

Best Regards,

Medical Team, Micro Labs Limited.

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Adjuvant nivolumab plus ipilimumab or nivolumab monotherapy versus placebo in patients with resected stage IV melanoma

Introduction

Cutaneous melanoma has the capacity to spread to remote organs and causes multiple deaths. Surgical excision with adjuvant treatment of the primary tumor decreases the possibility of recurrence and distant metastasis. Adjuvant immunotherapy with the cytotoxic T-lymphocyte-associated protein 4 inhibitor ipilimumab (10 mg / kg) demonstrated significant clinical advantage versus placebo in stage III melanoma. However, treatment-related toxicity was high. Recently, dabrafenib plus trametinib as well as the programmed cell death 1 (PD-1) blocking agents nivolumab and pembrolizumab demonstrated therapeutic efficacy improvement in resected stage III melanoma, contributing to adjuvant approval. The EORTC 1325 study of patients with stage III melanoma, which contrasted pembrolizumab to placebo, demonstrated substantially improved recurrence-free survival in favor of pembrolizumab, and likewise, the CheckMate-238 experiment, which checked nivolumab head-to - head with ipilimumab, resulted in significantly improved recurrence-free survival in favor of nivolumab. The CheckMate-238 analysis included not just patients with stage IIIB – C resected Melanoma but still around 20 per cent of patients with stage IV melanoma completely resected. For metastatic melanoma, PD-1 antagonists, ipilimumab CTLA-4 inhibitor,14 the mixture of nivolumab and ipilimumab, and combinations of BRAF and MEK antagonists for BRAF-mutated melanoma approved for many years.

Patients with stage IV melanoma without evidence of cancer were omitted from these studies as detectable tumor lesions were needed. There is a strong clinical need for patients with stage IV melanoma without signs of cancer, because their survival rate is lower than in patients with stage III. Statistics are low for recurrence-free recovery and general recovery in Stage IV patients. Recurrence-free survival in case series ranged from 5 to 7 months and total survival was recorded between 20-24 months. In this review, they intended to provide data on protection and effectiveness for a randomized interim examination of the combination of nivolumab & ipilimumab and nivolumab monotherapy as opposed to placebo in patients with stage IV melanoma without evidence of disease.

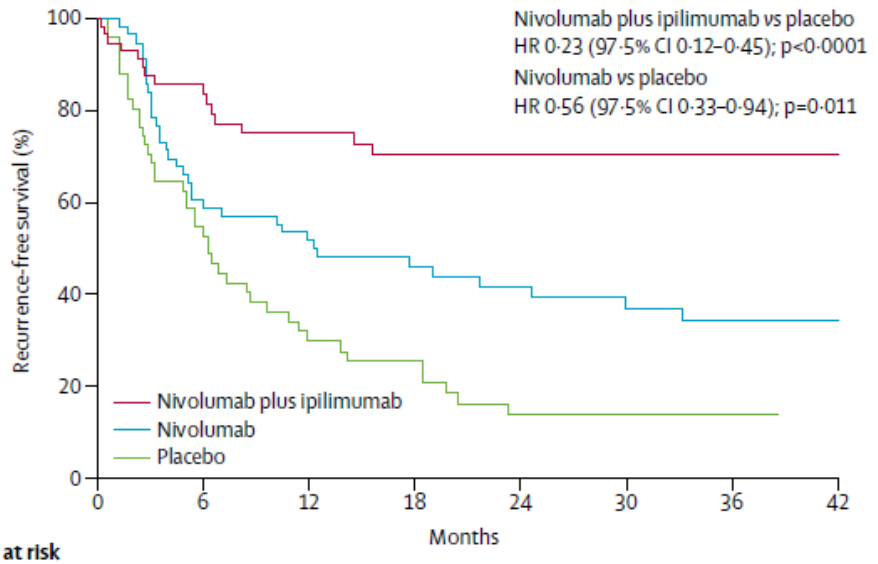
Methods

They did a randomised, double-blind, placebo-controlled, phase 2 trial in 20 German academic medical centres. Eligible patients were aged 18–80 years with stage IV melanoma with no evidence of disease after surgery or radiotherapy. Key exclusion criteria included uveal or mucosal melanoma, previous therapy with checkpoint inhibitors, and any previous immunosuppressive therapy within the 30 days before study drug administration. Eligible patients were randomly assigned (1:1:1), using a central, interactive, online system, to the nivolumab plus ipilimumab group (1 mg/kg of intravenous nivolumab every 3 weeks plus 3 mg/kg of intravenous ipilimumab every 3 weeks for four doses, followed by 3 mg/kg of nivolumab every 2 weeks), nivolumab monotherapy group (3 mg/kg of intravenous nivolumab every 2 weeks plus ipilimumab-matching placebo during weeks 1–

12), or double-matching placebo group. The primary endpoint was the recurrence-free survival in the intention-to-treat population. The results presented in this report reflect the prespecified interim analysis of recurrence-free survival after 90 events had been reported.

Results

Between Sept 2, 2015, and Nov 20, 2018, 167 patients were randomly assigned to receive nivolumab plus ipilimumab (n=56), nivolumab (n=59), or placebo (n=52). As of July 2, 2019, at a median follow-up of 28·4 months (IQR 17·7–36·8), median recurrence-free survival was not reached in the nivolumab plus ipilimumab group, whereas median recurrence-free survival was 12·4 months (95% CI 5·3–33·3) in the nivolumab group and 6·4 months (3·3–9·6) in the placebo group. The hazard ratio for recurrence for the nivolumab plus ipilimumab group versus placebo group was 0·23 (97·5% CI 0·12–0·45; p<0·0001), and for the nivolumab group versus placebo group was 0·56 (0·33–0·94; p=0·011). In the nivolumab plus ipilimumab group, recurrence-free survival at 1 year was 75% (95% CI 61·0–84·9) and at 2 years was 70% (55·1–81·0); in the nivolumab group, 1-year recurrence-free survival was 52% (38·1–63·9) and at 2 years was 42% (28·6–54·5); and in the placebo group, this rate was 32% (19·8–45·3) at 1 year and 14% (5·9–25·7) at 2 years. Treatment-related grade 3–4 adverse events were reported in 71% (95% CI 57–82) of patients in the nivolumab plus ipilimumab group and in 27% (16–40) of those in the nivolumab group. Treatment-related adverse events of any grade led to treatment discontinuation in 34 (62%) of 55 patients in the nivolumab plus ipilimumab group and seven (13%) of 56 in the nivolumab group. Three deaths from adverse events were reported but were considered unrelated to the study treatment.



Number at risk (number censored)								
Nivolumab plus ipilimumab	56 (0)	40 (7)	34 (9)	26 (15)	21 (20)	14 (27)	10 (31)	1 (40)
Nivolumab	59 (0)	34 (3)	29 (3)	22 (7)	19 (8)	16 (10)	11 (13)	3 (21)
Placebo	52 (0)	26 (2)	15 (3)	11 (4)	6 (4)	6 (4)	2 (8)	0 (10)

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Conclusion

Among patients with stage IV melanoma without signs of cancer, adjuvant treatment with nivolumab alone or in conjunction with ipilimumab improved recurrence-free survival dramatically compared with placebo. Grade 3–4 therapy-related AE levels in all successful patient classes were greater than the level recorded in previous landmark trials performed with detectable disease in advanced melanoma.

Source: Zimmer L, Livingstone E, Hassel JC, et al. Adjuvant nivolumab plus ipilimumab or nivolumab monotherapy versus placebo in patients with resected stage IV melanoma with no evidence of disease (IMMUNED): a randomised, double-blind, placebo-controlled, phase 2 trial. Lancet. 2020;395(10236):1558-1568.

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A Registry-Based Cross-Sectional Study of 13,538 Patients with Hidradenitis Suppurativa

Introduction

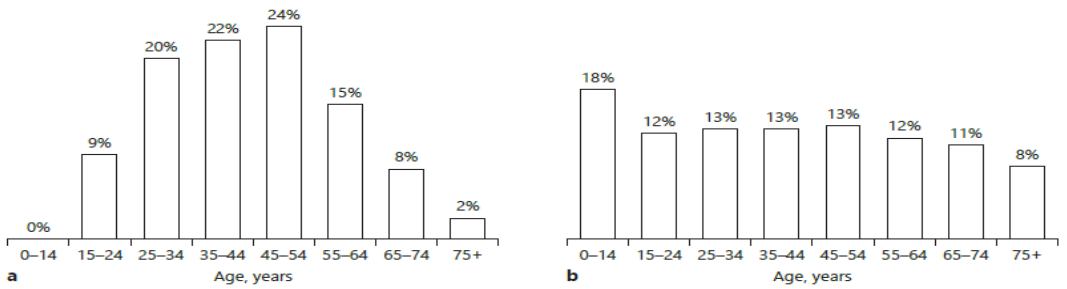
Hidradenitis suppurativa (HS) is a chronic, inflammatory skin condition with nodules and fistula formation and scarring. It is a debilitating disease with a severe negative impact on quality of life. There is a need for increased knowledge about the social and lifestyle characteristics of patients with HS in general, and pregnant women in particular. The aims of this study were to investigate and describe social characteristics and comorbidity in all HS patients in Sweden as well as to study the prevalence of lifestyle factors associated with negative impact on health and pregnancy in Swedish pregnant women with HS.

Methods

A registry-based cross-sectional study was performed by record linkage between Swedish registers covering the entire population. A cohort of 13,538 HS patients diagnosed with HS in specialised care during the years 2001–2014 and a subgroup of 1,368 HS patients who had undergone pregnancy during 2010–2015 were defined and described. Aggregated public data on the entire Swedish population and all pregnancies in 2014 were described for reference.

Results

The HS population had an average age of 44 years on December 31, 2014. The prevalence of HS was 0.14%. In comparison to the Swedish reference population the HS patients were more often women, unmarried (36 vs. 44% married), and had lower education (68 vs. 82% with an upper-secondary school degree or higher) and lower income (39 vs. 16% made SEK < 100,000 a year). Comorbidity was 3% for inflammatory bowel disease and 8% for type 2 diabetes. The subgroup analysis showed high prevalence of overweight, obesity, and smoking in pregnant women with HS.



Age distribution on December 31, 2014, in 10-year intervals. a. The HS population (n = 13,538). b. The Swedish reference population (n = 9,747,355).

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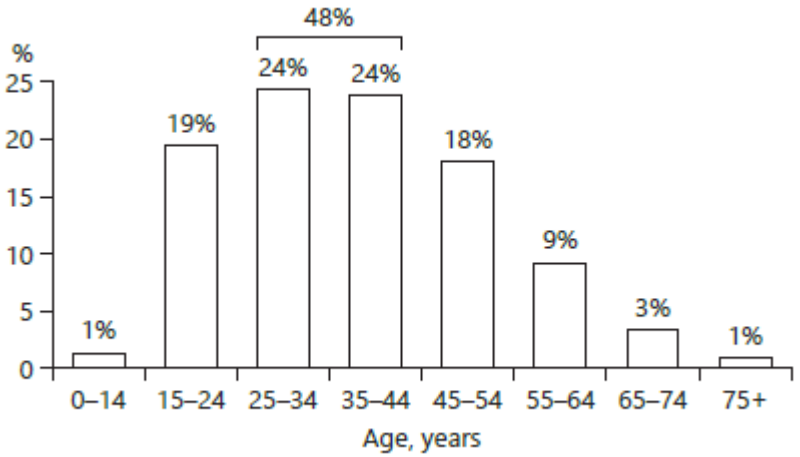
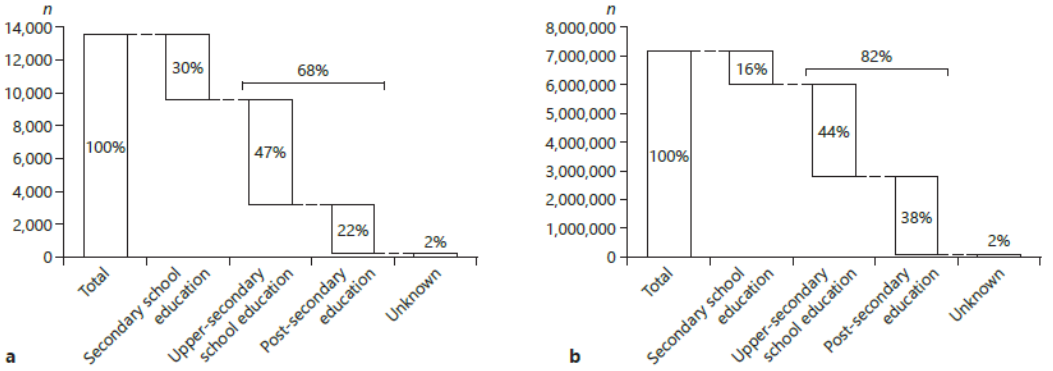
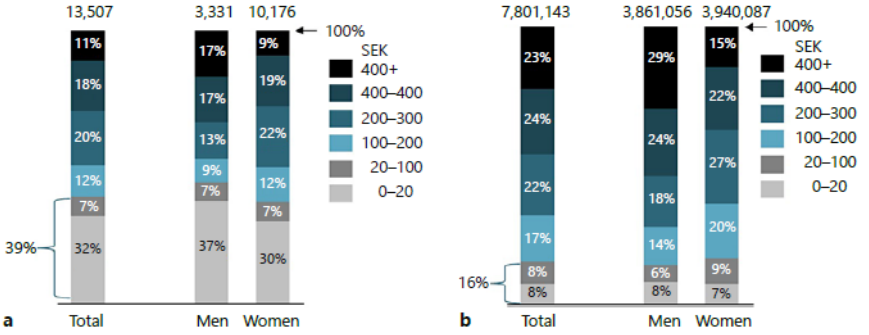


The age at which each patient in the HS population first received the diagnosis HS in specialised care (n = 13,538). The average age was 37.7 years. Almost half the patients (48%) were aged between 25 and 54 years at the time of the first registered HS diagnosis.



The highest completed education for each individual in the population on December 31, 2014 (primary school corresponds to 6 years of school, secondary school to 9 years, and upper-secondary degree to 12 years of education). a. The HS population (n = 13,538). Sixty-eight percent had an upper-secondary degree or higher. b. The Swedish reference population (n = 7,131,607), aged 16–74 years. Eighty-two percent had an upper-secondary degree or higher.



Annual taxable income of the individuals (aged 16 years or older) in the populations, expressed in thousands of Swedish kronor (SEK), 2014. Results are displayed for the entire groups and for men and women separately. Taxable income includes all income (except capital gain) from employment and pension, social, unemployment, and welfare benefits. a. The HS population (n = 13,507). Thirty-nine percent had a taxable income lower than SEK 100,000. b. The age-adjusted Swedish reference population (n = 7,801,143). Sixteen percent had a taxable income lower than SEK 100,000.

Conclusion

The results from this comprehensive characterisation of Swedish HS patients may be used to improve preventive measures, information, and care for this vulnerable group.

Source: Killasli H, Sartorius K, Emtestam L, Svensson Å. Hidradenitis Suppurativa in Sweden: A Registry-Based Cross-Sectional Study of 13,538 Patients. Dermatology. 2020;236(4):281-288.

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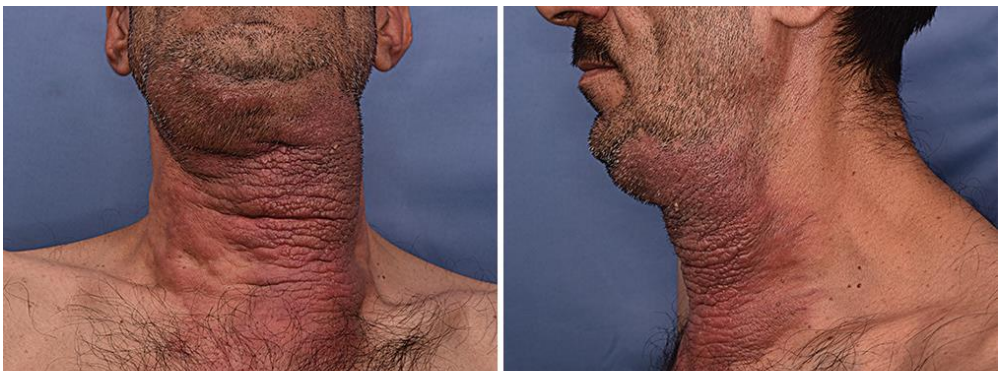
A Rare Instance of Tumoral Scleromyxedema

Case study

Introduction

Scleromyxedema is a progressive condition characterized by pronounced mucin deposition and fibrosis reported in the dermis with several hard waxy papules and plaques, systemic symptoms, and monoclonal gammopathies. The essay is meant to concentrate on an uncommon and ambiguous layout that has not been addressed in prior literature.

The authors report a case of a 53-year-old male patient with a steadily progressing infiltrative solid, reddish, nontender pruritic waxy plaque with a cobblestone appearance on the neck reaching up to the mandible and upper chest with some minimally conspicuous lymph nodes in bilateral jugular chains from 9 months ago. The patient has no history of weight loss or any other systemic symptoms Spiral CT scan of the neck, chest, abdomen, and pelvis showed the vascular soft-tissue mass with 80 mm × 48 mm size anterior to the thyroid and trachea with some axillary lympahdenopathy on both sides. Hypodense soft-tissue mass with 42 mm × 26 mm size encasing the left gastric artery also was seen. Serum protein electrophoresis and immunoelectrophoresis were normal, and no gammaglobulinemia were found. Lymph node biopsy was reactive. A biopsy was taken and showed proliferation of fibroblasts or fibrohistiocytes as interlacing bundles between collagen fibers, in a marked mucinous background which was compatible with the diagnosis of scleromyxedema. Immunohistochemistry (IHC) was done to support the diagnosis and to rule out other suggested diagnosis such as inflammatory myofibroblastic tumor and dermatofibrosarcoma protuberans. Linear endoscopic ultrasound examination was performed for the mass around the gastric artery showing ill-defined hypoechoic soft-tissue closed to the celiac region. Fine-needle aspiration was performed, but no malignant cells were found in the cytology.



(a) Infiltrative erythematous plaque on the neck (b) View from the lateral side

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After 3 months the lesion was more obvious and larger in size

DISCUSSION

Scleromyxedema is an uncommon disease. It affects the middle-aged adults without sex predilection. It is characterized by a widespread symmetric eruption of small, waxy, and firm papules that are closely spaced and often arranged linearly. The papules are typically 2–3 mm, dome-shaped, or flat-topped. The most commonly affected areas include the face, neck, distal forearms, and hands, with sparing of the palms, scalp, and mucous membranes. Itching is not rare. The affected skin may exhibit diffuse erythema, edema, and a brownish-discoloration. As the condition progresses, erythematous and infiltrated plaques may occur with skin stiffening, sclerodactyly, and decreased mobility of the mouth and joints. The systemic manifestations of scleromyxedema are serious and have been fatal in some cases. Mucin has been identified in adventitia around vessels in many systems, including the heart and lungs. Up to 83% of patients with scleromyxedema have been described as having a paraproteinemia, predominantly of the IgG-λ subtype. The disease may progress to multiple myeloma in 10% of cases. Other systemic manifestations include myositis, disturbances in the central nervous system and peripheral neuropathy, coma (preceded by flu-like illness), arthralgia and arthritis, renal disease, lung involvement, dysphagia, and laryngeal involvement. Intravenous immunoglobulin (IVIG), alone or in combination with systemic medications, has gained widespread acceptance as first-line therapy for both the cutaneous involvement and associated systemic manifestations, including the dermato-neuro syndrome. Melphalan used to be the main treatment for scleromyxedema; however, it may have contributed to patient's deaths from the inducement of hematologic malignancies. Other therapies includes steroids, methotrexate, cyclophosphamide, thalidomide, cyclosporine, oral retinoids, extracorporeal photopheresis, and plasmapheresis.

In such cases with growing infiltrative tumoral hard plaque, scleromyxedema could mimic other entities and the diagnosis becomes difficult, revealing the importance of clinicopathologic correlation. Scleromyxedema could be mistaken with nephrogenic systemic fibrosis (NSF), scleredema, localized myxedema, mycosis fungoides, nodular amyloidosis, metastasis, DFSP, other mesenchymal tumors, and inflammatory myofibroblastic tumor. It is easy to rule out nephrogenic

systemic fibrosis (NSF) clinically, as it develops in patients suffering from renal failure exposed to gadolinium-containing contrast media, and it usually tends to be distributed symmetrically on extremities. Scleredema lacks fibroblast proliferation despite mucin deposition and fibrosis, and myxedema usually appears on the shins with a previous history of Grave's disease or treatment of the thyroid disease.

Mycosis fungoides, nodular amyloidosis, and metastasis are easily differentiated on the basis of histologic findings, and general workup for any malignancy source as was done for this patient. Immunohistochemistry (IHC) is often required, in particular for the exclusion of DFSP. DFSP normally starts as a single, gradually developing plaque on the trunk, and histological observations indicate storiform fascicles of atypical spindle cells and the presence of the subcutaneous tissue in a pattern looks like a honeycomb, but in early stages low cellularity and limited atypia may occur. Inflammatory myofibroblastic tumor sometimes called inflammatory pseudotumor is a uncommon tumor located mainly in internal organs, such as heart, abdominal, mediastinal, vaginal, and soft tissue, although it may occasionally affect the skin. The key clinical results are spindle cell proliferation (predominantly myofibroblastic) and a influential inflammatory invasion consisting mainly of plasma cells. The IHC for the Desmin, SMA, and ALK-1 are optimistic. Unfortunately, patient commitment to every modality of care was low.

Source: Sadeghinia A, Al Salman M, Fazli JT, et al. A rare case of tumoral scleromyxedema. Indian J Dermatol 2020; 65:310-2