Skin and Breast Disease in the Differential Diagnosis of Chest Pain

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KEYWORDS

• Chest pain • Skin diseases • Herpes zoster
• Breast • Neoplasm

Pain is not a symptom commonly associated with skin disease. This is especially so when considering the known skin problems that have a presenting symptom of chest pain that could potentially be confused with chest pain from other causes.

PAINFUL SKIN CONDITIONS

Several extremely painful and tender skin conditions present with dramatic clinical signs. Inflammatory disorders such as pyoderma gangrenosum, skin malignancies, both primary and secondary, acute bacterial infections such as erysipelas or cellulitis, and multiple other infections are commonly extremely painful and tender. As these conditions manifest with obvious skin signs such as swelling, erythema, localized tenderness, fever, lymphangitis, and lymphadenopathy, there is little chance of misdiagnosis of symptoms as caused by anything other than a cutaneous pathology.

Several skin tumors can be painful or tender. These include blue rubber bleb nevus, eccrine spiradenoma, neuromas, neurilemmomas, glomus tumors, angiolipomas, leiomyomas, dermatofibromas, squamous cell carcinomas and other skin malignancies especially when perineural infiltration is present, endometriomas, and granular cell tumors. Once again in almost all cases of pain related to a skin tumor a lesion can be readily identified, often by the patient. For a painful skin condition to be misdiagnosed as cardiac, pulmonary, or other forms of chest pain, the pain must arise in the absence of readily identifiable skin disease.

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HERPES ZOSTER

The classic condition to cause significant pain without obvious skin changes is herpes zoster. Although herpes zoster affects 20% to 30% of people in their lifetime, up to 50% of those more than 80 years old will be affected.[1] Herpes zoster is the reactivation of varicella zoster (chicken pox) virus that has lain dormant in the spinal dorsal root ganglion since initial infection. This produces the well-known, dermatomally distributed eruption commonly known as shingles (**Fig. 1**). Most often unilateral and confined to a single dermatome, herpes zoster can involve multiple dermatomes and be bilateral. In severe cases, scarring and depigmentation may follow the healing of the acute lesions (**Fig. 2**). There is often significant associated pain preceding, accompanying, and following resolution of the skin eruption. Pain persisting more than a month after the typical skin eruption is termed postherpetic neuralgia.

The pain is variable in intensity but can be severe. It may be localized or more diffuse. The onset of pain is usually around 4 days before any skin lesions appear.[2] This prodromal pain has been labeled as "preherpetic neuralgia."[3] There may be associated fever, malaise, and often tenderness or hyperesthesia in the affected area. Obviously in the prodromal phase before the onset of the skin lesions, the source of this pain can be obscure and erroneously attributed to other causes. For example, involvement of abdominal dermatomes can lead to the diagnosis of intraabdominal pathology such as biliary colic,[4] duodenal ulcer, appendicitis, or renal colic. A rare presentation is where there is no skin eruption following the prodromal pain. This is termed "zoster sine eruption" or "zoster sine herpete." The diagnosis may be supported by demonstrating an increase in IgM and eventually IgG varicella antibody titers.[5,6]

Of particular interest are reports of 6 zoster patients in whom pain preceded any skin eruption for between 7 and more than 100 days. The distribution of the pain did not always occur in the same dermatomes where the rash eventually developed.[3] Clearly it would be extremely difficult to diagnose the cause of such a pain before the onset of skin signs. Pain from such an atypical presentation of zoster would be even more likely to be attributed to other causes.

During this phase of pain without skin lesions, there is the likelihood that diagnoses other than herpes zoster will be considered.[7] Of especial pertinence to chest pain is the fact that zoster-related pain is more likely in older patients and will more often be severe. As older patients are also more at risk of chest pain from cardiac and

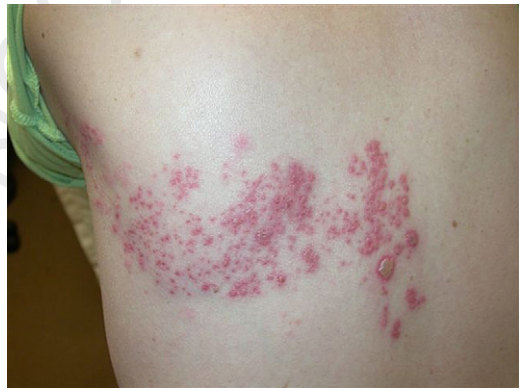

Fig. 1. Acute herpes zoster showing the typical changes of pustules on an erythematous base in a dermatomal distribution.

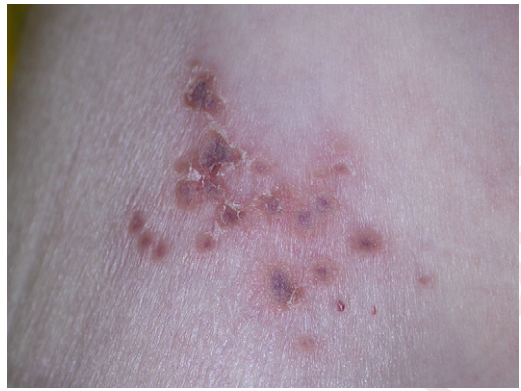

Fig. 2. Healing shingles approximately 10 to 14 days after the onset of the eruption.

pulmonary causes, the increasing incidence of zoster with increasing age also adds to the likelihood of diagnostic confusion.

Thoracic dermatomes are commonly affected. These features enhance the risk of confusion with cardiac pain[8,9] or pleurisy. Herpes zoster can be complicated by pleuropericarditis and even complete heart block.[10] Temporary electrocardiographic abnormalities can be seen.[11]

Diagnosing herpes zoster during this prodromal phase is clearly difficult. Clues to the diagnosis include a history of varicella or herpes zoster, the presence of localized skin tenderness or hyperesthesia in the painful area, and the localization of pain to a dermatome. Obviously all efforts would need to be made to exclude other serious or indeed life-threatening causes of chest pain. Often the diagnosis is only made with the onset of the typical skin lesions of grouped vesicles and pustules on an erythematous base in a dermatomal distribution (see **Fig. 1**). Then the diagnosis can usually be made on clinical grounds alone. Swabs from a blister base reveal varicella zoster virus DNA when submitted for confirmatory polymerase chain reaction. Only rarely is biopsy necessary.

Treatment is with pain relief and a variety of systemic antiviral agents (acyclovir, famciclovir, valacyclovir). Treatment should be instituted within 72 hours of the appearance of the rash and continued for 7 days.[12] There is evidence that valacyclovir is superior to acyclovir.[13] The former agent has the advantages of better bioavailability and less frequent dosing.

An episode of herpes zoster usually resolves completely within 4 weeks (see **Fig. 2**). Scarring and depigmentation may occur (**Fig. 3**). There should be no confusion as to the cause of pain once the typical skin lesions have developed. It should be noted that there are case reports of herpes zoster being temporally associated with and perhaps triggered by thoracic surgery with zoster arising in the surgical scars.[14]

Pain that persists or recurs more than a month after the onset of herpes zoster is termed postherpetic neuralgia. It is more common in older female patients especially if there was significant prodromal pain, a more severe rash, and more severe acute pain.[15] Again there is little risk of misdiagnosis of this pain as a history of acute herpes zoster will be found.

Once established postherpetic neuralgia is notoriously difficult to treat. Treatments used include gabapentin,[16] pregabalin,[17] topical capsaicin cream,[18] tricyclic antidepressants,[19] and in selected cases epidural injections of local anesthetic and steroid.[20]

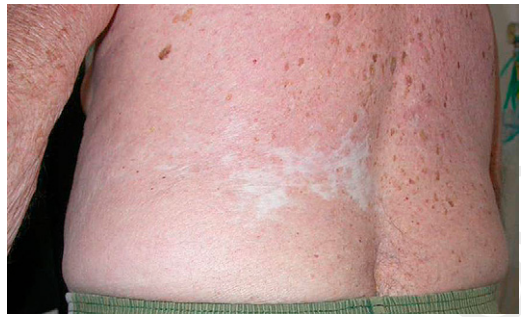

Fig. 3. Postherpetic scarring and depigmentation in a lower thoracic dermatome.

A condition little known outside of dermatologic circles is notalgia paresthetica. It is characterized by itch and less commonly pain in the interscapular region of the back. This is the area innervated by the posterior primary rami of the thoracic nerves T2 to T6. Entrapment of these nerves is speculated to be causal.[21] Typically the condition occurs in older patients and there is a long history of discomfort, itch, or even hyperesthesia in the region. Skin changes can be minimal or related to chronic rubbing and scratching with thickening and darkening of the skin in the affected area. Sensory disturbances may be detectable on pin-prick testing. Biopsy of the affected skin can reveal necrotic epidermal keratinocytes and melanophages in the dermis.[22] Amyloid deposition, which is probably reactive, is also documented. Treatment is difficult and the condition tends to run a prolonged course. Agents such as topical capsaicin, topical local anesthetics, and oral amitryptiline have been used in treatment. Unfortunately there is little published evidence to support any intervention.

SKIN NEOPLASMS

As outlined earlier, several skin neoplasms can be painful. It would be uncommon for any of these lesions to present diagnostic confusion as to the source of the pain. Histology is characteristic in each case.

Glomus tumors are benign vascular skin tumors that resemble the gloumus apparatus. They are essentially vascular lesions.[23] Typically these lesions are solitary, pink to purple, domed dermal nodules. They vary in size from 1 to 20 mm diameter. Classically they are found on the distal extremities and are very painful. Symptoms can be spontaneous or triggered by pressure and temperature change. Glomangiomas, which have more prominent vessels and less prominent glomus cells, are reported on the trunk. These present as larger hemangioma-like lesions that may be congenital, are not restricted to the extremities, and although less likely to be painful, they can be.[24] Treatment is usually by surgical excision.

Eccrine spiradenomas are tumors derived from sweat glands and present as single, gray to pink, dermal nodules. They arise on the head, neck, and trunk but less often the extremities. Several variants are described (multiple, giant, linear, congenital). Malignant transformation can occur. They can be tender and painful. Histology is distinctive. Treatment and often diagnosis is by excision.[25]

Leiomyomas in the skin are benign smooth muscle lesions that can be vascular (angileiomyoma) in origin or derived from arrector pili muscle (piloleiomyomas). Both forms can be painful but angioleiomyomas are more likely to cause symptoms. Piloleiomyomas are often multiple and occur on the face, back, and limbs. They are

firm red-brown nodules. Trauma and cold can trigger pain. Angioleiomyomas, on the other hand, are usually solitary nodules on the extremities (**Fig. 4**). Pain and tenderness are seen in most cases. Many treatments are described including excision, analgesics, nifedipine, phenoxybenzamine hydrochloride, gabapentin, and doxazosin. More recently botulinum toxin has been used with success.[26]

Angiolipomas, as the name suggests, arise in the subcutis and are far more vascular than lipomas. They are believed to be hamartomas of blood vessels and fat. Onset soon after puberty is common and they present as soft sometimes bluish nodules on the trunk or limbs and are often multiple. They are often easier felt than seen. Unlike simple lipomas, mild pain and tenderness with pressure or movement is common. There is a noninfiltrating and a more rare but aggressive infiltrating type. The latter can mimic malignancy and is likely to recur after surgery. Treatment is usually surgical for single lesions. If multiple, β blockers can be useful in relieving pain.[27]

The blue rubber bleb nevus syndrome is an extremely rare disorder characterized by multiple venous malformations affecting primarily the skin and gastrointestinal tract. Multiple other organs can be affected. The skin lesions are dark blue nodules up to several centimeters in diameter. As expected with vascular lesions, they are compressible. They can be widespread and disfiguring. Pain and tenderness may be seen. In most cases, onset occurs in childhood.[27]

Traumatic neuromas are a result of nerve injury. They thus complicate trauma, surgery, and scars. Lying in the subcutaneous tissue, these firm, oval, pea-sized lesions are more easily felt than seen. Spontaneous pain and tenderness can occur. Traumatic neuromas are a well-known complication of amputation stumps and are also found on the foot; they have been related to wearing high-heeled shoes. Intercostal nerve injury is felt to be a major factor in postthoracotomy pain. It has been reported that injury to these nerves occurs routinely with rib retraction.[28] Another painful lesion derived from nerve tissue is the neurilemmoma or schwannoma. These slow-growing benign tumors, derived from Schwann cells, usually arise in association with a major nerve. Bilateral acoustic schwannomas are typical of neurofibromatosis type 2. The other common sites are the head and neck and near the limb joints. Up to one-third are associated with pain, tenderness, and parasthesia. Rounded and well defined, they are usually solitary and up to 5 cm in diameter. Other sites include deep soft tissues, retroperitoneum, mediastinum, and tongue. Scwannomas can involve the intercostal nerves and cause pain.[29] They may be palpable.[30]

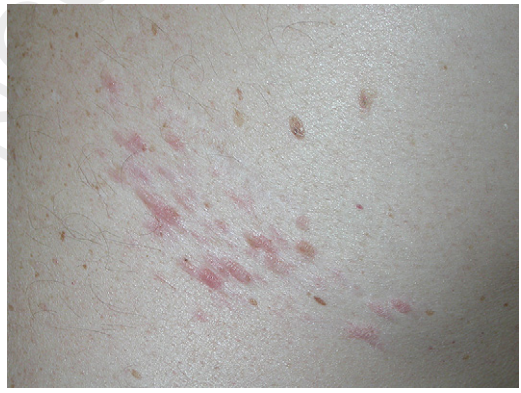

Fig. 4. Multiple painful dermal papules. Histology revealed angioleiomyomas.

Retroperitoneal schwannomas are a rarely reported cause of chest pain. Treatment is by local resection and recurrence is rare.[31]

BREAST LESIONS AND CHEST PAIN

Chest pain may also result from breast lesions. In a survey of presenting symptoms in patients with breast cancer in 2 health service districts in Wales, pain or soreness was the initial symptom in 12% of women, only second to a painless lump at 68%.[32] Similar figures of 10% for pain and 76% for painless lump as presenting symptoms of breast cancer were reported by an Australian breast unit.[33]

Not all painful breast lesions are malignant. Women with fibrocystic disease of the breast typically complain of pain and tenderness, most marked in the premenstrual period, with some continuing throughout the cycle.[34] The incidence of fibrocystic disease is 90 per 100,000 woman-years; the incidence increases up to the age of 45 years and then declines sharply.[35] In contrast, the incidence of breast cancer increase with age, being 50 per 100,000 woman-years in women less than 50 and 300 per 100,000 woman-years in women more than 50 years.[36]

Given these rates, breast lesions are still be a relatively uncommon source of chest pain, but breast examination and investigations, including mammography, ultrasound, and magnetic resonance imaging, may be indicated when other causes of chest pain are not found or if the pain is of a cyclical nature.

SUMMARY

There are several skin and breast lesions that can cause pain or tenderness. In most cases the presence of a skin lesion, if not its definitive diagnosis, will be clinically evident. In most instances treatment of these painful skin lesions is by simple excision, which will also provide histologic confirmation of the diagnosis. It would be rare for a cutaneous cause of skin pain to be mistaken for another cause. The prodromal pain of herpes zoster is most likely to cause diagnostic confusion. The painful skin lesions are usually identified by the patient as being the source of their discomfort. The specific diagnosis may not be apparent without submission of lesional tissue for histology. Chest pain is an uncommon presenting symptom of benign and malignant breast lesions. Breast examination and investigation may be appropriate when other causes of chest pain are not evident.

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