

## Importance of Case Reports in Medical Literature

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In a world of evidence-based medicine, where randomized trials are considered the gold standard of evidence, case reports and case series are at the bottom of this hierarchy. Whereas randomized control trials assess the level of uncertainty about a benefit or harm, case reports have a different fundamental function. Case reports typically highlight extremely unusual and novel findings. Case reports can rarely prove causation but generate a new hypothesis and stimulate further research. Only once a hypothesis is generated (a function of case reports), randomized trials will do final evaluation of therapies or tests.

Case reports or case series are the only way to bring a new disease to the attention of the medical community. AIDS is a good example in the recent history, when astute physicians noticed immunodeficiency-related diseases in a patient who had no reason to be immunodeficient [1]. New side effects of drugs are also usually reported in case reports or case series. The first case reports that suggested a link between the use of appetite suppressants and valvular heart disease were published in 1997 [2].

The importance of case reports or case series is not confined to identification of new diseases or drug side effects. New mutations responsible for certain genetic diseases are found frequently and reported in case reports or series, providing new clues to the pathogenesis of these diseases and thus opening new avenues of research for finding cures. We have recently reported a previously unknown mutation in a patient with Birt-Hogg-Dube syndrome [3]. The most common genetic cause of thrombophilia was discovered by meticulous search of clotting abnormalities in one family [4]. New indications for old drugs are also often based on case reports or series. This was the case with the development of oral hypoglycemic agents when patients treated with sulpham drugs were noticed to develop hypoglycemia [5]. Sometimes new treatment options are suggested by the case reports. Dapsone was first suggested as effective treatment for Behçet's disease in a case report and is now accepted a standard treatment for this condition [6].

Case reports have played a major role in human tetralogy. Association of limb malformations with use of thalidomide in pregnancy, warfarin causing hypoplastic nasal abnormalities in

children born to mothers taking warfarin during pregnancy, and hydrocephalus/microphthalmos association with the use of isotretinoin in pregnancy were all first described as case reports [7-9].

The fundamental requirements to be able to identify these new diseases, mutations or drug side effects are shrewd observation skills and a curious analytical mind to find reasons for unexplained features of a symptom complex. Case reports are highly sensitive for detecting novelty providing new ideas and discoveries, which is the basis of all scientific advancement. Once a suggestion of a new disease or association of a side effect with a particular drug is made by a case report, prospective or case-cohort studies will confirm the initial observation. While there are clear limitations to case reports and case series, astute observations can add to our understanding of pathogenesis, natural history and treatment of diseases.

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